
12/6/2022

8:00 AM - 8:25 AM

APOBEC and genome evolution in mBC

Presenting Author(s) and Co-Author(s):

Reuben Harris, PhD - *UT Health San Antonio*

City: San Antonio

State: Texas

Country: United States

12/6/2022

8:00 AM - 9:45 AM

Basic Science Workshop

Presenting Author(s) and Co-Author(s):

Alana Welm, PhD - *University of Utah*

City: Salt Lake City

State: Utah

Country: United States

12/6/2022

8:25 AM - 8:50 AM

Therapy-induced senescence: Friend or foe?

Presenting Author(s) and Co-Author(s):

Sheila Stewart, PhD - *Washington University School of Medicine*

City: St. Louis

State: MO

Country: United States

The stromal compartment plays a pivotal role in tumor progression. This is best illustrated in breast cancer bone metastases, where the stromal compartment supports tumor growth, albeit through poorly defined mechanisms. p38MAPK α is frequently expressed in tumor cells and surrounding stromal cells and its expression levels correlate with poor prognosis. Using clinically relevant breast cancer metastasis models, we show that orally administered, small-molecule inhibitors of p38MAPK α or its downstream kinase, MK2, each limited outgrowth of metastatic breast cancer cells in the bone and visceral organs. Further we found that this effect is mediated by inhibition of the p38MAPK α pathway within the stromal compartment. Beyond effectively limiting metastatic tumor growth, we also found that these inhibitors reduced tumor-associated and chemotherapy-induced bone loss, which is a devastating comorbidity for cancer patients that drastically impacts their quality of life. Mechanistic studies revealed that p38MAPK α 's ability to limit tumor growth within the bone is dependent on CD4 T cells and macrophages. To determine which cell types within the bone contribute to tumor growth and bone loss, we carried out single cell RNA-sequencing of stromal cells located within the bone metastatic lesion and cells outside the lesion. We found numerous differences that could explain how the stromal compartment contributes to tumor progression and bone loss and how inhibition of p38MAPK α or MK2 contribute. These data underscore the vital role stromal-derived factors play in tumor progression and identify the p38MAPK-MK2 pathway as a promising therapeutic target for metastatic disease and prevention of tumor-induced bone loss.

12/6/2022

8:50 AM - 9:15 AM

Drug-tolerant persister cells in cancer

Presenting Author(s) and Co-Author(s):

Joan Brugge, PhD - *Harvard Ludwig Cancer Center*

City: Boston

State: MA

Country: United States

Drug tolerant Persister cells in cancer

Joan S. Brugge

Despite favorable initial response to therapy, many cancer patients develop recurrent disease and succumb to it within five years of diagnosis. While there has been much progress in characterizing the pathways that contribute to stable genetic drug resistance, non-genetic mechanisms have recently emerged as important drivers of therapy failure in cancer. In my presentation, I will discuss different types of non-genetic, reversible mechanisms that confer therapy resistance, those involving immediate adaptive responses to stresses associated with therapies, and the other states associated with longer term persistence. I will include a discussion of strategies to target the vulnerabilities associated with each of these adaptive responses.

12/6/2022

9:15 AM - 9:45 AM

Clinical implications of tumor heterogeneity single cell genomics

Presenting Author(s) and Co-Author(s):

Nnennaya Kanu, PhD - *University College London*

City: London

Country: United Kingdom

An understanding of how and why somatic mutations accumulate is required to shed light on cancer evolution. DNA replication during each cell cycle is an essential and highly regulated process that ensures the correct duplication of the entire genome. The timing of DNA replication has been indirectly linked to mutation acquisition and genome instability. However, the extent and the importance of altered replication timing (ART) from normal to cancer cells, and whether this process directly influences mutation acquisition during cancer evolution, have not been explored. Here we evaluated the impact of ART by analysing data from 1271 whole-genome sequenced lung (100,000 Genomes Project ¹) and breast (560 breast cancer genomes from Nik-Zainal et al. ²) tumours, together with replication-timing sequencing data of multiple cancer and normal cell lines. We find that 6%-18% of the genome is subject to ART in cancer cells. Genomic regions subject to a shift from early to late replication in cancer cells exhibit an increased mutation rate in tumours and are associated with distinct mutational signatures compared to unaltered early replicated regions. In particular, we identify APOBEC3-mediated mutation clusters (omikli events) in unaltered early and late-to-early ART regions, associated with the acquisition of driver mutations. We demonstrate that ART is a relatively early event during the evolution of breast cancer and lung adenocarcinomas. Finally, genes replicated early in cancer but late in normal cells exhibit an up-regulated expression in tumour samples. The incorporation of single-cell DNA sequencing further enables accurate identification of proliferation rates. Taken together, replication timing alterations during malignant transformation are prevalent in cancer and significantly impact the genomic and transcriptomic landscape during tumour evolution.

12/6/2022

8:00 AM - 8:25 AM

Use of the postneoadjuvant setting to accelerate drug development

Presenting Author(s) and Co-Author(s):

Melinda Telli, MD - *Stanford University School of Medicine*

City: San Francisco

State: CA

Country: United States

Disclosure(s):

Melinda Telli, MD: AbbVie: Contracted Research (Ongoing); Arvinas: Contracted Research (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Bayer: Contracted Research (Ongoing); Biothera: Contracted Research (Ongoing); Blueprint Medicines: Consulting Fees (e.g., advisory boards) (Ongoing); Calithera Biosciences: Contracted Research (Ongoing); EMD Serono: Contracted Research (Ongoing); G1 Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Genentech: Contracted Research (Ongoing); Genentech/Roche: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead Sciences: Consulting Fees (e.g., advisory boards) (Ongoing); GSK: Contracted Research (Ongoing); Guardant Health: Consulting Fees (e.g., advisory boards) (Ongoing); Hummingbird Biosciences: Contracted Research (Ongoing), Contracted Research (Ongoing); Immunomedics: Consulting Fees (e.g., advisory boards) (Ongoing); Medivation: Contracted Research (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing); Natera: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); OncoSec: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); PharmaMar: Contracted Research (Ongoing); Reflexion Medical: Consulting Fees (e.g., advisory boards) (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing); Tesaro: Contracted Research (Ongoing); Vertex: Contracted Research (Ongoing)

12/6/2022

8:00 AM - 9:45 AM

Clinical Research Workshop

Presenting Author(s) and Co-Author(s):

Aditya Bardia, MD, MPH, *Associate Professor - Massachusetts General Hospital Cancer Center*

City: Boston

State: Massachusetts

Country: United States

Disclosure(s):

Aditya Bardia, MD, MPH: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); BioTheragnostics: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Foundation Medicine: Consulting Fees (e.g., advisory boards) (Ongoing); Genentech/Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Immunomedics/Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Phillips: Consulting Fees (e.g., advisory boards) (Ongoing); Radius Health: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing)

12/6/2022

8:25 AM - 8:50 AM

How to measure and improve drug adherence in clinical trials

Presenting Author(s) and Co-Author(s):

Dawn Hershman, MD, MS, FASCO - *Columbia University*

City: New York, NY

Country: United States

The past decade has seen a dramatic increase in the number of Food and Drug Administration approval of oral anti-cancer drugs (OACDs). In 2018 alone, OACDs comprised ten of the sixteen newly approved oncology therapeutics in the United States. Despite the clinical benefits and convenience of OACDs, these new oral options present potential challenges, including polypharmacy, and can result in increased toxicities, drug–drug interactions (DDIs), inappropriate consumption of medications, and medication non-adherence. Adverse drug events have the potential to affect quality of life, healthcare utilization, treatment response, and survival.

For the treatment of breast cancer, Endocrine therapies have remained a critical component of care for early stage and advance disease. Despite the proven efficacy adherence to therapy is suboptimal. Issues related to non-adherence are increasingly important, as analyses from prospective randomized trials show compliance to endocrine therapy is associated with improved disease-free survival. The reasons for non-adherence to hormonal therapy are multifactorial. Barriers to compliance include patient, physician, medication and system related variables and poor compliance is usually associated with a combination of these factors. Characteristics associated with non-adherence include very high and low age, minority race, being single, increased number of comorbidities, lack of knowledge about efficacy of AI therapy, history of non-adherence to other chronic medications, limited insurance status, and higher out of pocket costs. Side effects from hormonal therapy is the most common reason for early discontinuation. An understanding of factors that contribute to non-adherence and interventions that have been tested to improve adherence will be discussed.

Medication compliance has become a more salient issue in cancer care with the increased availability of oral antineoplastic therapies for breast cancer. The treatment of BC now routinely encompasses targeted therapies such as oral poly(ADP-ribose) polymerase (PARP) inhibitors and cyclin-dependent kinase 4 (CDK4) and CDK6 inhibitors, PI3 Kinase(PI3K) Inhibitors, in addition to traditional ET. Furthermore, as advances in BC treatment have improved long-term prognosis, the management of other chronic conditions has become an essential component of BC survivorship care. It remains unclear how this increased oral medication burden on BC survivors affects compliance with both ET and other chronic medications. Issues related to adherence measurement will be discussed.

Disclosure(s):

Dawn Hershman, MD, MS, FASCO: No financial relationships to disclose

12/6/2022

8:50 AM - 9:15 AM

Statistical considerations for precision medicine

Presenting Author(s) and Co-Author(s):

Nabihah Tayob, PhD - *Dana-Farber Cancer Institute*

City: Boston

State: MA

Country: United States

Disclosure(s):

Nabihah Tayob, PhD: No financial relationships to disclose

12/6/2022

9:15 AM - 9:40 AM

Bringing trials to all patients: A patient's perspective

Presenting Author(s) and Co-Author(s):

Thelma Brown, BSc - *University of Alabama at Birmingham*

City: Birmingham

State: AL

Country: United States

12/6/2022

9:45 AM - 10:00 AM

Break

12/6/2022

10:00 AM - 10:30 AM

Early palliative care

Presenting Author(s) and Co-Author(s):

Tara Kaufmann, MD, MSCE - *UT Health Austin*

City: Austin

State: Texas

Country: United States

This education session will review early palliative care in oncology and applications in patients with metastatic breast cancer. This presentation provides an overview of the field of research in early palliative care for patients with advanced solid tumors and discusses considerations specific to breast cancer. The speaker will present current challenges that we face in integrating palliative care into our practice and future areas for clinical innovation and research in palliative care. The speaker will present practical tips for how breast oncologists can deliver early palliative care to patients. The speaker will present guiding principles on when to consider referral to interdisciplinary, specialty palliative care.

12/6/2022

10:00 AM - 12:00 PM

Educational Session: Living with Metastatic Breast Cancer

Presenting Author(s) and Co-Author(s):

Anne Blaes, MD - *University of Minnesota*

City: Minneapolis

State: MN

Country: United States

12/6/2022

10:30 AM - 11:00 AM

Support for patients with MBC

Presenting Author(s) and Co-Author(s):

Abbey Kaler, MS, APRN, FNP-C - *UT MD Anderson Cancer Center*

City: Houston

State: TX

Country: United States

Over the last decade we have witnessed rapid advances in the treatment of patients with metastatic breast cancer (MBC) with seminal discoveries in cancer biology, correlative biomarkers and clinical trials leading to multiple new drug approvals. While these milestones have improved survival, the science of survivorship in this population is just beginning. The diagnosis of MBC is life-changing and requires individualized and multidisciplinary support. The NCI defined the areas of epidemiology and surveillance, symptom management, psychosocial research, health-care delivery, and health behaviors as necessary fields to advance the state of the science in advanced cancer survivors. A multifaceted program addressing these domains is needed to assess MBC patients and their unique and ever-changing needs. With input from patients and providers, program components should include: therapeutic clinical trials, multidisciplinary specialty care, individualized patient navigation, peer support, continuing education, and patient reported outcome (PRO) collection to support patients living with MBC. Input for a program for MBC patients can be guided by a multidisciplinary steering committee in which patient advocates are a major voice. Patients can provide insight into what works for them, and what they are facing may be very different from the experience of an early-stage breast cancer patient.

Clinical trials designed to advance the current scientific knowledge of breast cancer treatment are essential to patients living longer, more fulfilled lives with MBC. Clinical trials may include systemic therapy, local therapies such as surgery and radiation for MBC patients, side-effect management and quality of life (may put elsewhere). A comprehensive systemic therapy portfolio should include all biological subtypes as well as recommended treatment options (hormonal therapy, targeted therapy, chemotherapy, and immunotherapy).

Multidisciplinary care is necessary to diagnose and treat any condition the MBC patient may encounter and is essential in providing quality care. Comorbidities and debilitating side effects arising from cancer treatment are known to be associated with inferior outcomes. MBC patients may experience lack of familiarity of some providers with novel MBC cancer treatment, side effects, and interactions of their cancer treatment with non-cancer conditions and treatment. With the increasing life expectancy of MBC patients, it is important to manage the medical comorbidities in coordination with the MBC patient's cancer treatment. Integrative Medicine helps support the quality of life of patients through providing clinical modalities such as stress management, yoga, meditation, acupuncture, massage and lifestyle counseling. Supportive care helps support cancer related fatigue and sleep challenges, geriatrics and hospice and palliative care for advanced cancer patients.

The role of navigation for MBC patients is unique and should be designed to support the patient's many individual needs. Navigation requires assessment of individual knowledge deficit, coordination of care challenges, internal resource utilization, cultural requests, and emotional health. Navigation should also address the patient's financial and disability questions, medication assistance, symptom management, advanced care planning and goals of care

discussions. Additional items to be discussed during navigation visits include primary care provider utilization, COVID-19 vaccination, illness and medication questions, and other patient questions as they arise.

A comprehensive registry of MBC patient's medical records and histories will assist researchers in designing future therapeutic and quality of life clinical trials. The categories of patient demographics, clinical variables, pathological variables, treatment variables, outcomes of MBC, and PROs will create a robust registry. A comprehensive patient registry can create a rich database which can guide and inspire future innovative research.

Peer support through support groups and peer-to-peer matching is pivotal to MBC patients finding and utilizing their patient voice, emotionally supporting each other and learning from other's similar experiences. Connection between patients and the creation of a community of survivors can empower patients to positively impact their care through self-advocacy and self-efficacy.

Continuing patient education is also essential to providing quality cancer care. The format of a weekly virtual education webinars are helpful in creating an engaged patient community and a platform to disseminate educational resources in a reoccurring digestible format. Frequent educational webinars covering a wide variety of topics can positively influence patient interactions with their healthcare providers and influence how patients living with MBC view their own cancer experience. Educational webinars provide opportunities for patients to connect with subject matter experts, other patients like themselves, and share information with their family and friends. Informed patients can discuss and ask questions more confidently with their health care providers about information and services presented during the educational webinars.

The symptom profile of patients living with MBC are impacted by numerous variables such as disease burden, treatment plan, comorbidities, supportive regimen etc.. The collection of PROs has been shown to improve patient satisfaction with his/her care, improve quality of life, decrease emergency room visits and hospitalizations, and increased overall survival. The routine measurement and management of MBC patients' symptoms has been found to be integral in providing comprehensive cancer treatment. The collection of PROs improves patient and provider communication and elicits the outcome to symptoms that matter most to each patient.

Patients diagnosed with MBC are living longer because of the recent advancements in therapeutic treatments. A multifaceted and comprehensive program consisting of therapeutic clinical trials, multidisciplinary specialty care, individualized patient navigation, peer support, continuing education, and PROs collection is integral to fully support patients living with MBC.

12/6/2022

11:00 AM - 11:30 AM

Financial toxicity

Presenting Author(s) and Co-Author(s):

Fumiko Chino, MD - *Memorial Sloan Kettering Cancer Center*

City: New York

State: New York

Country: United States

People with cancer spend more out of pocket for medical care than others with chronic diseases, a pattern that persists years after initial cancer diagnosis and treatment. Patients and their families are at risk for financial toxicity including problems paying medical bills, increased stress and/or symptom burden, and delaying or forgoing care due to costs. In this talk, Dr. Fumiko Chino provides an overview of financial toxicity in cancer care and its real-life impact on people with cancer. Factors contributing to financial toxicity are addressed as well potential solutions.

1. Define financial toxicity as a negative consequence of cancer diagnosis/treatment
2. Describe effects of financial toxicity on quality of life, adherence, and outcomes
3. Name potential solutions to financial toxicity on a health system, provider, and patient level

12/6/2022

11:30 AM - 12:00 PM

Patient perspective

Presenting Author(s) and Co-Author(s):

Christine Hodgdon, MS - *GRASP - Guiding Researchers & Advocates To Scientific Partnerships*

City: Baltimore

State: MD

Country: United States

Stephanie Walker, BSN - *MBC Alliance*

City: Tarboro

State: NC

Country: United States

12/6/2022

10:00 AM - 10:40 AM

Contralateral mastectomy in patients with germline mutations

Presenting Author(s) and Co-Author(s):

Katharine Yao, MD - *Northshore Medical Group*

City: Evanston

State: IL

Country: United States

The educational session titled "Contralateral mastectomy in patients with germline mutations" will cover contralateral mastectomy in affected gene carriers. The session will first cover trends in contralateral mastectomy in germline mutation carriers and the impact of genetic testing on contralateral mastectomy utilization. Second, the session will review guidelines on contralateral mastectomy for gene carriers. Literature on potential beneficial impacts of contralateral mastectomy for gene carriers will be reviewed. Impact to contralateral risk, survival outcomes and patient quality of life will be examined. Lastly, the session will review new surgical approaches for prophylactic mastectomy and protocols to reduce pain and enhance recovery after mastectomy.

12/6/2022

10:00 AM - 12:00 PM

Educational Session: Local Therapy - Best Breast Practice

Presenting Author(s) and Co-Author(s):

Peter Dubsky, MD, PhD - *Breast Center Hirslanden Klinik St. Anna*

City: Zurich

Country: Switzerland

12/6/2022

10:40 AM - 11:20 AM

RT: How short can it be

Presenting Author(s) and Co-Author(s):

David Krug, Dr Med - *Universitätsklinikum Schleswig-Holstein*

City: Kiel

Country: Germany

Adjuvant whole-breast radiotherapy for breast cancer has traditionally been delivered over the course of 5 weeks. In the past decades, there has been a paradigm shift towards moderate hypofractionation with 15-16 fractions over 3 weeks based on randomized controlled trials demonstrating comparable oncological safety, decreased acute toxicity and similar long-term toxicity compared to conventional fractionation. More recently, ultra-hypofractionated whole-breast radiotherapy delivered with 5 fractions over 1 week or 5 weeks has been introduced into the clinic. Furthermore, the increasing use of partial-breast irradiation with a de-escalation of the target volume to the region of the lumpectomy cavity has further allowed acceleration of radiotherapy delivery for patients with breast cancer. This lecture will summarize recent advances and data on hypofractionation for breast cancer.

Disclosure(s):

David Krug, Dr Med: Merck KGaA: Research funding (Ongoing); Merck Sharp & Dohme: Honoraria (Ongoing); Pfizer: Honoraria (Ongoing)

12/6/2022

11:20 AM - 12:00 PM

How to reconcile novel reconstructive techniques with the need to radiate

Presenting Author(s) and Co-Author(s):

Christine Solbach, MD, PhD - *University Hospital Frankfurt*

City: Frankfurt

Country: Germany

The indication for postmastectomy radiotherapy (PMRT) is mainly based on tumor stage and the extent of lymph node involvement. The results of EBCTCG meta-analysis (EBCTCG Lancet, 2014) support the need of radiation therapy (RT) for patients with one to three axillary metastatic lymph nodes (LN), as well as for patients with > 3 affected LN.

In nearly 40% of patients with mastectomy (ME) RT is required. According to the plastic surgery statistics report 2020 approximately 80% of patients seeking breast reconstruction in the USA receive an implant-based breast reconstruction (IBBR), while 18% undergo autologous reconstruction (ASoPS 2020). PMRT, regardless of reconstructive method, has been found to have a detrimental effect on outcomes with increased postoperative complications and decreased patient satisfaction. Nevertheless, even in this cohort the number of breast reconstruction (BR) is increasing over time. Surgical techniques for ME and BR are advancing constantly. With the increasing use of skin-sparing ME (SPM) techniques, particularly nipple-sparing ME (NSM), one stage IBBR (single-stage direct-to-implant, DTI) become more popular. With the availability of supportive materials such as synthetic/biological mesh or acellular dermal matrix (ADM) there has been a significant improvement in pre-pectoral implant reconstruction. The impact of PMRT on the outcomes of pre-pectoral IBRR has been recently summarized in a systemic review and meta-analysis by Awadeen (Aesth Plast Surg, 2022). Wound infection, capsular contraction and implant loss were significantly more frequent in the irradiated than in the non-irradiated breasts. Several studies describe the delayed/2-stage IBBR in the setting of PMRT as more promising and discuss different timings of exchange from expanders to implant. In one systematic review, PMRT to permanent implants reduced the rate of reconstructive failure compared to TE (J Surg Oncol,2015). After prosthetic-based BR and RT, conversion to autologous reconstruction can always be considered. Recommendations for immediate autologous reconstruction vary when PMRT is required. PMRT can result in wound complications, fat necrosis and volume loss, but overall cosmetic results are better than with IBBR and PMRT. When undergoing delayed reconstruction after PMRT, the optimal time from PMRT to reconstruction is unknown. In patients with a history of RT, NCCN-guidelines (V.4.2022) recommend autologous reconstruction as the preferred reconstruction option. Fat grafting, which can optimize tissue perfusion and wound healing, is playing an emerging role in breast surgery. Lipofilling can be used to improve the thickness of the mastectomy flap and to recontour breast defects after PMRT. There is an increasing awareness for better understanding of the different reconstruction types to define target volumes depending on the varying risk for residual tissue and potential recurrences. The ESTRO-ACROP guidelines discuss adapted dose distribution in accordance with the different locations of the implant (pre- or sub-pectoral) (Radiotherapy and Oncology, 2019).

The risks and benefits of immediate versus delayed as well as implant-based versus autologous reconstruction must be considered for each individual patient and should be planned in a multidisciplinary setting, especially when PMRT is required.

Disclosure(s):

Christine Solbach, MD, PhD: Lilly: Lecture (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Lecture (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing)

12/6/2022

10:00 AM - 10:40 AM

Pol-theta inhibitors in HRD tumors

Presenting Author(s) and Co-Author(s):

Alan d'Andrea, MD - *Dana-Farber Cancer Institute*

City: Boston

State: MA

Country: United States

Pol-theta inhibitors in HRD tumors

Alan D. D'Andrea, M.D.

Center for DNA Damage and Repair, Dana-Farber Cancer Institute, Boston, MA, USA.

Susan F. Smith Center for Women's Cancers, Dana-Farber Cancer Institute, Boston, MA, USA.

Deficiency of homologous recombination (HR)-mediated DNA repair occurs through genetic or epigenetic inactivation of the BRCA1 and BRCA2 (BRCA1/2) genes, and it plays a role in the initiation and progression of many tumor types. HR-deficiency also provides unique opportunities for targeted therapy, as exemplified by the extreme sensitivity of BRCA1/2-mutated tumors to poly (ADP-ribose) polymerase inhibitors (PARPi). In the last decade, several PARP inhibitors have been approved for clinical use. At first, PARPi were solely used in combination with chemotherapeutics, and platinum sensitivity was used as a surrogate marker of HR-deficiency for enrolling patients for treatment. The promising clinical response of patients with germline BRCA1/2-mutations prompted the use of PARPi for patients with somatic BRCA1/2 mutations as well. In addition, it also opened the possibility for extended use of PARPi for the treatment of various types of ovarian, breast, pancreatic and prostate tumors with HR defects. PARPi efficacy is currently being evaluated in different clinical settings such as first line chemotherapy, neoadjuvant therapy, and combination therapy with chemo- or immuno-therapies.

Despite initial sensitivity to PARPi, resistance to these drugs is emerging as the major obstacle to its clinical effectiveness in patients with HR-deficient tumors. PARPi resistance can result from several independent mechanisms, often leading to the restoration of Homologous Recombination and/or Replication Fork stabilization. In addition, resistance to PARPi often correlates with platinum resistance, which remains the backbone therapy for most BRCA1/2-mutated tumors. The absence of alternative therapeutic options for patients with tumors with innate or acquired resistance underlines the urgency to develop additional therapeutics. While several mechanisms of PARPi resistance have been described, an effective method for overcoming such resistance is still lacking.

DNA polymerase theta (POL θ or POLQ) recently emerged as a new promising drug target for the treatment of HR-deficient tumors. POL θ expression is particularly high in subtypes of breast and ovarian tumors with defects in HR, where it mediates backup DNA double-strand breaks (DSBs) repair, thus compensating for the loss of HR. As a result, POL θ is synthetic lethal with HR, and POL θ inhibition in HR-deficient tumors induces cell death. In addition, POL θ inhibition synergizes with PARPi in the killing of HR-deficient tumors.

Synthetic lethality between HR-deficiency and POL θ inhibition hinges on several functions of POL θ . The enzyme maintains genomic stability and prevents tumorigenesis. It is a crucial enzyme in the mutagenic microhomology-mediated end joining (MMEJ) repair of DSBs, a pathway that plays critical role in genomic stability. Inhibiting PARP1, a key enzyme in MMEJ, prevents POL θ recruitment to sites of laser micro-irradiation. Since POL θ inhibition and PARPi have additive effects on HR-deficient cells, these data suggest that POL θ also functions outside the PARP-mediated MMEJ pathway and in pathways that are critical to the survival of HR-deficient cells.

POL θ is a large protein that contains 3 domains and is structurally and functionally distinct from other polymerases. The N-term contains a helicase-like ATPase domain that can unwind several types of DNA structures, while the central domain binds RAD51, displaces RPA proteins from resected DSBs, and antagonizes HR repair in an ATP-hydrolysis dependent manner. Finally, the C-term contains a nuclease domain which trims DNA ends and a polymerase domain that fills in nucleotides during MMEJ. Both the ATPase and polymerase domains are required for MMEJ repair.

POL θ has several functions that preserve genomic stability, and POL θ -mediated MMEJ repair can compensate for the loss of HR. It remains unclear which of the many functions of POL θ underlies the synthetic lethality with HR. Nevertheless, POL θ exhibits unique features of druggability, providing a strong rationale for developing POL θ inhibitors.

We have recently performed a small-molecule screen for inhibitors of POL θ ATPase activity and identified the antibiotic novobiocin (NVB) as a specific and potent inhibitor of human POL θ . NVB binds to purified POL θ protein, prevents its recruitment to DNA damage, and inhibits MMEJ repair. Importantly, we have shown that NVB selectively kills HR-deficient (BRCA1- and BRCA2-deficient) cells over wild-type cells and potentiates the cytotoxic effect of PARPi in HR-deficient tumor cells *in vitro* and *in vivo*. Moreover, NVB kills HR-deficient, PARPi-resistant tumor cells. These results suggest that NVB can be used alone or in combination with PARPi for treating HR-deficient tumors, even after they have acquired PARPi resistance. Accordingly, clinical trials have now been initiated for the use of NVB in the management of these tumors.

12/6/2022

10:00 AM - 12:00 PM

Educational Session: New Agents Targeting HRD in Breast Cancer

Presenting Author(s) and Co-Author(s):

Erica Stringer-Reasor, MD - *University of Alabama at Birmingham*

City: Birmingham

State: AL

Country: United States

Disclosure(s):

Erica Stringer-Reasor, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Immunomedics: Consulting Fees (e.g., advisory boards) (Terminated, December 12, 2021); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); SeaGen: Consulting Fees (e.g., advisory boards) (Ongoing)

12/6/2022

10:40 AM - 11:20 AM

Mechanisms of sensitivity and resistance to HRD targeting agents in breast cancer – PARPi and beyond

Presenting Author(s) and Co-Author(s):

Christopher Lord, MD - *Institute of Cancer Research*

City: London

Country: United Kingdom

Although PARP inhibitors (PARPi) deliver significant and sustained anti-tumour responses in those with HR defective cancers, PARPi resistance is a common clinical phenomenon and limits the overall effectiveness of these agents. I will discuss how reversion mutations in BRCA1 and BRCA2 cause PARPi resistance and how the emergence of reversions might be targeted by immune responses against the neopeptides caused by reversion mutations. I will also discuss how other mechanisms of PARPi resistance such as 53BP1/Shieldin complex dysfunction could be targeted by evolutionary “double binds” using drugs such as Pol-theta inhibitors that exploit new vulnerabilities put in place by emerging PARPi resistance mechanisms

12/6/2022

11:20 AM - 12:00 PM

ATR inhibitors and PARP1 selective PARP inhibitors

Presenting Author(s) and Co-Author(s):

Andrew Tutt, MB ChB, MRCP, FRCR, PhD - *Institute of Cancer Research*

City: London

Country: United Kingdom

“ATR inhibitors and PARP1 selective PARP inhibitors”

The targeting of Homologous Recombination deficient (HRD) malignancy using a synthetic lethal strategy based on the inhibition and trapping of PARP1 on DNA in manner that leads to tumour selective effects via dependency on the function of HR gene products such as BRCA1, BRCA2 and PALB2 for DNA replication fitness is now well established. However, there is a need to improve both the frequency and duration of response in the licensed indications and to explore combination PARP inhibitor (PARPi) strategies that may be effective a broader range of breast cancers with functional deficiencies in HR and the wider DNA damage response. ATR inhibitors exacerbate replication stress that is toxic to HR deficient cells. Combinations of an ATR inhibition (ATRi) and PARPi have been shown to be synergistic and to be active in PARPi resistant pre-clinical model contexts. The development of combination strategies of these agents and of platinum and ATRi have been limited by combinatorial toxicity but have recently reported results in breast cancer. PARP1 is part of a family of PARP enzymes and currently licensed PARPi inhibit several family members that underpin some of their toxicity. New PARP1 selective agents have recently reported results in early phase trials. I will review some of the mechanistic rationale, preclinical data and relevant clinical trial data in my lecture.

Disclosure(s):

Andrew Tutt, MB ChB, MRCP, FRCR, PhD: AACR: AACR Team Prize (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Honoraria - ESMO Symposium 2021 (Ongoing), Travel/accomodation/expenses (Ongoing); Cancer Panel: Honoraria (Ongoing); EM Partners: Consulting Fees (e.g., advisory boards) (Ongoing); GBCC: Honoraria - GBCC conference (Ongoing); GE Healthcare: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); IBCS: Honoraria - IBCS conference (Ongoing); InBiomotion: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); MD Anderson: Consulting Fees (e.g., advisory boards) (Ongoing); Medivation: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Merck Serono: Consulting Fees (e.g., advisory boards) (Ongoing); Myriad genetics: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Pfizer: Travel/accomodation/expenses (Ongoing); Research to practice survey: Honoraria (Ongoing); SABCS: Honoraria - SABCS 2020 (Ongoing); The Institute of Cancer Research: I have in the past and may in the future be in receipt of payments under my employer (ICR London) Rewards to Inventors Scheme associated with patents (Ongoing); VJ Oncology: Honoraria (Ongoing)

12/6/2022

10:00 AM - 10:40 AM

Hormone receptor positive breast cancer

Presenting Author(s) and Co-Author(s):

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Estrogen receptor (ER) positive breast cancer is a heterogeneous group of diseases. While the major goal of neoadjuvant treatment in patients with locally advanced disease is to downstage the cancer to facilitate resectability and breast-conserving surgery, there is increasing evidence that response in the neoadjuvant setting has prognostic implications in predicting long term relapse outcomes. However, questions remain as to strategies that optimize neoadjuvant treatment selection of endocrine therapy versus chemotherapy, and whether adjuvant therapy could be tailored based on treatment response in the neoadjuvant setting. In this lecture, we will discuss evolving data regarding pathologic and molecular characteristics of ER positive breast cancer that assist with treatment selection in the neoadjuvant setting and the potential role of pathologic and biomarker response to neoadjuvant endocrine therapy in tailoring adjuvant chemotherapy decisions.

Disclosure(s):

Cynthia Ma, MD, PhD: Agendia: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Athenex: Consulting Fees (e.g., advisory boards) (Ongoing); Bayer Healthcare: Consulting Fees (e.g., advisory boards) (Ongoing); Biovica: Consulting Fees (e.g., advisory boards) (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); Inivata: Consulting Fees (e.g., advisory boards) (Ongoing); Jacobio: Consulting Fees (e.g., advisory boards) (Ongoing); Natera: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Olaris: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Phillips Electronics: Consulting Fees (e.g., advisory boards) (Ongoing); Puma: Contracted Research (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing); Tempus: Filled out Surveys for Tempus regarding these tests. Did not impact clinical or research activity. (Ongoing)

12/6/2022

10:00 AM - 12:00 PM

Educational Session: Predictive Value Of Treatment Response And Residual Disease After Neoadjuvant Therapy

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12/6/2022

10:40 AM - 11:20 AM

HER2 positive breast cancer

Presenting Author(s) and Co-Author(s):

Luca Gianni, MD - *Fondazione Michelangelo*

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“Clinical relevance and value of neoadjuvant therapy of HER2+ early breast cancer at individual and at trial level”

Luca Gianni, MD - *Fondazione Michelangelo*, Milan Italy

Giampaolo Bianchini, MD - *Medical Oncology*, San Raffaele Hospital, Milan, Italy

Neoadjuvant therapy of HER2+ breast cancer has been groundbreaking. It showed the superior results in terms of pathologic complete response (pCR) and event free survival (EFS) of adding trastuzumab to chemotherapy in women with locally advanced breast cancer (NOAH trial) that led to the first regulatory approval of a neoadjuvant approach in the field of breast cancer. In addition, neoadjuvant studies (NeoSphere, neoALLTO) clearly showed the improved antitumor activity of dual blockade of the HER2 receptor, paved the way to the Aphinity adjuvant study and justified the current worldwide use of dual block of HER2 in high/moderate risk HER2+ early breast cancer.

In the above scenario the design and results of the Katherine study were a landmark achievement. By proving the clinical value of shifting treatment from trastuzumab to trastuzumab-DM1 in women with residual disease after neoadjuvant therapy the study provided firm clinical evidence that residual disease can be used as a surrogate of relative resistance that per se justifies the adoption of alternative non cross resistant regimens/therapies at the individual level.

The clinical success of neoadjuvant trials in HER2+ early breast cancer went hand-to-hand with translational studies that are identifying markers predicting for pCR and EFS that are and will be used to fine tuning a more individually tailored approach to treatment, and eventually effective and safe de-escalation strategies.

The rich collection of neoadjuvant studies that shaped the modern approach to treatment of women with early HER2+ breast cancer will be enriched of studies with new drugs, trastuzumab deruxtecan and tucatinib to name some of the front runners. All current and future treatments will greatly depend on the neoadjuvant approach as a tool for a quick assessment of the clinical value of new therapies. Such approach has so far been used as basis or supporting evidence for regulatory approvals worldwide, based on the concept that pCR can be viewed as surrogate of long-term benefit. Individual trials and meta-analyses are challenging the dependability of pCR to predict EFS at trial level. However, the benefits of tumor eradication (pCR) at individual level continue to support the simple clinical concept that more pCR is better and that regimens leading to it deserve full credit.

Acknowledgment: The work of Luca Gianni is supported by grants of the BCRF

12/6/2022

11:20 AM - 12:00 PM

Triple negative breast cancer

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12/6/2022

12:00 PM - 2:00 PM

Special Session 1: Big Data and Health Equity

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12/6/2022

12:10 PM - 12:30 PM

Keynote Speaker 1

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12/6/2022

12:30 PM - 1:00 PM

Panel 1: The use of data to provide services to specific populations, telemedicine, virtual clinical trials

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12/6/2022

1:05 PM - 1:25 PM

Keynote Speaker 2

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12/6/2022

1:25 PM - 2:00 PM

Panel 2: Patient privacy & use of data to provide services

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12/6/2022

12:00 PM - 2:00 PM

Special Session 2: Overcoming the Big Obstacles to Find Solutions for Breast Cancer

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12/6/2022

2:00 PM - 2:15 PM

GS1-01

GS1-01 Race and clinical outcomes in the RxPONDER Trial (SWOG S1007)

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Introduction:

Racial disparities in breast cancer (BC) outcomes continues to be a major health care challenge. The 21-gene recurrence score (RS) is an important tool to guide treatment (tx) decisions among women with early-stage BC. We report an analysis of clinical characteristics,

survival outcomes and race in association with RS in participants (pts) in the RxPONDER trial.

Methods:

We analyzed clinical outcomes with respect to race and ethnicity. Unreported race excluded 18.7% of the pts, with most due to privacy rules. The primary outcome was invasive disease-free survival (IDFS). Distant relapse-free survival (DRFS) was also evaluated. Analyses adjusted for assigned tx arm, RS, and grade were performed. There were too few events to include Native American/Pacific Islander (NAPI) women in the survival analyses.

Results:

A total of 4,048 trial women with Hormone Receptor positive, HER2 negative (HR+/HER2-) BC, 1-3 involved axillary lymph nodes (LNs), RS \leq 25 and known race/ethnicity were included in this analysis including the following: 2,833 non-Hispanic (NH) White pts (70%), 248 NH Black pts (6.1%), 610 Hispanic pts (15.1%), 324 Asian pts (8.0%), and 33 NAPI pts (0.8%). Asian and Hispanic women were younger than NH Whites (by 7.1 and 2.4 years, respectively) but NH Blacks did not differ in age. RS distribution did not differ among all racial subgroups ($p=0.49$). There were also no significant differences in tumor size ($p=0.10$) or number of positive LNs ($p=0.26$) across all racial groups. However, tumor grade was found to be significantly different with grade 3 tumors higher for NH Blacks (18.0%), NH NAPI (21.1%), and Hispanics (14.5%) vs. NH Whites (10.4%) and Asians (6.5%) ($p < 0.001$). Overall five-year IDFS was lower for NH Blacks (87.0%) compared to that for Asians (93.9%), NH Whites (91.5%), and Hispanics (91.4%) (Table 1). A multivariable Cox model adjusting for RS and tx arm showed worse IDFS for NH Blacks compared to NH Whites (HR=1.38; 95% CI 1.00-1.90; $p=0.048$), although Asian pts had better IDFS than NH Whites (HR=0.65; 95% CI 0.44-0.97; $p=0.034$). In a separate analysis by menopausal status the magnitude of the IDFS hazard ratios (HRs) for NH Blacks was similar, although no longer statistically significant (premenopausal HR=1.37; 95% CI 0.69-2.72; postmenopausal HR=1.38; 95% CI 0.96-1.98). While there was no statistically significant interaction between NH Blacks vs. NH Whites and tx arm for either premenopausal ($p=0.99$) or postmenopausal women ($p=0.44$), adjusting for RS, the small number of events in the NH Black cohort, particularly in premenopausal women ($n = 9$ IDFS events), limit power and inference about differences in chemotherapy benefit. Among postmenopausal women, NH Blacks had worse DRFS compared to NH Whites (HR=1.69; 95% CI 1.12-2.53; $p=0.01$), adjusting for tx and RS. A similar trend was seen among premenopausal women (HR=1.74; 95% CI 0.79-3.82; $p=0.17$), although not statistically significant. Data on tx adherence over 5 years was not mature, although NH Blacks were more likely to accept tx assignment compared to NH Whites at randomization (93% vs. 86%, $p=0.004$).

Conclusion:

Black women with HR+/HER2- BC, 1-3 involved LNs and RS \leq 25 have worse outcomes compared to White women despite similar RS results. There was no significant interaction between NH Blacks vs. NH Whites and tx arm, although this analysis was limited due to sample size. There remains an important need for novel approaches to improve clinical outcomes particularly for NH Black Women.

Table 1. IDFS by Race and Ethnicity

Table 1. IDFS by Race and Ethnicity

Race/ethnicity	N	IDFS Events	5-year IDFS, %	Adjusted HR (95% CI)
NH Whites	2,833	353	91.5%	1.00 (referent)
Asians	324	27	93.9%	0.65 (0.44-0.97)
Hispanics	610	72	91.4%	0.91 (0.70-1.17)
NH Blacks	248	42	87.0%	1.38 (1.00-1.90)

Disclosure(s):

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12/6/2022

2:00 PM - 5:00 PM

General Session 1

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12/6/2022

2:15 PM - 2:30 PM

GS1-02

GS1-02 Racial disparity in tumor microenvironment and outcomes in residual breast cancer treated with neoadjuvant chemotherapy

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Background: Black, compared to White women with localized breast cancer have higher mortality and worse distant recurrence free survival (DRFS). This has been attributed to social determinants of health and higher prevalence of triple negative breast cancer (TNBC) in Black compared to White women. Recent studies indicate that racial disparity in outcome is present in patients with estrogen receptor-positive (ER+), but not ER- disease, in particular in patients with residual disease after neoadjuvant chemotherapy (NAC). It has been shown that in some patients NAC may induce pro-metastatic changes in tumor microenvironment, such as increased density of tumor associated macrophages and portals for cancer cell dissemination to distant sites called TMEM doorways (TMEM score). TMEM score correlates with metastasis in patients with ER+/HER2- breast cancer. We hypothesized that racial disparity in DRFS in patients with residual ER+/HER2- disease is due to enhanced pro-metastatic components (macrophage and TMEM doorway density) in the tumor microenvironment post-chemotherapy in Black compared to White women.

Methods: We performed a retrospective, multi-institutional study of TMEM score and macrophage density in the residual disease after NAC from 196 patients diagnosed with unilateral invasive ductal cancer of breast between 2004 and 2014. 99 patients self-identified as Black and 97 as White. TMEM doorways were visualized by triple immunohistochemistry for macrophages (CD68), tumor cells (panMena), and endothelial cells (CD31). The evaluation of TMEM score and macrophage density was done using automated image analysis. Tumor characteristics and patient survival were compared between Black and White patients. The relationship between TMEM score, macrophage density and DRFS was examined by log-rank test and multivariate Cox regression model. The covariates in Cox model included TMEM score, age (continuous), race (Black vs White), surgery type (mastectomy vs lumpectomy), tumor stage (T3 vs T1; T2 vs T1), lymph node status (positive vs negative), and tumor subtype (triple negative [TN] vs ER+/HER2-; other vs ER+/HER2-).

Results: Black compared to White women were more likely to develop distant recurrence (49.5% vs 34%, $p=0.04$), receive mastectomy (69.7% vs 51.5%, $p=0.014$), and have higher grade ($p=0.001$). Tumors from Black patients had more macrophages and a higher TMEM score in the entire cohort ($p=0.004$; $p=0.001$ respectively) and in the ER+/HER2- subset ($p=0.008$; $p=0.008$ respectively), but not in the TNBC subset. High TMEM score was associated with worse DRFS in all patients ($p=0.004$) and in the ER+/HER2- ($p=0.03$), but not in TNBC. In multivariate Cox model, TMEM score was an independent prognostic factor in the entire cohort (HR, 1.92; 95%CI, 1.15-3.22; $p=0.01$) and trended towards significance in ER+/HER2- disease (HR, 2.13; 95%CI, 0.96-4.71; $p=0.06$). TN, compared to ER+/HER2- cancers had higher TMEM

score ($p=0.01$), and macrophage density ($p=0.001$).

Conclusion: Racial disparity in outcome in patients with localized breast cancer may be due to a more pronounced pro-metastatic response to chemotherapy in Black, compared to White patients with ER+/HER2- disease. Thus, higher prevalence of TNBC in Black patients may not be the controlling factor in racial disparity.

Disclosure(s):

Burcu Karadal, MD: No financial relationships to disclose

Gina Kim, MD: No financial relationships to disclose

Ved Sharma, PhD: No financial relationships to disclose

Jessica Pastoriza, MD: No financial relationships to disclose

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12/6/2022

2:30 PM - 2:45 PM

GS1-03

GS1-03 Discussant for GS1-01 and GS1-02

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12/6/2022

2:45 PM - 3:00 PM

GS1-04

GS1-04 Patient-reported cognitive impairment in women participating in the RxPONDER trial (SWOG S1007) by menopausal status

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Introduction: Breast cancer treatment is associated with cancer-related cognitive impairment (CRCI). However, the differential effect of endocrine therapy (ET) vs chemotherapy followed by endocrine therapy (CET), including the impact of menopausal status, on CRCI is not well understood.

Methods: Participants (pts) with hormone receptor positive, HER2 negative breast cancer with 1-3 positive lymph nodes and an Oncotype DX recurrence score of 0-25 enrolled in the RxPONDER trial were randomly assigned to ET alone versus CET. Until the health-related quality of life (HRQoL) accrual goal was reached, English speaking pts in the US were invited to complete HRQoL questionnaires including the 8-item PROMIS Perceived Cognitive Function Concerns (PCF) Short Form questionnaire shortly after randomization (baseline), as well as 6, 12, and 36 months after baseline. Analysis of measures of anxiety and fatigue is presented separately. Standardized T scores (mean 50; SD 10) for PCF were computed with higher scores indicating less cognitive impairment. The primary endpoint of this exploratory analysis was to compare mean PCF T scores by treatment arm and menopausal status. Separately by

menopausal status, a generalized estimating equations (GEE) model was fit to the three timepoints adjusting for baseline to estimate the difference between treatment arms and whether there was a time trend over the three follow-up measures.

Results: The HRQoL accrual exceeded the goal of 500 patients, with 74% of pts participating voluntarily until the QOL invitation was removed from the protocol (Dec 1, 2012). A total of 139 pre and 429 postmenopausal pts completed the questionnaires at baseline. T scores were similar between ET and CET arms at baseline [Table]. In the ET arm, T scores decreased from baseline to 6 and 12 months but recovered to baseline at 36 months. In the CET arm, T scores decreased from baseline to 6 months and 12 months but did not return to baseline at 36 months. The mean score difference between CET and ET over time was -3.02 (p=0.01) and -2.36 (p=0.003) for pre and postmenopausal pts, respectively. Adjusting for baseline, there was no significant time trend over the three follow-up periods for either premenopausal (p=0.12) or postmenopausal (p=0.49) pts. Dropoff occurred over time with 79%, 76%, 60% of pts at baseline participating at 6, 12, and 36 months. Complete endocrine treatment adherence data are not yet available at each timepoint.

Conclusion: Chemoendocrine therapy has a greater negative effect on patient-reported CRCI compared to ET alone in both pre- and post-menopausal pts and it is sustained over 36 months. Interventions to prevent or treat CRCI are needed to improve the long-term quality of life of patients treated with CET.

Comparisons of mean Cognitive Function score by treatment arm and menopausal status

Table. Comparisons of mean Cognitive Function score by treatment arm and menopausal status

Menopausal status	Treatment Arm	Timepoint				CET vs. ET difference
		Randomization	6 months	12 months	36 months	
Premenopausal	CET	52.84	49.27	47.95	48.80	-3.02 (p=0.01)
	ET	53.53	51.49	51.35	53.50	
Postmenopausal	CET	50.65	48.32	47.30	48.43	-2.36 (p<0.003)
	ET	51.73	51.35	51.30	51.89	

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GS1-05

GS1-05 Trial Assigning Individualized Options for Treatment (TAILORx): An Update Including 12-Year Event Rates

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Background: Late recurrence of breast cancer after 5 years accounts for about 50% of recurrences in hormone receptor (HR)-positive early breast cancer (EBC). TAILORx established non-inferiority of adjuvant endocrine therapy (ET) given for at least 5 years to chemotherapy plus ET (CET) in EBC and a 21-gene recurrence score (RS) of 11-25, although there was some chemotherapy benefit in women

Methods: Eligibility criteria included women 18-75 years with HR-positive, HER2-negative, T1b-T2N0 EBC who agreed to have CT assigned or randomized based on the RS assay. The primary endpoint was invasive disease-free survival (iDFS) in the RS 11-25 group. The “primary analysis” refers to the original prespecified analysis for the primary IDFS endpoint (836 IDFS events at full information in the RS 11-25 group) after a median of 7.5 years. The “updated analysis” was performed after a median followup of 11.0 and 10.4 years in the randomized and overall populations, respectively.

Results: 10,253 eligible women enrolled between 4/7/06-10/6/10. The updated analysis includes substantially more events than the primary analysis, including IDFS events (1819 vs. 1210), distant recurrences (561 vs. 384), locoregional +/- distant recurrences (764 vs. 543), and deaths (910 vs. 499). The table provides 5 and 12-year event rates (and standard errors) for all arms, and comparisons of the randomized arms. The primary trial conclusions remain unchanged: ET was non-inferior to CET in the randomized group with a RS 11-25. Although recurrence occurred in < 10% by 12 years for a RS 0-25, late recurrence events beyond 5 years exceeded earlier recurrence. Non-recurrence events occurred in about 13% at 12 years (~1%/year), contributing substantially to the IDFS rates. For women
Conclusions: The current updated analysis confirms findings from the original primary analysis that ET is non-inferior to CET in HR-positive, HER2-negative, node-negative EBC and a RS 11-

25. As in the original primary analysis, the subgroup of women

Event Rate	Arm A RS <11 ET (n=1619)	Arm B RS 11-25 ET (n=3399)	Arm C RS 11-25 CET (n=3312)	Arm D RS >25 CET (n=1389)		Hazard Ratio: Arm B vs. C (95% C.I.)
5-year	94.0% (0.6)	92.8% (0.5)	93.1% (0.5)	87.6% (1.0)	IDFS	Primary analysis: 1.08 (0.94, 1.24, p=0.26)
12-year	75.9% (1.3)	76.8% (0.9)	77.4% (0.9)	65.9% (2.9)		Updated analysis: 1.08 (0.96, 1.20)
5-year	99.3% (0.2)	98.0% (0.3)	98.2% (0.2)	93.0% (0.8)	DRFI	Primary analysis: 1.10 (0.85, 1.41, p=0.48)
12-year	93.2% (0.8)	92.6% (0.5)	92.8% (0.5)	84.8% (1.8)		Updated analysis: 1.11 (0.90, 1.36)
5-year	98.8% (0.3)	96.9% (0.3)	97.0% (0.3)	91.0% (0.8)	RFI	Primary analysis: 1.11 (0.90, 1.37, p=0.28)
12-year	91.4% (0.9)	89.6% (0.6)	90.5% (0.6)	80.9% (2.2)		Updated analysis: 1.15 (0.96, 1.36)
5-year	98.0% (0.4)	98.0% (0.2)	98.1% (0.2)	95.9% (0.6)	OS	Primary analysis: 0.99 (0.79, 1.22, p=0.89)
12-year	89.8% (0.8)	89.8% (0.6)	89.8% (0.6)	87.0% (1.7)		Updated analysis: 1.06 (0.91, 1.24)

DRFI: distant relapse-free interval; RFI: relapse-free interval; OS: overall survival
(Funded by the National Cancer Institute and others; ClinicalTrials.gov identifier NCT00310180)

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12/6/2022

3:15 PM - 3:30 PM

GS1-06

GS1-06 Evaluation of the Breast Cancer Index in premenopausal women with early-stage HR+ breast cancer in the SOFT trial

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Background:

The landmark Suppression of Ovarian Function Trial (SOFT) in premenopausal breast cancer patients revealed that the addition of ovarian function suppression (OFS) to adjuvant endocrine therapy with either tamoxifen (T+OFS) or exemestane (E+OFS) reduces the risk of recurrence compared with adjuvant tamoxifen alone. The benefit from the addition of OFS was most clinically meaningful for patients at higher clinico-pathologic risk of recurrence. There are no biomarkers to aid decision-making about intensification of endocrine therapy with OFS and its resultant toxicities. The Breast Cancer Index (BCI) is a gene expression-based signature that stratifies patients based on the risk of overall (0-10 years) and late (post-5 years) distant recurrence (DR) and predicts the likelihood of benefit from extended endocrine therapy in early stage HR+ breast cancer. The purpose of this study is to assess BCI's prognostic and predictive ability in premenopausal women randomly assigned to 5-years treatment with E+OFS or T+OFS vs T alone in the SOFT trial.

Methods:

All available FFPE tumor samples from the SOFT trial (n=1718 of 3047) were included in the study. BCI testing was performed blinded to clinical characteristics, treatment and outcome. Median follow-up was 13 years. Primary endpoint was breast cancer-free interval (BCFI). Secondary endpoints were distant recurrence-free interval (DRFI) and disease-free survival (DFS). Kaplan-Meier analysis and Cox proportional hazards regression models, stratified by prior chemotherapy and lymph node status, were used to evaluate the predictive performance of BCI (H/I) status (High vs Low), and secondarily H/I as a continuous score. Hypothesis testing for interaction was performed by stratified log-rank tests.

Results:

Tumor samples from 1687 (98%) patients (30.4% < 40 years, 64.1% T1, 50.1% G2, 65.8% N0, 85.5% HER2-, 53.3% received prior chemotherapy) were successful in BCI testing and included in the final analysis. Patient characteristics in the translational cohort are representative of the parent SOFT trial. 42.4% of patients' tumors had H/I-High status. Prognostic and predictive analyses are ongoing and will be presented at the meeting.

Disclosure(s):

Ruth O'Regan, MD: Biotheranostics: Consulting Fees (e.g., advisory boards) (Ongoing); Genentech: Consulting Fees (e.g., advisory boards) (Ongoing); Genomic Health: Consulting Fees (e.g., advisory boards) (Ongoing); Immunomedics: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); MacroGenics: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); puma: Consulting Fees (e.g., advisory boards) (Ongoing)

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12/6/2022

3:30 PM - 3:45 PM

GS1-07

GS1-07 Results from a phase III randomized, placebo-controlled clinical trial evaluating adjuvant endocrine therapy +/- 1 year of everolimus in patients with high-risk hormone receptor-positive, HER2-negative breast cancer: SWOG S1207

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BACKGROUND: Abnormalities of the PI3kinase/AKT/mTOR signaling network are common in breast cancer (BC) and are associated with endocrine resistance. Everolimus, an mTOR-

inhibitor increased PFS when combined with endocrine therapy (ET) in the metastatic setting and is thought to revert endocrine resistance. S1207 is a phase III randomized, placebo-controlled trial evaluating the role of everolimus in combination with ET in the adjuvant setting among patients with high-risk hormone receptor-positive, HER2-negative BC (NCT01674140). METHODS: Eligible patients were >18 years of age with histologically confirmed invasive hormone receptor-positive and HER2-negative high-risk BC. Four risk groups were defined as: 1) > 2cm node-negative disease (or pN1mi), and either an Oncotype DX® Recurrence Score (RS) > 25 or MammaPrint® high-risk category (MP high); 2) 1-3 positive nodes and either RS >25, MP high or a pathological grade 3 tumor; 3) >4 positive lymph nodes. Patients treated with neoadjuvant chemotherapy were eligible if: 4) after surgery had >1 lymph node involvement. Patients were randomized 1:1 to physician's choice adjuvant ET in combination with one year of everolimus (10 mg PO daily) or ET plus placebo stratified by risk group. The primary endpoint was invasive disease-free survival (IDFS) evaluated by a stratified log-rank test. Secondary endpoints included overall survival (OS) and safety. The hazard ratio (HR) for treatment efficacy was estimated using Cox regression with stratification by risk groups. Subset analyses included preplanned evaluation within risk group and exploratory analyses of menopausal status and age. RESULTS: 1,939 patients were randomized between September 2013 and May 2019, of them 1,792 were eligible and included in the analysis (896 per arm). Primary reason for ineligibility was timing after chemotherapy/radiation or not high risk. Median age was 54 years (22-85) and 32% were premenopausal. With a median follow-up of 50.5 months, there were 389 IDFS events as of May 2022 (data cutoff). 5-year IDFS was 74.8% among patients treated with everolimus and 73.9% among patients treated with placebo, HR=0.93 (95% CI 0.76-1.14). However, the proportional hazards assumption was violated (p=0.02) suggesting differential treatment effect over time. The HR during the one year of treatment was 0.72 (95% CI 0.47-1.10) while after one year it was 1.00 (95% CI 0.80-1.26). The 5-year OS was 87.6% in the everolimus arm and 85.5% in the placebo arm, HR=0.98 (95% CI 0.75-1.28). Analysis by risk group did not show higher everolimus benefit as risk increased. No difference in IDFS or OS was seen among postmenopausal patients (IDFS HR=1.08 [95% CI 0.85-1.36], OS HR=1.19 [95% CI 0.87-1.61]). Among premenopausal patients, everolimus was associated with improved IDFS (HR=0.63 [95% CI 0.43-0.93]) and OS (HR=0.48 [95% CI 0.26-0.88]). Treatment completion of randomized therapy was lower in the everolimus arm compared to placebo (47.9% v 72.7%). Grade 3 and 4 toxicities were noted in 6.5% and 0.5% of patients in the placebo arm and in 31.2% and 3.7% in the everolimus arm respectively. CONCLUSIONS: Addition of one year of adjuvant everolimus to standard adjuvant ET did not improve IDFS or OS and was associated with low completion rate and increased AEs. Among premenopausal patients there was a benefit in IDFS and OS that is hypothesis generating. Future translational studies will evaluate potential predictors of everolimus benefit and drug toxicity.

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12/6/2022

3:45 PM - 4:00 PM

GS1-08

GS1-08 Discussant for GS1-06 and GS1-07

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12/6/2022

4:00 PM - 4:15 PM

GS1-09

GS1-09 Abemaciclib plus endocrine therapy for HR+, HER2-, node-positive, high-risk early breast cancer: results from a pre-planned monarchE overall survival interim analysis, including 4-year efficacy outcomes

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Background Adjuvant abemaciclib (a CDK4 and 6 inhibitor) combined with ET resulted in significant and clinically meaningful improvement in invasive disease-free survival (IDFS) and distant relapse-free survival (DRFS) in patients (pts) with HR+, HER2-, node-positive, high risk EBC in the monarchE trial, and is an approved adjuvant therapy for these patients. Here we present efficacy results from a pre-specified overall survival interim analysis (OS IA2) which was planned to occur 2 years (yrs) after the primary outcome analysis. Methods Pts were

randomized (1:1) to receive ET for up to 10 yrs +/- abemaciclib for 2 yrs (study treatment period). High-risk EBC was defined as either ≥ 4 positive axillary lymph nodes (ALN), or 1-3 ALN with either Grade 3 disease and/or tumor ≥ 5 cm (Cohort 1). While the proliferation biomarker Ki-67 was centrally assessed in all pts with available tissue sample, an additional smaller group of pts with 1-3+ ALN and central Ki-67 $\geq 20\%$ as the only high-risk feature were included (Cohort 2). The intent-to-treat (ITT) population consisted of both Cohort 1 (5120 pts) and Cohort 2 (517 pts). Hazard ratios (HR) were estimated using Cox proportional hazard model. Results At a median follow-up of 42 months, all pts were off abemaciclib. IDFS and DRFS data illustrate a sustained benefit beyond the treatment period. In the ITT population, the HR for IDFS was 0.664 (95% CI: 0.578, 0.762) and DRFS was 0.659 (95% CI: 0.567, 0.767). At 4 yrs, this reflected an improvement in IDFS rates from 79.4% to 85.8% (absolute difference 6.4%), and in DRFS rates from 82.5% to 88.4% (absolute difference 5.9%). The continued separation of the curves was associated with an increase in absolute benefit in IDFS 4-year rates compared to 2- and 3-year IDFS rates (absolute difference 2.8% and 4.8% respectively). While OS remained immature, there was a lower number of deaths observed in the abemaciclib plus ET arm compared to the ET alone arm (157 [5.6%] vs 173 [6.1%], HR 0.929 [95% CI: 0.748, 1.153], $p = 0.503$), suggesting that the robust benefit in IDFS and DRFS began to translate into a numerically favorable OS HR. As previously described, within Cohort 1, a Ki-67 index of $\geq 20\%$ was associated with a worse prognosis, but similar abemaciclib treatment effects were observed regardless of Ki-67 index. No new safety signals were observed. Conclusion The clinically meaningful benefit of adjuvant abemaciclib added to ET in HR+, HER2-, node-positive, high-risk EBC persists beyond completion of abemaciclib therapy, yielding an increase in absolute IDFS and DRFS benefit at 4 yrs. While OS remains immature at this time, the lower number of deaths in the abemaciclib arm compared to the ET arm suggest that a survival signal favoring abemaciclib is emerging.

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4:15 PM - 4:30 PM

GS1-10

GS1-10 Primary results from the randomized Phase II RIGHT Choice trial of premenopausal patients with aggressive HR+/HER2- advanced breast cancer treated with ribociclib + endocrine therapy vs physician's choice combination chemotherapy

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Background: Combination chemotherapy (CT) remains a standard of care in advanced breast cancer (ABC) with aggressive disease features (rapidly progressing or highly symptomatic disease, including life-threatening visceral crisis). To date, no data have been published on a head-to-head comparison of CDK4/6 inhibitor (CDK4/6i) + endocrine therapy (ET) vs combination CT in this patient (pt) population. RIGHT Choice, a randomized, open-label, multi-national, Phase II trial, investigated the efficacy and safety of first-line ribociclib (RIB) + ET vs

combination CT in pre/perimenopausal pts with HR+/HER2- ABC with aggressive disease (where combination CT is clinically indicated by physician's judgment). Here we report the results of the primary endpoint of progression-free survival (PFS) and key secondary endpoints from this study.

Methods: Pre/perimenopausal pts with HR+/HER2- ABC (>10% estrogen receptor-positive [ER+]) and no prior systemic therapy for ABC were randomized 1:1 to receive either RIB (600 mg daily, 3 weeks on/1 week off) with letrozole/anastrozole + goserelin or investigator's choice of CT (docetaxel + capecitabine, paclitaxel + gemcitabine, or capecitabine + vinorelbine). Randomization was stratified by presence of liver metastases and whether the disease-free interval (duration from date of complete tumor resection for primary breast cancer lesion to the date of documented disease recurrence) was less than two years. Pts included in the trial had ABC not amenable to curative therapy for which combination CT was clinically indicated by physician's judgment (i.e., symptomatic visceral metastases, rapid progression of disease or impending visceral compromise, or markedly symptomatic non-visceral disease). Median PFS (mPFS) and median time to treatment failure (mTTF) were evaluated by Kaplan-Meier methods. Overall response rate (ORR) was also analyzed, with quality of life and biomarker analyses planned. RIGHT Choice is registered at ClinicalTrials.gov (NCT03839823).

Results: A total of 222 pts (112 RIB + ET; 110 CT) were enrolled from Feb 2019 to Nov 2021. Pts with symptomatic visceral metastases (n=150; 67.6%), rapid disease progression (n=41; 18.5%), and markedly symptomatic non-visceral metastases (n=31; 14.0%) were included. Overall, 116 pts (52.3%) had visceral crisis based on guideline definitions. A majority of pts (n=190; 85.6%) had tumors that were ≥50% ER+. At data cutoff (Apr 12, 2022), median follow-up was 24.1 mo; 45.5% and 23.6% of pts remained on treatment in the RIB + ET arm and combination CT arm, respectively. The primary endpoint was met, with a statistically significant PFS benefit of ≈1 year for RIB + ET vs combination CT (mPFS, 24.0 vs 12.3 mo; hazard ratio, 0.54; 95% CI, 0.36-0.79; P=.0007). OS data were immature at data cutoff. The mTTF was ≈10 mo longer for RIB + ET vs CT (18.6 vs 8.5 mo; hazard ratio, 0.45; 95% CI, 0.32-0.63). The ORR was similar for RIB + ET vs CT (65.2% vs 60.0%). No new safety signals were observed in pts on RIB. Lower rates of treatment-related serious adverse events (AEs; 1.8% vs 8.0%) and lower rates of discontinuation due to treatment-related AEs (7.1% vs 23.0%) were seen with RIB + ET vs CT, respectively. AEs observed with combination CT were consistent with the published data.

Conclusions: This analysis demonstrated a statistically significant and clinically meaningful PFS benefit with RIB + ET over combination CT in the first-line pre/perimenopausal pt population with aggressive HR+/HER2- ABC disease. This is the first study comparing a CDK4/6i + ET vs combination CT and demonstrating the superiority of RIB + ET in aggressive HR+/HER2- ABC. This evidence supports RIB+ ET use as a preferred option for this pt population.

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GS1-11

GS1-11 Sacituzumab Govitecan (SG) vs Treatment of Physician's Choice (TPC): Efficacy by Trop-2 Expression in the TROPiCS-02 Study of Patients (Pts) With HR+/HER2- Metastatic Breast Cancer (mBC)

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Background: HR+/HER2- mBC, the most common subset of breast cancer, is treated with sequential endocrine therapy + targeted agents followed by sequential single-agent chemotherapy (CT), with increasingly shorter benefit duration with each subsequent treatment. High Trop-2 expression is observed in breast cancer regardless of subtype. SG is a Trop-2-directed antibody-drug conjugate approved for pre-treated metastatic triple-negative breast cancer. In the phase 3 TROPiCS-02 study, SG showed both significant progression-free survival (PFS) benefit (HR, 0.66; $P < 0.001$; median 5.5 vs 4.0 mo; JCO 2022) at the primary analysis and overall survival (OS) benefit (median 14.4 vs 11.2 mo; HR, 0.79; $P = 0.02$; ESMO 2022) at the 2nd planned interim OS analysis vs TPC in pretreated HR+/HER2- mBC. Here we compare efficacy outcomes for SG and TPC by Trop-2 expression. Methods: Eligible pts had HR+/HER2- locally recurrent inoperable or mBC; received ≥ 1 prior taxane, endocrine therapy, a CDK4/6 inhibitor; and received 2-4 prior CT regimens for mBC. Pts were randomized 1:1 to receive SG (10 mg/kg IV on d 1 and 8, every 21 d) or TPC (eribulin, gemcitabine, capecitabine, or vinorelbine) until disease progression or unacceptable toxicity. The primary endpoint was PFS by independent review per RECIST v1.1; OS and objective response rate (ORR) were key secondary endpoints. ORR was assessed by blinded independent central review per RECIST v1.1. Membrane Trop-2 expression on archival tumor tissue was assessed by immunohistochemistry and expressed as a histochemical score (H-score; range, 0-300); efficacy outcomes were assessed in H-score < 100 and ≥ 100 groups. The H-score < 100 group was further divided into H-score ≤ 10 and > 10 - < 100 subgroups to assess the activity of SG in pts with very low Trop-2 expression. Results: Data cut-off was January 3, 2022 for PFS (median follow-up, 10.2 mo) and July 1, 2022 for OS (median follow-up, 12.5 mo). In total, 543 pts were randomized to receive SG (n=272) vs TPC (n=271). Pts had a median of 3 prior CT regimens for mBC; 95% had visceral metastases. There were 238 (88%) vs 224 (83%) Trop-2-evaluable pts in the SG vs TPC groups, respectively; of these, 95% had tumors with Trop-2 H-score > 0 . Of Trop-2-evaluable pts, 192 (42%) and 270 (58%) had H-scores < 100 and ≥ 100 , respectively. Demographics and baseline characteristics were generally consistent across H-score groups. PFS and OS benefit was observed for SG vs TPC across both Trop-2 groups (Table). Median PFS was 5.3 vs 4.0 mo (HR, 0.77; 95% CI, 0.54-1.09) and 6.4 vs 4.1 mo (HR, 0.60; 95% CI, 0.44-0.81) in the H-score < 100 and ≥ 100 groups; median OS was 14.6 vs 11.3 mo (HR, 0.75; 95% CI, 0.54-1.04) and 14.4 vs 11.2 mo (HR, 0.83; 95% CI, 0.62-1.11), respectively. Disease response was observed in the 34 pts with H-score ≤ 10 who received SG. In pts who received SG, those with H-score ≤ 10 , > 10 - < 100 , and ≥ 100 had ORRs of 24%, 18%, and 23%, respectively. The safety profile for SG by Trop-2 H-score was consistent with previous reports. Conclusions: In this TROPiCS-02 post-hoc analysis, improved efficacy with SG vs TPC was observed regardless of Trop-2 expression, and there was no clear level of

Trop-2 expression at which a better treatment effect for SG was observed. These results support SG as an effective novel treatment option for patients with pretreated, endocrine-resistant HR+/HER2- mBC, and reinforce that Trop-2 testing is not required for SG treatment.

Table

	n (SG/TPC)	Median PFS (SG vs TPC), mo	PFS HR (95%CI)	Median OS (SG vs TPC), mo	OS HR (95%CI)
Trop-2 expression, H-score					
<100	96/96	5.3 vs 4.0	0.77 (0.54-1.09)	14.6 vs 11.3	0.75 (0.54-1.04)
≥100	142/128	6.4 vs 4.1	0.60 (0.44-0.81)	14.4 vs 11.2	0.83 (0.62-1.11)
≤10	34/45	5.5 vs 4.3	0.89 (0.51-1.57)	17.6 vs 12.3	0.61 (0.34-1.08)
>10-<100	62/51	5.0 vs 3.5	0.67 (0.42-1.07)	13.7 vs 11.0	0.81 (0.54-1.23)
>10	204/179	5.6 vs 4.0	0.62 (0.48-0.80)	14.1 vs 11.1	0.82 (0.65-1.04)

H-score, histochemical score; OS, overall survival; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

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Ongoing Trials 1

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A randomised phase II trial of palbociclib and fulvestrant vs standard endocrine therapy in patients with ER positive HER2 negative breast cancer and ctDNA detected molecular relapse during adjuvant endocrine therapy (TRAK-ER)

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Background: Most patients with early stage oestrogen receptor positive (ER+) and HER2 negative breast cancer will be cured of their cancer. However, up to 20% of patients may experience disease recurrence in the first 10 years. Molecular relapse of ER+ breast cancer can be detected with circulating tumour DNA (ctDNA) before clinical relapse occurs. Palbociclib, a CDK4/6 inhibitor, plus fulvestrant, a selective oestrogen receptor degrader, is a standard first line therapy for patients with ER+ breast cancer who have relapsed on standard endocrine therapy. We designed TRAK-ER to establish a surveillance system for ctDNA detection and then to assess whether treating patients, who have ctDNA detected molecular relapse, with palbociclib and fulvestrant may defer or prevent relapse. Design: TRAK-ER is a phase 2 multi-centre, randomised, open-label parallel superiority trial in patients with ER+ early breast cancer, recruiting at centres in the UK and France. In the surveillance phase patients will be monitored for molecular recurrence with ctDNA testing. To be eligible for the surveillance phase patients must be aged 18 or over, have ER+ ($\geq 10\%$ or Allred score 6/8 or greater) and HER2 negative breast cancer and have completed their primary surgery, chemotherapy and radiotherapy. Standard endocrine therapy (GnRH analogues, aromatase inhibitors and tamoxifen) must have been received for a minimum of 6 months and a maximum of 7 years and be planned to continue for at least another 3 years. Inclusion criteria in patients who did not receive neoadjuvant chemotherapy are at least one of: (a) four or more involved axillary or positive supraclavicular lymph node; (b) tumour size $>5\text{cm}$; (c) one to three involved axillary lymph nodes together with at least one of: tumour size $>3\text{cm}$, grade 3 or a high genomic risk score. Patients who received neoadjuvant chemotherapy require at least one lymph node positive or a tumour size $>3\text{cm}$ after chemotherapy. Invitae Personalized Cancer Monitoring (PCM TM) will be used for ctDNA analysis, a pan-cancer, tumour-informed liquid biopsy test that uses next-generation sequencing to detect minimal or molecular residual disease (MRD) in solid tumours. ctDNA analysis will be every 3 months for up to 3 years. Detection of ctDNA will trigger staging imaging. If no overt metastatic disease is identified, patients will be able to enter the treatment phase of the study, and be 1:1 randomised using minimisation to either remain on standard endocrine therapy or switch to palbociclib plus fulvestrant. Those who are allocated to remain on endocrine therapy are allowed to continue on the same therapy or change standard endocrine therapy. Duration of palbociclib and fulvestrant will be 2 years, or until relapse. Up to

1300 patients will enrol for tissue screening to allow 1100 patients to enter into ctDNA surveillance. 132 patients will enter the treatment part of the study. The primary endpoint of the surveillance phase is ctDNA detection rate. The primary endpoint of the treatment phase is relapse free survival (RFS). RFS will be calculated in the intention to treat population using Kaplan Meier methods from the date of randomisation to the date of recurrence or death from any cause. Secondary endpoints include relapse free interval, invasive disease free survival, distant recurrence free survival, overall survival and ctDNA clearance. (NCT04985266)

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EMBER-4: A phase 3 adjuvant trial of imlunestrant vs standard endocrine therapy (ET) in patients with ER+, HER2- early breast cancer (EBC) with an increased risk of recurrence who have previously received 2 to 5 years of adjuvant ET

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Background: Adjuvant ET has been the standard of care for patients with estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) EBC. A significant proportion of patients with increased risk still experience disease relapse despite available ET and more optimum ET is needed to prevent patients developing incurable metastatic cancer. Distant recurrence risk ranges from 20% to 40% after 5 years of adjuvant ET, depending on clinicopathological (clin-path) features at diagnosis. Consequently, there is a need to further optimize adjuvant treatment, particularly in those patients who are at increased risk of recurrence. Imlunestrant is an orally bioavailable selective estrogen receptor degrader (SERD) with pure antagonistic properties and the potential to overcome ET resistance. In early phase trials, imlunestrant monotherapy showed favorable safety with pharmacokinetic (PK) exposures exceeding fulvestrant and preliminary efficacy in ER+, HER2- advanced breast cancer patients (EMBER, Jhaveri 2022) along with robust biological/pharmacodynamic activity and tolerability in EBC (EMBER-2, Neven). Trial Design: EMBER-4 is a randomized, open-label, global phase 3 study comparing imlunestrant versus physicians' choice of ET, in patients who are at an increased risk of recurrence based on clin-path features and who have received 2 to 5 years of standard adjuvant ET. Approximately 6,000 patients will be randomized 1:1 to receive imlunestrant (400 mg daily) for 5 years or physicians' choice of adjuvant ET (tamoxifen or an aromatase inhibitor, AI, dosed per label). Study treatment duration is 5 years. Males and pre-/peri-menopausal women will receive concomitant treatment with a GnRH agonist if receiving imlunestrant or an AI. Stratification factors include time from initial adjuvant ET, use of prior adjuvant cyclin dependent kinase 4/6 inhibitors, nodal status, menopausal status, and geographic region. Eligibility criteria: Eligible patients are adult males and females (pre-, peri- or postmenopausal) with ER+, HER2- EBC who have completed definitive locoregional therapy and have received 2 to 5 years of prior adjuvant ET without disease recurrence, but who are at increased risk of recurrence based on clin-path features at diagnosis. Prior (neo) adjuvant chemotherapy and/or targeted therapy with a CDK4/6- or PARP- inhibitor is permitted. Study endpoints: The primary endpoint is invasive disease-free survival (IDFS), excluding second non-breast primary invasive cancers. Key secondary endpoints include distant relapse-free survival, overall survival, IDFS including second non-breast primary invasive cancers, safety, PK and patient reported outcomes. Recruitment for EMBER-4 begins globally in Q4 2022.

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5:00 PM - 6:15 PM

OT1-02-01

4CAST: A Phase 1b dose exploration and dose expansion, open-label study evaluating the safety and efficacy of INO-464 in combination with Chemotherapy in patients with metASTatic breast cancer.

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Abstract: Trials in progress **Authors:** Dr Rachel Dear, A/Prof Christine Chaffer, Dr Beatriz Perez San Juan **Title:** 4CAST: A Phase 1b dose exploration and dose expansion, open-label study evaluating the safety and efficacy of INO-464 in combination with Chemotherapy in patients with metASTatic breast cancer. **Problem statement:** Metastatic triple negative breast cancer (mTNBC) has poor outcomes, with rapid progression and a median overall survival of 16 months. Standard treatment includes chemotherapy, with a possible role for immunotherapy. The antibody-drug conjugate sacituzumab govitecan was been granted recent approval. The development of new targeted treatments remains an unmet need. The androgen receptor is a mediator of chemotherapy-resistance in triple-negative breast cancer. Taxane and platinum-based chemotherapy induces cell plasticity and the emergence of chemotherapy-resistance. The androgen receptor (AR) antagonist, INO-464, but not abiraterone or enzalutamide, blocks chemotherapy induced cell plasticity to inhibit and primary and metastatic tumour growth. Three early-phase prospective clinical studies investigating anti-androgen therapy have demonstrated clinical benefit of single-agent AR-targeted agents in women with metastatic AR positive TNBC. The 450 mg daily start dose of INO-464 was well-tolerated and declared the recommended phase 2 dose. Preliminary laboratory data demonstrates an increase in survival and suppression of metastatic TNBC when INO-464 is used in combination with docetaxel. **Methods:** To determine the feasibility, safety and efficacy of INO-464 in combination with chemotherapy for the treatment of metastatic breast cancer. In Part 1 (dose exploration) of the trial we aim to establish the tolerability and safety and determine the recommended phase 2 dose of INO-464 when used in combination with docetaxel. Part 1 will recruit 6-18 females or males with locally advanced or metastatic breast cancer ie hormone receptor positive, HER2-positive or triple-negative breast cancer. In Part 2 (dose expansion) the clinical activity INO-464 and docetaxel in participants with metastatic triple negative breast cancer will be assessed. **Results:** Ethics approval for Part 1 of the trial was granted in May 2021. The trial received governance approval from St Vincent's Hospital governance in June 2022. Recruitment commenced on the 1 July 2022. The trial has received 40 enquiries, of which three patients

were eligible and one patient has consented to the trial and will be ready to start in the next two weeks. Conclusion: This investigator-initiated trial is an example of a collaborative effort between the Garvan Institute of Medical Research and the Kinghorn Cancer Centre at St Vincent's Hospital. If the combination of INO-464 and docetaxel is shown to be safe we look forward to recruiting to the part 2 dose expansion phase across multiple Australian sites. This study is registered with ClinicalTrials.gov NCT04947189. Disclosure of interests: A/Prof Christine Chaffer is the Managing Director of Kembi Therapeutics that is providing the investigational product for the clinical trial.

Disclosure(s):

Rachel F. Dear, MBBS PhD FRACP: No financial relationships to disclose

Kathleen Batty, MBBS: No financial relationships to disclose

Beatriz Perez, PhD: No financial relationships to disclose

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5:00 PM - 6:15 PM

OT1-02-02

A phase 1/2 study to evaluate the safety and efficacy of EP0062, an oral Selective Androgen Receptor Modulator (SARM), for the treatment of AR+/HER2-/ER+ advanced breast cancer

Presenting Author(s) and Co-Author(s):

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There is growing interest in targeting the androgen receptor (AR) in advanced/metastatic breast cancer. It has been recently demonstrated preclinically that AR activation, rather than AR suppression, exerts potent antitumor activity across a number of ER+ /AR+ breast tumors, including those resistant to standard-of-care endocrine therapy and CDK4/6 inhibitors (Hickey et al, *Nature Medicine* 2021 27: 310-320). Mechanistically, agonist activation of AR altered the genomic distribution of ER and essential co-activators resulting in repression of ER-regulated cell cycle genes and upregulation of AR target genes, including known tumor suppressors. EP0062 is an oral, non-steroidal, SARM currently being developed for the treatment of AR+/HER2-/ER+ advanced breast cancer. The efficacy and safety of EP0062 has previously been investigated in a Phase 1 clinical trial of AR+/HER2-/ER+ advanced breast cancer, and demonstrated that EP0062 has acceptable tolerability with evidence of clinical efficacy (LoRusso et al. *Clinical Breast Cancer* 2022 22;1 67-77). This new study is designed to further extend the evaluation of EP0062 as a potential therapy for AR+/HER2-/ER+ advanced breast cancer. The primary aim of the study is to assess tolerability and identify an optimal RP2D dose. The study will also explore the relationship between efficacy of EP0062 and AR expression, to establish a threshold for future patient selection, and undertake an initial evaluation of the safety and efficacy of EP0062 in combination with established standard of care therapies. The study will recruit up to 128 patients with AR+/HER2-/ER+ advanced breast cancer. Module A is a dose finding cohort to investigate safety, tolerability, PK and PD and to define the maximum tolerated dose (MTD) and/or Recommended Phase II Dose (RP2D). Dose finding will be based on a 3+3 design and is expected to recruit up to 32 patients. Once

potential recommended doses are identified, approximately 60 evaluable patients will be randomised to two different dose cohorts in Module B in order to further optimise the RP2D dose, by further evaluation of safety and tolerability, as well as prospectively evaluate the relationship between efficacy and AR expression. In Module C, EP0062 will be combined with select standard of care targeted therapies in patients with relapsed AR+/HER2-/ER+ advanced breast cancer to confirm safety and explore efficacy. This will include approximately 36 patients across a number of single arm expansion cohorts. The key inclusion criteria are as follows: • Post-menopausal women, ≥18 years • ECOG performance status of 0 to 1 • Locally advanced or metastatic breast cancer • ER+, HER2- as per ASCO CAP guidelines • AR+, as defined as ≥ 10% AR nuclei staining by IHC • Endocrine-sensitive defined as greater than 3 years endocrine treatment prior to recurrence if recurrence occurred in the adjuvant setting, or ≥ 6 months treatment and response if recurrence occurred from primary treatment in the advanced setting • Relapsed, defined as clear and documented evidence of disease progression following ≥ 1 lines and ≤2 prior lines of previous endocrine therapy and ≤ 2 lines of chemotherapy in the advanced/metastatic setting • Measurable disease defined by RECIST version 1.1, or measurable bone-only disease EP0062 will be dosed to progression. Endpoints include incidence of DLTs during Cycle 1 of EP0062 treatment (28 days), MTD, RP2D (Module A), incidence and severity of AEs and SAEs, plasma PK parameters, Clinical Benefit Rate (complete response, partial response, or stable disease) at 24 weeks, ORR, duration of response, PFS, OS and quality of life. Clinic follow-up will be at 2 and 4 weeks, then every 4 weeks until disease progression. Recruitment is scheduled to initiate in Q4 2022.

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12/6/2022

5:00 PM - 6:15 PM

OT1-03-01

XMT-1660: A Phase 1b trial of a B7-H4 targeted Antibody Drug Conjugate (ADC) in Breast, Endometrial, and Ovarian Cancers

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Background: Breast cancer (BC) is the most commonly diagnosed cancer and one of the leading causes of cancer death in women. Despite significant therapeutic advances, the

majority of patients with unresectable or recurrent/metastatic disease eventually develop resistance to available standard of care (SOC) therapies. B7-H4 is a poor prognostic factor and is overexpressed in several cancers including endometrial, ovarian, and breast. As a member of the CD28/B7 family of cell surface proteins, it promotes tumorigenesis by suppressing anti-tumor immunity. XMT-1660 is a B7-H4-targeted Dolasynthen antibody drug conjugate with a precise, optimized drug-to-antibody ratio and a DolaLock microtubule inhibitor payload with controlled bystander effect. In the preclinical setting, XMT-1660 has demonstrated anti-tumor activity in TNBC and ER+/HER2- patient-derived xenograft mouse models, which included tumors from heavily pre-treated patients (Collins et al, AACR 2022). Increased anti-tumor activity tended to be more frequent in models with higher B7-H4 expression, providing rationale for a Ph1 clinical trial. Methods: The Ph1 trial includes a first-in-human open-label dose escalation (DES) portion followed by dose expansion (EXP) evaluating XMT-1660 in patients with BC, EC, and OC following progression on SOC as applicable (i.e., CDK4/6i + ET; platinum-based chemotherapy). In the DES, Bayesian Optimal Interval (BOIN) design will be used to determine the MTD. Patients will receive XMT-1660 IV Q3 weeks. Primary endpoints in DES are to assess safety and determine a recommended phase 2 dose (RP2D) and assessment of preliminary efficacy as a secondary endpoint. In the EXP portion, cohorts enrolling TNBC, ER+/HER2- BC, EC/OC are planned and additional patients may be enrolled based on emerging data. The primary endpoint of EXP is to assess safety and tolerability, overall response rate, disease control rate, and duration of response. Secondary endpoints include pharmacokinetic analysis and antidrug antibodies. Patients are not selected by B7-H4 status, but baseline tumors samples are collected for retrospective tumor tissue evaluation. The trial is currently enrolling patients. NCT05377996

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12/6/2022

5:00 PM - 6:15 PM

OT1-03-02

Efficacy and safety of SKB264 for previously treated metastatic triple negative breast cancer in Phase 2 study

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Background: The therapeutic options for patients (pts) with previously treated metastatic TNBC are limited compared with other breast cancer subtypes. SKB264 is an antibody drug conjugate (ADC) composed of an anti-TROP2 antibody coupled to the cytotoxic belotecan-derivative via a novel linker. Here, we present results from a Phase 2 expansion cohort for pts with mTNBC (NCT04152499). Methods: Pts with previously treated mTNBC were enrolled to receive SKB264 4 mg/kg Q2W or 5 mg/kg Q2W in a non-randomized fashion until disease progression/unacceptable toxicity. The assessment for tumor response was performed every 8 weeks per RECIST v1.1 assessed by investigator. The TROP2 expression was scored using the semi-quantitative H-score method, and cut off point was set to 200. TROP2 expression and its association with anti-tumor activity was retrospectively analyzed. Results: At data cut-off date (May 15, 2022), 59 pts were enrolled (23 in 4 mg/kg, 36 in 5 mg/kg), 88% of them (52 pts) had received ≥ 3 prior therapies for metastatic disease. Among 53 patients with tissue available for TROP2 testing, 29 patients (55%) had TROP2 high (H-score $>200-300$) tumors. The median follow up was 9.6 months. Of 55 pts (21 in 4 mg/kg and 34 in 5 mg/kg) evaluable for response assessment (≥ 1 on-study scan), the confirmed ORR (cORR) was 40% (22/55) and disease control rate (PR+CR+SD) was 80% (44/55). The cORR was 55% (16/29) in the subset of patients with high TROP2 expression. The median duration of response (DoR) was not reached with range from 1.0+ to 11.0+ months and the 6-month DoR rate was 82%. Median PFS was 5.7 months (95% CI: 3.9, 7.6). Treatment-related adverse events (TRAEs) of \geq Grade 3 were reported in 55.9% (33/59) of pts. The most common \geq Grade 3 TRAEs ($\geq 10\%$) were neutrophil count decreased (23.7%), anemia (20.3%) and platelet count decreased (16.9%). TRAEs led to dose reduction in 15.2% (9/59) of pts and to discontinuation in 6.8% (4/59) of pts. No treatment-related AEs leading to death or interstitial lung disease (ILD) were reported. Safety and anti-tumor activities of SKB264 by dose level will be presented. Conclusions: SKB264 demonstrates a manageable safety profile and promising antitumor activity in pts with heavily pretreated mTNBC. SKB264 toxicity was mainly hematologic. A Phase 3 study of SKB264 vs investigator selected chemo alone in pts with locally advanced inoperable or metastatic TNBC was initiated (NCT05347134).

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OT1-03-03

Phase 1 open-label study of ladiratumumab vedotin in patients with first-line unresectable locally advanced or metastatic triple-negative breast cancer (SGNLVA-001, part F, trial in progress)

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Background LIV-1 is a highly expressed transmembrane protein in breast cancer cells. Ladiratumab vedotin (LV) is an investigational antibody–drug conjugate directed to LIV-1 via a humanized IgG1 monoclonal antibody conjugated to monomethyl auristatin E (MMAE) by a protease-cleavable linker. LV is internalized when it binds LIV-1 on cell surfaces and MMAE is released, which binds tubulin and induces apoptosis. We established that weekly doses of LV up to 1.5 mg/kg were clinically active and generally well tolerated in patients with second-line metastatic triple-negative breast cancer (mTNBC) (Tsai 2021). Based on pharmacokinetic and pharmacodynamic (PK/PD) modeling and simulation analysis, we are evaluating an intermittent LV dosing schedule to improve antitumor activity while maintaining a manageable safety profile. There is currently an unmet medical need for front-line novel therapies in patients with programmed death ligand 1 (PD-L1) low or negative mTNBC, where response rates to standard of care chemotherapy are poor. Part F of this study focuses on this patient population. Methods SGNLVA-001 (NCT01969643) is an ongoing phase 1 study assessing the safety, tolerability, and preliminary efficacy of LV. Part F will enroll ~30 patients with first-line unresectable locally advanced (LA)/mTNBC. Eligible patients must not have received prior cytotoxic therapy in the unresectable LA/mTNBC setting and have tumors with a PD-L1 combined positive score < 10. Patients must also have at least 1 measurable lesion per RECIST v1.1, adequate organ function, and an ECOG status of ≤ 1 . Patients with Grade ≥ 2 peripheral neuropathy and prior therapy with LV or MMAE-containing agents are not eligible. Tumor LIV-1 expression is not required for enrollment. Patients in Part F will receive LV 1.5 mg/kg by intravenous infusion on Days 1 and 8 every 3 weeks, until progression or unacceptable toxicity. Tumor assessments will be conducted every 6 weeks (± 1 week) for the first 10 cycles and every 12 weeks thereafter. All patients will be followed for safety. The primary safety endpoint is the incidence of adverse events. Key efficacy endpoints include confirmed overall response rate, duration of response, progression-free survival, and overall survival. PK and markers of PD will be assessed. Safety, PK, and efficacy measures will be summarized using descriptive statistics. Enrollment for Part F is ongoing in the US.

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Datopotamab deruxtecan (Dato-DXd), a TROP2 antibody-drug conjugate, vs investigators' choice of chemotherapy in previously-treated, inoperable or metastatic HR+/HER2- breast cancer: TROPION-Breast01

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Background: Chemotherapy is the main treatment in patients with pre-treated endocrine-resistant HR+/HER2– metastatic breast cancer, but has limited efficacy and substantial toxicities. The antibody-drug conjugate Dato-DXd consists of a humanized IgG1 mAb targeting TROP2 attached via a stable cleavable linker to a topoisomerase I (TopI) inhibitor payload. Heavily pre-treated patients with metastatic triple-negative breast cancer in the TROPION-PanTumor01 (NCT03401385) study of Dato-DXd showed a manageable safety profile and highly encouraging objective response rates (ORR by blinded independent central review [BICR]: 34% in all patients; 52% in patients treatment-naïve to TopI inhibitor-based therapies). The metastatic HR+/HER2– breast cancer cohort of TROPION-PanTumor01 has completed enrollment (n=41); data are currently maturing. Trial design: TROPION-Breast01 (NCT05104866) is an ongoing, global, phase 3, open-label, randomized trial evaluating efficacy and safety of Dato-DXd vs investigators' choice of chemotherapy (ICC) in patients with inoperable or metastatic HR+/HER2– breast cancer. Patients (n≈700) are randomized 1:1 to Dato-DXd 6 mg/kg IV Q3W or ICC (eribulin, capecitabine, vinorelbine, or gemcitabine) until progression. Adults with an ECOG performance status of 0–1, who experienced progression on or are unsuitable for endocrine therapy, and received 1–2 prior lines of standard-of-care chemotherapy in the inoperable or metastatic setting are eligible. Monotherapy treatment with inhibitors of mTOR, PD-[L]1, CDK4/6 and PARP do not count as prior chemotherapy lines. Patients must have ≥1 measurable lesion per RECIST 1.1 and an archival or fresh formalin-fixed and paraffin-embedded tumor sample. Clinically inactive brain metastases are permitted. Dual primary endpoints are progression-free survival (PFS) by BICR, and overall survival. Secondary endpoints include PFS per investigator, ORR, disease control rate, patient-reported outcomes, and Dato-DXd pharmacokinetics and immunogenicity. Exploratory endpoints include TROP2 expression and exposure–efficacy relationship. Patients are stratified by number of prior chemotherapy lines, prior CDK4/6 inhibitor use, and region. At the time of writing 236 patients have been enrolled across 19 countries.

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OT1-03-05

TROPION-Breast02: Phase 3, open-label, randomized study of first-line datopotamab deruxtecan versus chemotherapy in patients with locally recurrent inoperable or metastatic TNBC who are not candidates for anti-PD-(L)1 therapy

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Introduction: Despite recent treatment advances, the prognosis for patients diagnosed with locally recurrent inoperable or metastatic triple-negative breast cancer (TNBC) remains poor. Single-agent chemotherapy has been the mainstay of treatment for metastatic TNBC for many years, with very limited treatment options for patients who are not candidates for anti-PD-1/PD-L1 therapy; consequently, there remains an urgent unmet need. Trophoblast cell surface protein 2 (TROP2) is a type I transmembrane glycoprotein highly expressed on various solid tumors, including breast. Datopotamab deruxtecan (Dato-DXd) is an antibody-drug conjugate (ADC) composed of a humanized anti-TROP2 IgG1 monoclonal antibody covalently linked to an exatecan derivative (DXd) – a highly potent topoisomerase I inhibitor payload – via a stable, tumor-selective, tetrapeptide-based cleavable linker. Dato-DXd has previously been evaluated in TROPION-PanTumor01 (NCT03401385) – an ongoing Phase I clinical trial across multiple advanced solid tumors, including heavily-pretreated, metastatic TNBC. As of the July 30, 2021 cut-off date, the objective response rate (ORR) by blinded independent central review (BICR) was 34% (15/44) in all patients with TNBC and 52% (14/27) in those patients treatment-naïve to topoisomerase I inhibitor-based ADC therapies, with measurable disease (per RECIST 1.1) at baseline. Furthermore, a manageable safety profile was reported, with no new safety signals identified; low grade nausea and stomatitis were most frequent, with neutropenia and diarrhea being uncommon. The aim of the phase 3 TROPION-Breast02 trial is to evaluate the efficacy and safety of Dato-DXd versus investigator's choice of chemotherapy (ICC) in patients with TNBC who are not candidates for PD-1/PD-L1 inhibitor therapy. Methods: TROPION-Breast02 (NCT05374512) is an ongoing Phase 3, open-label, randomized study of Dato-DXd versus ICC in first-line treatment of patients with locally recurrent inoperable or metastatic TNBC. Approximately 600 patients will be randomized 1:1 to receive either Dato-DXd 6 mg/kg IV every three weeks or ICC (paclitaxel, nab-paclitaxel, carboplatin, capecitabine, or eribulin mesylate). Patients ≥18 years with histologically/cytologically confirmed TNBC who have not received prior chemotherapy or targeted systemic therapy for metastatic or locally recurrent inoperable disease are eligible for inclusion. Patients are also required to have an ECOG PS of 0 or 1 and be eligible for treatment with one of the ICC options per investigator assessment. Patients must have ≥1 measurable lesion per RECIST v1.1 not previously irradiated, along with a formalin-fixed and paraffin-embedded tumor sample available. Those with a previously treated neoplastic spinal cord compression or clinically inactive brain metastases can be included. Key exclusion criteria are history of another primary malignancy; persistent toxicity from previous anti-cancer treatments; uncontrolled infections; current/prior interstitial lung disease/pneumonitis or clinically severe pulmonary function compromise; clinically significant corneal disease; and prior treatment with topoisomerase I inhibitors, TROP2-targeted therapy, or the same chemotherapy agent chosen for on-study ICC. The dual primary endpoints are progression free survival (PFS) per RECIST 1.1 by BICR, and OS. Secondary endpoints include ORR, duration of response, PFS by investigator assessment, time to deterioration for patient-reported outcomes, time to first subsequent therapy, time to second subsequent therapy, time to second progression or death, pharmacokinetics and immunogenicity of Dato-DXd, and safety. Recruitment for this study is ongoing as of June 2022.

Disclosure(s):

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5:00 PM - 6:15 PM

OT1-03-06

Phase 1b/2 study of ladiratumumab vedotin (LV) in combination with pembrolizumab for first-line treatment of triple-negative breast cancer (SGNLVA-002, trial in progress)

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Background Patients with metastatic triple-negative breast cancer (mTNBC) have a poor prognosis. Treatment combinations of anti-programmed death protein 1 (anti-PD-1) agents with chemotherapy have shown promise in mTNBC. Ladiratuzumab vedotin (LV) is an investigational antibody-drug conjugate directed to LIV-1, a protein highly expressed on breast cancer cells, via a humanized IgG1 monoclonal antibody conjugated to approximately 4 molecules of monomethyl auristatin E (MMAE) by a protease-cleavable linker. LIV-1-mediated delivery of MMAE disrupts microtubules and induces cell cycle arrest and apoptosis. LV has also been shown to drive immunogenic cell death (ICD) to elicit an immune response. LV + pembrolizumab may result in synergistic activity through LV-induced ICD, creating a microenvironment favorable for enhanced anti-PD-1 activity. Interim results from an ongoing, multi-part, open-label study investigating the safety and efficacy of LV in patients with metastatic breast cancer (SGNLVA-001, NCT01969643), showed weekly LV monotherapy at doses up to 1.5 mg/kg were clinically active and generally well tolerated (Tsai 2021). Based on pharmacokinetic and pharmacodynamic modeling and simulation analysis, an intermittent LV + pembrolizumab dosing regimen is being evaluated to further enhance efficacy and improve the tolerability profile. Due to an unmet medical need for patients with unresectable locally advanced (LA)/mTNBC who are programmed death ligand 1 (PD-L1) low or negative, Part D will focus on this patient population. Trial Design SGNLVA-002 (NCT03310957) is an ongoing global single-arm, open-label phase 1b/2 study of LV + pembrolizumab as 1L therapy for patients with unresectable LA/mTNBC. Part D is currently enrolling ~40 patients. Eligible patients must have advanced disease with no prior cytotoxic/anti-PD-1 treatment, PD-L1 combined positive score < 10, measurable disease per RECIST v1.1, and an ECOG performance status ≤1. Patients with Grade ≥2 pre-existing neuropathy or active central nervous system metastases are not permitted. Patients will receive LV at 1.5 mg/kg on Days 1 and 8 every 21 days plus pembrolizumab 200 mg on Day 1 q3w. The primary objectives are to evaluate the safety/tolerability and objective response rate of LV + pembrolizumab. Secondary objectives include duration of response, disease control rate, progression-free survival, and overall survival. Safety and efficacy endpoints will be summarized with descriptive statistics. Global enrollment is ongoing in the US, EU, and Asia.

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5:00 PM - 6:15 PM

OT1-04-01

AMEERA-6: Phase 3 Study of Adjuvant Amcenestrant Versus Tamoxifen for Patients With Hormone Receptor-Positive Early Breast Cancer, Who Have Discontinued Adjuvant Aromatase Inhibitor Therapy Due to Treatment-related Toxicity

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Background: About 30% of patients (pts) with hormone receptor (HR)-positive early breast cancer (EBC) on adjuvant aromatase inhibitor (AI) therapy discontinue due to toxicity with 22% of pts discontinuing during the first year (Henry et al. JCO 2012). For these patients who struggle with adjuvant AIs, there are limited alternatives including switch to a different AI which may have similar side effects, tamoxifen, or observation. This paucity of effective and tolerable options may contribute to poor adherence and/or early discontinuation of adjuvant endocrine therapy, which is associated with worse outcomes. Amcenestrant (SAR439859) is an optimized oral selective estrogen receptor degrader (SERD) with potent dual activity which antagonizes and degrades the estrogen receptor (ER), resulting in inhibition of the ER signaling pathway. In the phase 1/2 AMEERA-1 first-in-human trial (SABCS 2020 PD8-08), amcenestrant showed strong antitumor activity and favorable safety profile in the treatment of HR+ metastatic breast cancer. The phase 2 window-of-opportunity study AMEERA-4 evaluating two doses of amcenestrant demonstrated robust Ki67 reductions, strong engagement of the ER target, and

continued to show a favorable safety profile in an early breast cancer population. Based on pharmacodynamic activity, safety, and emerging results from other ongoing amcenestrant trials, the 200 mg daily dose of amcenestrant was selected for the AMEERA-6 study. Trial Design: This is a prospective, randomized, international, double-blind, double-dummy, phase 3 superiority study of amcenestrant versus tamoxifen. Eligible pts are men and women with any menopausal status with HR+ stage IIB/III breast cancer, irrespective of human epidermal growth factor receptor 2 (HER2) status. If neoadjuvant systemic therapy was administered, pts must have residual nodal disease after definitive breast surgery (ypN1-3). Pts will be centrally assessed to have ER-positive and/or progesterone receptor-positive ($\geq 10\%$ positive stained cells) status by immunohistochemistry assay. Pts must have received at least 6 months of adjuvant AIs (≥ 3 months in the adjuvant setting if they received prior neoadjuvant AI) and discontinued within 30 months of initiation due to AI-related toxicity. Pts may have been treated with more than one AI. All adjuvant therapies including chemotherapy, anti-HER2 treatment, cyclin-dependent kinase (CDK) 4/6 inhibitor, and/or poly (ADP-ribose) polymerase (PARP) inhibitors must be completed or stopped prior to randomization. 3738 pts will be randomized 1:1 to receive either amcenestrant 200 mg daily or tamoxifen 20 mg daily for 5 years and will be followed for 10 years from randomization. Men and pre/peri-menopausal women will also receive a GnRH analog. Extended adjuvant endocrine therapy upon completion of study treatment is allowed per investigator discretion. Stratification factors include duration of prior AI therapy, HER2 status and prior chemotherapy, prior CDK4/6 inhibitors, geographic region, and menopausal status. The primary endpoint is invasive breast cancer-free survival (IBCFS) based on STEEP criteria version 2.0 defined as occurrence of first recurrence of the disease: ipsilateral or regional invasive, distant recurrence, contralateral invasive breast cancer and death. Key secondary endpoint is invasive disease-free survival (IDFS) and other secondary endpoints include overall survival, safety, patient reported outcomes, and pharmacokinetics of amcenestrant. Adherence to treatment and biomarkers are exploratory endpoints. AMEERA-6 recruited the first patient in March 2022 and is being conducted in partnership with AFT, BIG, EORTC, and Sanofi. Clinical trial information: NCT05128773

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Anastrozole dose escalation for optimal estrogen suppression in postmenopausal early stage breast cancer: A prospective trial

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Introduction: We performed matched case-control studies utilizing cohorts of postmenopausal women with ER+ breast cancer receiving adjuvant aromatase inhibitors (AI) on MA.27 [anastrozole, exemestane] or PreFace [letrozole] to assess the association between estrogen suppression after 6 months of treatment and an early breast cancer (EBC) event within 5 years of AI initiation (Clin Cancer Res 2020;26:2986-98). We found a significant 3.0-fold increase in risk of an EBC event for those taking anastrozole with levels of estrone (E1) ≥ 1.3 pg/mL and estradiol (E2) ≥ 0.5 pg/mL, but not for exemestane or letrozole. Given these findings we designed a prospective pharmacodynamic (PD) study to evaluate the impact of anastrozole (1 mg/day: ANA1) on E1 and E2 levels, and among those with inadequate estrogen suppression (IES: E1 ≥ 1.3 pg/mL and E2 ≥ 0.5 pg/mL), to evaluate the safety and PD efficacy of high-dose anastrozole (10 mg/day: ANA10), which has been found to be safe in prior clinical trials (Cancer 1998;83:1142-52). Methods: Post-menopausal women with stage I-III, ER $\geq 1\%$ positive/HER2-negative breast cancer who were candidates for anastrozole were eligible after completion of locoregional therapy and chemotherapy, as clinically indicated. Women who were pre-menopausal at diagnosis were not eligible. All patients received 8-10 weeks of ANA1, after which those with adequate estrogen suppression (AES: E1 < 1.3 pg/mL or E2 < 0.5 pg/mL) came off study. Those with IES went on to receive ANA10 for 8-10 weeks, followed by letrozole (2.5 mg/day: LET) for 8-10 weeks. All patients were managed at their treating oncologist's discretion following study discontinuation. E1 and E2 blood levels were measured pre-treatment

and after completion of each treatment cycle by a CLIA-approved liquid chromatography with tandem mass spectrometry in the Immunochemical Core Laboratory at Mayo Clinic. With a sample size of 29 patients with IES after ANA1, a one-sided binomial test of proportions with a significance level of 0.05 will have an 87% chance of rejecting the proportion with AES after ANA10 is at most 25% (H_0) when the true proportion is at least 50%. Specifically, the null hypothesis is rejected if the number of women with AES after ANA10 is 12 or more. Data lock was July 6, 2022. Results: Of the 161 women enrolled from April 2020 through May 2022, 3 withdrew consent prior to start of ANA1 and 2 were ineligible; thus, 156 women comprised the study cohort. Median patient age was 64 years (range 44-86), 10% of patients were of Hispanic ethnicity and/or non-white race, and 15% received chemotherapy. Six patients remain on ANA1, and 10 discontinued ANA1 due to refusal (7), adverse event (AE) (2), or COVID-19 (1). Forty-one of the remaining 140 patients (29.3%; 95%CI: 21.9-37.6%) had IES with ANA1. Nine of these 41 patients did not go on to ANA10 due to refusal (6) or AE (3). Of the 32 patients who started ANA10, 8 remain on treatment, 5 discontinued due to refusal (3) or AE (1-grade 2 urinary tract infection; 1-grade 1 palpitations), and 19 had a blood draw 45 days or more after starting ANA10. No grade 3-5 AEs or grade 2 hot flashes or arthralgias were reported. Of these 19 patients, 14 achieved AES with ANA10 (73.7%; 95%CI: 48.8-90.9%). All 19 patients switched to LET of which 3 remain on treatment, 1 is missing E1/E2 data, and 15 had a blood draw 45 days or more after starting LET. Of these 15 patients, 10 maintained AES, 2 acquired AES with LET, and 3 no longer had AES. Anastrozole and letrozole drug levels will be reported at the meeting. Conclusions: Approximately 29% of postmenopausal women with ER+/HER2-BC receiving adjuvant anastrozole 1 mg/daily had IES. A majority of these patients achieved AES with dose escalation to ANA10 without tolerability issues. E1 and E2 levels are logical biomarkers given the mechanism of action of anastrozole, and further study utilizing them to determine the optimal dose of anastrozole for a given patient should be performed.

Disclosure(s):

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5:00 PM - 6:15 PM

OT1-05-02

Efficacy and safety of sintilimab in combination with anlotinib plus metronomic chemotherapy in advanced triple negative breast cancer (SPACE): preliminary results of a single-arm, multicenter phase II trial

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Background : Anti-PD-1 antibody combined with antiangiogenic drugs have demonstrated antitumor activity in advanced triple negative breast cancer (TNBC). Anlotinib, an oral multi-targeted tyrosine kinase inhibitor (TKI), has synergistic effect with anti-PD-1 antibody. Preclinical studies showed that metronomic chemotherapy inhibited angiogenesis and enhanced immunotherapy efficacy in TNBC via modulation of tumor immune microenvironment. We hereby conducted a single-arm, multicenter, phase II trial to investigate the efficacy and safety of sintilimab (anti-PD-1 antibody) in combination with anlotinib plus metronomic chemotherapy as a potential novel therapeutic strategy in advanced TNBC and explore potential biomarkers. Methods : Forty-three cases were planning to be included in this trial. The eligible patients who had received no more than two lines of chemotherapy for metastatic disease were enrolled and received sintilimab (200 mg iv q3w) in combination with anlotinib (12

mg po d1-14 q3w) plus capecitabine (500 mg po, tid) or vinorelbine (40 mg po, tiw) until disease progression or intolerable toxicity. The primary endpoint is objective response rate (ORR) and secondary endpoints are disease control rate (DCR), progression free survival (PFS), and overall survival (OS). The safety profile has also been assessed. Blood samples collected at different time points of the baseline, first and second cycle post-treatment, and disease progression were used for next-generation sequencing of ctDNA containing 654 tumor-related genes. Results: As of July 2022, a total of 32 patients were enrolled, and 29 patients were evaluable for efficacy. 2 patients (6.9%) achieved complete response (CR). 6 patients (20.7%) achieved partial response (PR). The ORR is 27.6% (8/29) and DCR is 79.3% (23/29). The median PFS was not reached. The most common grade 1 or 2 adverse events (AEs) include elevated thyroid stimulating hormone (37.0%, 10/27), hand-foot syndrome (18.5%, 5/27), elevated aspartate aminotransferase (14.8%, 4/27), elevated bilirubin (11.1%, 3/27) and hypertension (11.1%, 3/27). Grade 3 AEs include elevated bilirubin (3.7%, 1/27) and hypertension (3.7%, 1/27). No grade 4 or 5 AEs occurred. By analyzing ctDNA mutations of blood samples in 10 patients at baseline, we found that genes with high mutation frequency were HLA-DRB5 (8/10, 80%), TP53 (7/10, 70%), HLA-DRB1 (5/10, 50%) and PIK3CA (4/10, 40%). Among these 10 patients, 2, 3 and 5 patients achieved PR, SD and PD, respectively. The number of gene mutations in patients with PD was higher than that in patients with PR or SD at baseline. This indicate that mutations in ctDNA may be associated with poor efficacy in advanced TNBC. But this still needs further verification. Dynamic analysis of gene mutations at different time points showed that the amplification of HLA-DRB5 or the elimination of KMT2D, RELN and TP53 occurred in patients with PR and SD, but not in patients with PD. Conclusions: Sintilimab in combination with anlotinib plus metronomic chemotherapy has shown favorable efficacy and acceptable safety profile in patients with advanced TNBC. The clinical significance of ctDNA dynamic monitoring needs further validation. Clinical trial information: ChiCTR2100044725

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5:00 PM - 6:15 PM

OT1-06-01

Preservation of axillary lymph nodes in breast cancer patients undergoing mastectomy with 1-2 metastatic sentinel lymph nodes: The current status and future perspectives of the multicenter randomized clinical trial SINODAR-ONE

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Introduction: Axillary lymph node dissection (ALND) has always been part of breast cancer (BC) treatment. However, during the past 25 years, the surgical management of the axilla has shifted towards a more conservative approach. Until now, ALND has remained the standard surgical technique when the sentinel lymph node (SLN) is macrometastatic. However, ALND may now be considered overtreatment for early-stage BC. The SINODAR-ONE trial is a prospective non-inferiority multicenter randomized study aimed at assessing the role of ALND in patients undergoing either breast-conserving surgery (BCS) or mastectomy for T1-2 BC presenting 1-2 macrometastatic SLNs. Objectives: The primary endpoint was to evaluate whether sentinel lymph node biopsy (SLNB) only was associated with clinically relevant worsening of the prognosis compared with ALND in terms of overall survival (OS). The secondary endpoint was to evaluate whether there was increased regional (lymph node recurrence) or distant recurrence in terms of recurrence-free survival (RFS) in patients with macrometastatic SLN who did not undergo ALND. Methods: Patients were randomly assigned (1:1 ratio) to either removal of ≥ 10 axillary level I/II non-SLNs followed by adjuvant therapy (standard arm) or no further axillary treatment (experimental arm). Results: The trial started in April 2015 and ceased in April 2020, involving 889 patients. The majority of the patients (75.2%) underwent BCS; 328 of 439 patients (74.7%) in the standard treatment arm, and 333 of 440 patients (75.7%) in the experimental treatment arm. 218 patients (24.8%) underwent mastectomy. SLN status at randomization was comparable between the two groups of treatment, with a median number of two SLNs removed and a median number of one positive SLN in both arms. The median number of non-SLNs identified at definitive histopathological evaluation was 16 (interquartile range [IQR] 12–21) in the ALND group. Overall, 193 of 439 patients (44.0%) in the standard treatment arm had additional macrometastases in the removed axillary lymph nodes. However, the median number of positive non SLNs was 0 (IQR 0–1) in the ALND group. Median follow-up was 34.0 months. There were eight deaths (ALND, 4; SNLB only, 4), with a 5-year cumulative mortality of 5.8% and 2.1% in the standard and experimental arm, respectively ($p = 0.984$). There were 26 recurrences (ALND 11; SNLB only, 15), with a 5-year cumulative incidence of recurrence of 6.9% and 3.3% in the standard and experimental arm, respectively ($p = 0.444$). Only one axillary lymph node recurrence was observed in each arm. The 5-year OS rates were 98.9% and 98.8%, in the ALND and SNLB only arm, respectively ($p = 0.936$). Conclusion: The 3-year survival and relapse rates of T1-2 BC patients with 1-2 macrometastatic SLNs treated with SLNB only, and adjuvant therapy, were not inferior to those of patients treated with ALND. These results do not support the use of routine ALND in patients undergoing BCS. However, given the low number of patients treated with mastectomy, there is no certainty that ALND omission can be extended also to this sub-group. In order to collect further evidence regarding the safety of the experimental treatment in patients candidates for mastectomy, the reopening of the enrollment of these patients as part of a single-arm experimental study started in June 2022.

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5:00 PM - 6:15 PM

OT1-07-01

Omission of SLNB in triple-negative and HER2-positive breast cancer patients with radiologic and pathologic complete response in the breast after NAST: a single-arm, prospective surgical trial (EUBREAST-01 trial, GBG 104)

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Background: Currently, axillary surgery for breast cancer is considered a staging procedure that does not seem to influence breast cancer mortality since the risk of developing metastasis depends mainly on the biological behavior of the primary (seed-and-soil model). Based on this, postsurgical therapy should be considered based on biological tumor characteristics. Retrospective data of cancer registry trials showed a strong correlation between breast pathologic complete response (pCR) and nodal pCR depending on intrinsic subtypes. Improvements in systemic treatments for breast cancer have increased the rates of pCR in patients receiving neoadjuvant systemic therapy (NAST), offering the opportunity to decrease, and perhaps eliminate, surgery in patients who have a pCR. Trial design: The EUBREAST network designed a clinical trial (NCT04101851) in which only patients with the highest likelihood of having a pCR after NAST (triple-negative or HER2-positive breast cancer) will be included, and type of surgery will be defined according to the response to NAST rather than on the classical T and N status at presentation. In the ongoing trial, axillary surgery will be eliminated (no axillary sentinel lymph node biopsy [SLNB]) for initially clinical node-negative (cN0) patients with radiologic complete remission (rCR) and a breast pCR (ypT0/ypTis) as determined in the lumpectomy specimen. The trial design is a multicenter single-arm study with a limited number of patients (N=440 as the screening population with an expected 80% pCR-rate) which might give practice-changing results in a short period, sparing the time and the costs of a randomized comparison. Patients will be recruited in European countries (Austria, Germany, Italy, and Spain) over 36 months. Inclusion criteria: -Written informed consent - Histologically confirmed unilateral primary invasive carcinoma of the breast (core biopsy). Multifocal or multicentric tumors are allowed if breast-conserving surgery (BCS) is planned. - Age at diagnosis at least 18 years -imaging techniques with estimated tumor stage between cT1-T3 before NAST -triple-negative (TNBC) or HER2-positive invasive breast cancer -TNBC is defined by: ER-negative (< 10% positive cells in IHC) and PgR-negative (< 10% positive cells in IHC), HER2-negative -clinically and sonographically tumor-free axilla before core biopsy (cN0/iN0) -in cases with cN0 and iN+, a negative core biopsy or fine-needle aspiration biopsy of the sonographically suspected lymph node is required -no evidence for distant metastasis (M0) -standard NAST with rCR -planned BCS with postoperative external whole-breast irradiation (conventional fractionation or hypofractionation) Primary objective: 3-year rate of axillary recurrence-free survival (ARFS) after BCS Statistics: The calculated total case number for per-protocol analysis is N=350, and the expected total number of screened patients is N=440. The assumption for acceptable 3-year ARFS $\geq 98.5\%$ in the experimental arm is based on previous study findings. Timelines: -First patient in: January 2021 -Last patient in: December 2023 - Primary outcome analysis: Q1/2027 Current accrual: In June 2022, 150 patients were recruited in Germany and Italy. Contact: Prof. Dr. Toralf Reimer (eubreast-01@kliniksued-rostock.de), study chair Dr. Oreste D. Gentilini (gentilini.oreste@hsr.it), study co-chair Funding by Else Kroener-Fresenius Foundation, German Society of Senology, University of Rostock (Germany), and San Raffaele Hospital (Milan, Italy)

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OT1-08-01

AXSANA – EUBREAST3: An international prospective multicenter cohort study to evaluate different surgical methods of axillary staging in clinically node-positive breast cancer patients treated with neoadjuvant chemotherapy

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Background The optimal surgical staging procedure of the axilla in patients who convert from a clinically positive (cN+) to a clinically negative node status (ycN0) through neoadjuvant chemotherapy is still controversial. Widely diverse techniques such as full Axillary Lymph Node Dissection (ALND), Targeted Axillary Dissection (TAD), Targeted Lymph Node Biopsy (TLNB) and Sentinel Lymph Node Biopsy (SLNB) alone are given preference in different international guidelines. So far, no comparative data on the oncological outcome or the morbidity of the different procedures are available. Further research is needed to safely de-escalate the extent of axillary surgery in this patient group. **Trial design** The AXSANA study is an international prospective cohort study including cN+ patients converting to ycN0 status and treated with different axillary staging techniques according to the standard at their treating institution. The study was initiated by the EUBREAST network. The trial includes patients with cT1-4c tumors, who present initially with clinically axillary lymph node involvement metastasis scheduled for neoadjuvant chemotherapy. According to an amendment in 2020 the inclusion of patients with highly suspicious nodes without confirmation using a minimally invasive biopsy is allowed. All patients converting to ycN0 status undergo follow-up for 5 years irrespectively of the ypN status. **Primary endpoints:** Invasive disease-free survival, axillary recurrence rate and health-related quality of life (HRQoL). HRQoL are evaluated using four standardized questionnaires (EORTC QLQ-C 30, EORTC QLQ-BR23, Lymph-ICF and SOC 13) at baseline and after 1, 3 and 5 years after surgery. **Secondary endpoints** are the feasibility and performance of different axillary staging techniques (detection rate, number of removed lymph nodes and association with complications, arm morbidity and quality of life, operating time and use of clinical and economic resources); impact of learning curve, and the detailed mapping of surgical and oncological treatment standards in different countries. The impact on different regional treatment strategies (radiotherapy, ALND) in patients with ypN0(i+), ypN1(mi) and ypN1 is assessed. **Current status of the study:** 2347 patients from 247 study sites and 23 countries were enrolled in the study between June 2020 and June 2022. Among 1804 patients with a defined surgical concept 758 women were scheduled for ALND, 722 for TAD, 232 for SLNB, 16 for TLNB and 19 for other procedures. A target lymph node was marked in 1215 patients, most frequently using clips/coils (982, 82.0%), followed by magnetic seeds (100, 8.4%), carbon ink (99, 8.3%), radar marker (21, 1.8%), radioactive seeds (5, 0.4%), and other techniques (8, 0.7%).

Disclosure(s):

Thorsten Kühn, MD, PhD: No financial relationships to disclose

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OT1-09-01

Axillary surgery de-escalation after neoadjuvant chemotherapy in breast cancer patients with initially involved node: the GANEA 3 trial.

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Background : In breast cancer patients, neoadjuvant chemotherapy (NAC) allows to obtain pathological complete response (pCR). In case of initially involved node before NAC, pCR after NAC could make it possible to avoid axillary surgery. The aim of our study was to address parameters to build a tool able to accurately select patients at a high probability of axillary pCR after NAC. Method : GANEA 3 was a French prospective multi institutional cohorts of breast cancer patients with a proven axillary involved node treated with NAC (NCT03630913). Initially involved node was clipped before treatment. Each patient received, before and after NAC, a bilateral mammography, a Magnetic Resonance Imaging (MRI), an axillary sonography. After NAC breast, conservative or radical, and axillary surgery, were performed. Breast surgery allowed to measure breast tumor residual and to perform a Sataloff classification. Targeted axillary detection (TAD) was defined as the combination of the resection of the clipped node and SLN dissection. Axillary clipped node, sentinel lymph node (SLN) and axillary lymph node dissection (ALND) were always performed. ALND allowed to assess the false negative rate (FNR) of axillary clipped node and SLN dissection. A total of 500 included patients is planned to close this still ongoing trial. Results : From January 2019 to March 2022, 405 patients were included from 18 institutions. We present here the results of the 260 first patients, who experienced a complete treatment with NAC courses and post NAC breast and axillary surgery. Among these patients, SBR grade was III in 52%, OR and PR were positive in 59% and 46% respectively, HER2 was overexpressed in 40%, 26% were triple negative and pCR was present in 28%. FNR of the SLN detection was 21.1%, 9% for the clipped node alone and 6% for the TAD. Histopronostic grading, progesteron receptors, HER2 expression, MRI results and Sataloff grading of breast residual tumor were indepently linked with global pCR (breast and axilla) in multivariate analysis. The Area Under the Curve (AUC) model was 0.91 with 82% correctly patients classified. The false negative rate of no pCR classified patients was 14%. Conclusion : Intermediate results of Ganea 3 trial showed that operable breast cancer patients with an initially involved axillary node treated with NAC, showed that TAD allows to reduce the FNR of axillary surgery. Patients with histopronostic grade 3, negative progesteron receptors, HER2 overexpression, a normal MRI after NAC and a breast Sataloff A, have a low risk of axillary tumour residual burden and could be safely spare from any axillary surgery. Large prospective trials are needed to confirm the safety of this surgical de-escalation.

Disclosure(s):

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OT1-09-02

ATNEC: A multicentre, randomized trial investigating whether axillary treatment can be avoided in T1-3N1M0 breast cancer patients with no residual cancer in the axillary lymph nodes after neoadjuvant chemotherapy

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Background: For patients who are node positive at presentation and are found to have a complete nodal tumour response (ypN0) post-neoadjuvant chemotherapy (NACT), we do not yet know whether local axillary therapy can be modified based on the response to NACT. ATNEC addresses whether axillary treatment can be de-escalated, post-surgery, in T1-3N1M0 breast cancer patients who have no residual nodal disease post-NACT. Methods: Design: ATNEC is a phase III, randomized (1:1), multi-centre trial, with embedded economic evaluation. Patients with proven axillary node metastases on needle biopsy receive NACT followed by sentinel node biopsy (SNB). If the sentinel nodes have converted to ypN0, ATNEC randomizes patients to axillary treatment (nodal radiotherapy [ART] or axillary nodal clearance [ANC]) vs. no further axillary treatment. Stratification: Institution, type of surgery (breast conserving surgery vs mastectomy), receptor status (triple negative vs HER2 positive vs ER positive and/or PR positive and HER2 negative). Inclusion criteria: • Age \geq 18 • Male or female • T1-3N1M0 breast cancer at diagnosis (pre-NACT) • FNA or core biopsy confirmed axillary nodal metastases at presentation • ER and HER2 status evaluated on primary tumour • Received standard NACT as per local guidelines • Imaging of the axilla to assess response to NACT • Dual tracer SNB post-NACT and at least 3 nodes removed (sentinel nodes and marked node).
o If a single tracer is used, the patient is eligible if the involved node is marked pre-NACT and at least 3 nodes removed (including the marked node)
o If axillary node sampling is performed following failed localization of sentinel nodes, patient is eligible if at least 3 nodes removed (including the marked node).
o If node is not marked, or marked node is not removed, patient is eligible if the histology report shows evidence of down-staging with complete pathological response in at least one node of the 3 removed nodes. • No evidence of nodal metastases post-NACT (ypN0) Exclusion criteria: • Bilateral invasive breast cancer • SNB prior to NACT • Previous ipsilateral axillary nodal surgery • Previous cancer within last 5 years or concomitant malignancy Aims: To assess whether omitting further axillary treatment (ART or ANC) for patients with early stage breast cancer and axillary nodal metastases on needle biopsy - who post NACT have no residual nodal disease on SNB (ypN0) - is non-inferior to axillary treatment in terms of disease-free survival, and whether lymphoedema is reduced at 5 years. Statistical methods: All analyses will be carried out on an intention-to-treat basis to preserve randomization, avoid bias from exclusions and preserve statistical power. Radiotherapy Quality Assurance: ATNEC has in-built radiotherapy QA coordinated by National Radiotherapy Trials QA (RTTQA) group. The RTQA monitors trial protocol compliance ensuring clinical outcomes reflect differences in randomization schedules rather than departures from the protocol. ATNEC is the only trial in the UK that offers QA for IMC radiotherapy. Screening Data: ATNEC collects screening data to monitor acceptance rates and reasons why patients decline the trial to identify ways to improve recruitment. Screening data until 30-Jun-22 shows that 69% of eligible patients were approached (244/354) and, of those approached, 45% were consented (109/244). For the 81 patients who declined, the most common reasons were; preference for axillary treatment (31%), preference for no axillary treatment (10%), no reason documented (23%) and ineligibility (21%). ClinicalTrials.gov: NCT04109079 Target accrual: 1900 Target sites: 100 Trial Status: Recruiting. As of 30-Jun-22: 52 sites open, 158 patients enrolled, 54 randomised. ATNEC is open to new sites and international collaboration.

Disclosure(s):

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12/6/2022

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OT1-10-01

Treatment with Tucatinib in addition to Pertuzumab and Trastuzumab in patients with HER2-positive metastatic breast cancer (HER2+ MBC) after local therapy of isolated brain progression: InTTercePT, a UCBG/GINECO study.

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Treatment with Tucatinib in addition to Pertuzumab and Trastuzumab in patients with HER2-positive metastatic breast cancer (HER2+ MBC) after local therapy of isolated brain progression: InTTercePT, a UCBG/GINECO study. Background HER2+ MBC patient on first line treatment with pertuzumab and trastuzumab have a 13% risk of developing brain metastasis (BM) as the first site of progression. For such patient with isolated brain progression, guidelines recommend to use central nervous system (CNS) directed therapy whenever possible (stereotactic radiosurgery or surgery or both). These patients will have a higher risk of subsequent brain and systemic progression after local treatment. Therefore, whether systemic treatment should be continued or changed remains an open question. The tyrosine kinase inhibitor tucatinib is an orally bioavailable HER2 inhibitor with validated antineoplastic activity and the ability to cross the blood brain barrier. The randomized HER2CLIMB study, demonstrated that adding tucatinib to trastuzumab/capecitabine improved both progression-free survival (PFS) and overall survival (OS) among HER2+ MBC patients previously treated with trastuzumab, pertuzumab and T-DM1. Particularly, this regimen demonstrated improved antitumor activity in patients with BM, in terms of CNS-PFS and OS. Exploratory analysis of HER2CLIMB and in a phase 1b study, showed patients who continued systemic treatment with tucatinib (in combination either with trastuzumab/capecitabine or TDM-1) after CNS-directed treatment had a better outcome compared with those that discontinued systemic tucatinib-based treatment. These results suggest that for patient in the first line metastatic setting who experience isolated brain progression, adding tucatinib to the trastuzumab/pertuzumab regimen could help control BM, improve PFS, OS and patients' quality of life. Trial design InTTercePT is an open-label, single-arm, national, multicentric, phase II trial assessing the combination of tucatinib, pertuzumab and trastuzumab. Tucatinib will be administered orally twice daily at 300 mg. Pertuzumab and trastuzumab will be administered at the initial dose of 840 mg and 8 mg/kg respectively following by a maintenance dose of 420 mg and 6mg/kg respectively, 3-weekly. If indicated, hormone therapy is allowed in combination with HER2-directed therapy. Eligibility criteria include HER2+ MBC with isolated brain progression (new or progressive BM with stable or responding systemic disease) under pertuzumab/trastuzumab treatment (\pm taxane) after complete local treatment (surgery and/or radiation therapy). There is no limit to the number and size of BM. Specific aims To evaluate the efficacy, in terms of PFS rate (RECIST v1.1) of tucatinib in combination with pertuzumab/trastuzumab. Secondary endpoints include OS, brain PFS (RECIST v1.1) and BM response in patient not in complete remission at the brain level after local treatment and safety (NCI-CTCAE v5.0). Statistical methods Given the lack of safety data from this association, two interim safety analysis are planned: after 10 and 20 patients having received at least one dose of the treatments combination during at least one cycle. The number of patients to be included was calculated using Fleming's single-stage procedure for phase II trials. The sample size calculation was based on a minimum success (non-progression rate at 6 months) considered of interest of $p_1 = 75\%$ and an uninteresting rate of $p_0 = 60\%$. Assuming a unilateral type I error alpha of 10% and a power of 85%, 52 patients are needed. Considering 5% of the patients may be non-evaluable, 55 patients will be included. At the time of analysis, if at least 37 successes are observed, the treatment will be considered as interesting for further investigation. The study is recruiting. By July 1, 2022, 10 patients have been screened and 8 treated (NCT05041842). Funding SeaGen Contact information thomas.bachelot@lyon.unicancer.fr

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OT1-10-02

Trial of Neratinib Plus Capecitabine in Subjects With HER2-Negative Metastatic Breast Cancer With Brain Metastases and Abnormally Active HER2 Signaling

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Background: Development of brain metastasis (BM) portends poor prognosis in patients (pts) with metastatic breast cancer (MBC) mainly due to lack of systemic therapy with strong activity in CNS. While survival in HER2+ BC BMs has improved due to development of various HER2 therapies with activity against BM, outcome for HER2- BC BMs remains dismal. A novel assay (CELsignia) which measures underlying HER2 signal (HS) of live cancer cells in response to HER2 agonists & antagonists showed that about 25% of BC deemed HER2- by standard methods have underlying abnormal HS. Preclinical data showed various HER2 therapies inhibit tumor growth of such HER2- BC with abnormal HS. Among tested HER2 inhibitors with known CNS activity, neratinib had the lowest IC50. We propose a trial which identifies HER2- BC BM pts with abnormal HS & assesses activity of neratinib based therapy. Design: This is a phase II single arm study with 2 steps- step 0 (biopsy) & step 1 (treatment). Pts eligible for Step 0 will be registered as "Immediate Treatment (IT)" (intent to register to Step 1 immediately) or "Future Treatment" [registration can be delayed up to 28 weeks (wks)] & undergo biopsy of most accessible extra CNS (eCNS) tumor. Tumor will be sent for CELsignia testing (2 wks turn around). Additional biopsies may be obtained for standard of care (SOC). IT pts can be treated

with a brief course of capecitabine 1gm/m² BID for 1 wk followed by 1 wk off while waiting for CELSigia result. Pts with BC having abnormal HS will be screened & registered to step 1. Enrolled pts will receive neratinib 240mg daily (with SOC anti-diarrheal prophylaxis) + capecitabine 750mg/m² BID for 2 wks in every 3 wks cycle (C). Tumor assessments will be done prior to C3, 5 & 7 then every 12 wks with MRI brain, CT chest abdomen pelvis & bone scan using RECIST1.1 (eCNS disease) and a modified BM RANO criteria (>5mm, measurable disease, CNS). In isolated CNS progression, investigators have option of treatment beyond progression after SOC local treatment of progressing BMs. Key Eligibility Criteria: Step 0: Inclusion Criteria (IC): histologically confirmed HER2- BC (primary or metastatic); has radiological evidence of BM; prior treatment with CDK4/6 inhibitor + endocrine therapy required for hormone receptor+ BC, no prior specific treatment required for triple negative BC; radiological evidence of eCNS measurable disease (RECIST1.1) accessible for biopsy. Exclusion Criteria (EC): prior use of capecitabine in metastatic setting; known/suspected leptomeningeal disease. Step 1: IC: Abnormal HS; New or progressing BM that is measurable (>5mm); minimum washout periods in wks: last chemotherapy 2, hormonal therapy 1 except fulvestrant 4, targeted therapies 3, eCNS radiation 1, any investigational treatment 4. ECOG performance status 0-2; adequate end organ functions. EC: whole brain radiation in last 3 months (m). Endpoints: Co-primary: Overall survival (OS) and CNS progression free survival (CNS PFS). Key Secondary: Objective response rate, clinical benefit rate and duration of response (CNS using BM RANO, eCNS using RECIST1.1), eCNS PFS, various feasibility endpoints. Safety. Statistical methods: To detect 70% improvement in this trial in CNS PFS and OS compared to historical control (BEACON trial BM subset) 2.7m vs. 4.6m and 4.8m vs. 8.2 m with 80% power and 1-sided 5% significance level, a sample size of 22 is required. About 88 patients will undergo biopsy to enroll 22 pts in step 1. One fertility assessment is planned when the first 12 pts have been treated for at least 6 wks or have failed (died or progressed) prior to 6 wks. If 9 or more in the first 12 have died or progressed by 6 wks of treatment, the study will close for fertility. PFS and OS will be analyzed using Kaplan-Meier survival functions. Contact: Ajay Dhakal MBBS, ajay_dhakal@urmc.rochester.edu NCT#: NCT04965064 Funding: Celcuity, Puma Biotechnology Status: IRB approved. Anticipated activation Aug 2022, Accrual duration: 2 years. Seeking participating sites.

Disclosure(s):

Ajay Dhakal, M.B.B.S.: Celcuity: Contracted Research (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); MJH Sciences: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Puma: Contracted Research (Ongoing)
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OT1-11-01

Phase II study of talazoparib, a PARP inhibitor, in somatic BRCA1/2 mutant metastatic breast cancer identified by cell-free DNA or tumor tissue genotyping

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Background: PARP inhibitors are currently approved for the treatment of germline BRCA1/2 mutant metastatic breast cancer (MBC), which accounts for 5-10% of breast cancer. We hypothesize that a PARP inhibitor may also have efficacy in somatic BRCA1/2 mutant MBC, expanding the potential clinical applicability of PARP inhibitors. We previously demonstrated that somatic BRCA1/2 mutations can be identified by both cell-free DNA and tumor tissue genotyping in a subset of patients with MBC who are not germline BRCA1/2 carriers. Furthermore, a PARP inhibitor was demonstrated to induce cell growth inhibition in a circulating tumor cell culture model generated from a patient with pathogenic somatic BRCA1 mutant MBC (Vidula, Dubash, CCR, 2020). In this trial, we are evaluating the efficacy of a PARP inhibitor in somatic BRCA1/2 mutant MBC. Trial Design: This phase II investigator-initiated clinical trial is enrolling 30 patients with somatic BRCA1/2 mutant MBC identified via cell-free DNA or tumor tissue genotyping. Patients are treated with talazoparib, a PARP inhibitor, until disease progression. At baseline and every 3 months, patients undergo CT chest, abdomen, and pelvis, and a bone scan for disease assessment. Patients undergo blood collection at baseline for the Cancer Risk B (CR-B) assay, a novel flow variant assay to assess double-strand break repair mutations in circulating blood cells (Syeda, 2017) and monthly blood collection for cell-free DNA analysis to evaluate changes in the genomic environment. Eligibility Criteria: Patients with MBC with a pathogenic somatic BRCA1/2 mutation identified by cell-free DNA or tumor tissue genotyping are eligible. Both patients with triple-negative breast cancer (≥ 1 prior chemotherapy) or hormone receptor positive/HER2- MBC (≥ 1 prior hormone therapy) are eligible. Patients should not be known germline BRCA1/2 carriers. There is no limit on prior therapies including receipt of a prior platinum (in the absence of disease progression on prior platinum). A prior PARP inhibitor is not allowed. Adequate performance status and organ function are needed. Specific Aims: Primary aim is progression-free survival (PFS) assessed by RECIST 1.1. Secondary aims include objective response rate and toxicity assessed by NCI CTCAE v 5.0. Exploratory aims include assessing impact of BRCA1/2 reversion mutations in cell-free DNA, studying serial changes in BRCA1/2 mutant allelic frequency in cell-free DNA, comparing pre- and post-treatment cell-free DNA results to identify changes in the genomic environment, assessing the CR-B assay positivity rate, and correlating these biomarker analyses with patient response. Statistical Methods: This study uses a two-stage design with 80% power to demonstrate that talazoparib is associated with "success" (PFS > 12 weeks) in 53% patients (4% alpha). Accrual: This study (NCT03990896) is open at Massachusetts General Hospital, MD Anderson, University of California San Francisco, and Emory, with pending activation at Northwestern, Cornell, and Vanderbilt. Five patients are enrolled as of 7/2022. Funding: This study is supported by a Pfizer ASPIRE award and Conquer Cancer Foundation of ASCO–Breast Cancer Research Foundation- Career Development Award. Contact information: Neelima Vidula, MD, Massachusetts General Hospital, nvidula@mgh.harvard.edu

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OT1-12-01

A phase III trial evaluating De-escalation of Breast Radiation (DEBRA) following breast-conserving surgery (BCS) of stage 1, HR+, HER2-, RS ≤18 breast cancer: NRG-BR007

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BACKGROUND: Approximately 50% of newly diagnosed breast cancers are stage 1, with the majority being ER/PR-positive, HER2-negative. Genomic assays such as Oncotype DX® have identified pts with reduced distant metastasis and without benefit from chemotherapy, freeing patients from excess toxicity. Also, these genomic assays are prognostic of local-regional recurrence (LRR). The de-escalation of therapy is of interest to pts, providers, and payers. Low risk, as identified by Oncotype and MammaPrint®, is associated with low LRR after BCS and breast radiotherapy (RT). **METHODS:** We hypothesize that BCS alone is non-inferior to BCS plus RT for ipsilateral breast recurrence (IBR) and breast preservation in women intending appropriate endocrine therapy (ET) for stage 1 (ER and/or PR positive, HER2-negative, with an Oncotype DX Recurrence Score [RS] of ≤18) breast cancer. Stratification is by age (< 60; ≥60), tumor size (≤1 cm; >1-2cm), and RS (< 11; 11-18). Pts are randomized post-BCS to Arm 1 with breast RT using standard methods (hypo- or conventional-fractionated whole breast RT with or without boost, APBI) plus 5 years of ET (tamoxifen or AI) or Arm 2 with 5 years of ET (tamoxifen or AI) alone. The specific regimen of ET in both arms is at the treating physician's discretion. Eligible pts are stage 1: pT1 (≤2 cm), pN0, age ≥50 to < 70 years, s/p BCS with

negative margins (no ink on tumor), s/p axillary nodal staging (SNB or ALND), ER and/or PR positive (ASCO/CAP), HER2-negative (ASCO/CAP), and have an Oncotype DX RS of ≤ 18 (diagnostic core biopsy or resected specimen). Primary endpoint is IBR. Secondary endpoints are breast conservation rate, invasive in-breast recurrence, recurrence-free interval, distant disease-free survival, overall survival, patient-reported breast pain, patient-reported worry about recurrence, and adherence to ET. We assume a clinically acceptable difference in IBR of 4% at 10 years to judge omission of RT as non-inferior (10-year event-free survival for RT group is 95.6% versus 91.6% for the omission-of-RT group). The study is designed to be able to detect non-inferiority with 80% power and a one-sided $\alpha=0.025$, and assuming that there would be a ramp-up in accrual in the first two years of the study (leveling off in Years 3-5), 1,670 (835 per arm) patients are required to be randomized. Conservative loss to follow-up is 1% per year. Some of the T1a pts screened will have Oncotype DX scores >18 , making them ineligible for the study. In the accrual process, pts will be required to register (1,714 patients) to ensure that our final randomized cohort is 1,670 pts. Accrual as of 6-30-2022 is 169 screened and 147 randomized. Contact information: Protocol: CTSU member website: <https://www.ctsu.org>. NRG Oncology Pgh Clinical Coordinating Dpt: 1-800-477-7227 or ccdPGH@NRGOncology.org. Support: U10CA180868, -180822, UG1CA189867. NCT04852887.

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OT1-12-02

Preliminary report of the PRECISION Trial (Profiling Early Breast Cancer for Radiotherapy Omission): A Phase II Study of Breast-Conserving Surgery Without Adjuvant Radiotherapy for Favorable-Risk Breast Cancer

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Background: Breast conserving surgery (BCS) is typically followed by adjuvant radiotherapy (RT) based on several landmark trials demonstrating improvements in disease control and survival. Since completion of these historical trials, the advent of molecular subtyping has revealed that breast cancer is not a single disease entity, but rather a class of cancers with differential risk profiles. We evaluated whether RT could be safely omitted following BCS for patients with the most favorable subtype as defined by the Prosigna PAM50 assay. Methods: We conducted a multicenter prospective single-arm cohort study with IRB approval and an FDA investigational device exemption (IDE). Eligible patients were women 50 to 75 years of age (inclusive) who had undergone BCS revealing tumors ≤ 2 cm in size, that were estrogen or progesterone receptor positive (HR+), HER2 negative, grade 1-2, node negative (N0), with negative excision margins (no ink on tumor). Intent to take endocrine therapy was required. Upon registration, tumors were submitted for central Prosigna testing and those with Risk of Recurrence (ROR) score ≤ 40 were deemed eligible for the investigational omission of RT. The primary endpoint was the 5-year locoregional recurrence rate (LRR). Anticipating a total of 345 RT-omitting patients to enroll over 3.5 years, the study was designed with 90% power to exclude a 5-year LRR of 5% using a one-sample exponential test with one-sided type I error of 0.025. Results: From 2016 to 2020, 671 patients were registered from 13 centers, inclusive of affiliated regional network sites. Of these, 382 patients had a ROR Score ≤ 40 and opted to forego RT, comprising the main intention-to-treat (ITT) study population. Median age was 65 years (range 50 to 75), and median tumor size was 0.9 cm (range 0.1 to 2.0 cm). At a median follow-up of 26.9 months, 12 events were observed: 4 patients had ipsilateral in-breast recurrences, 7 had contralateral breast cancers, and 1 developed an unrelated melanoma. There were no regional-nodal or distant recurrences. The 2-year cumulative rate of LRR was 0.3% (95% CI: 0 – 1.0%). Of the 4 ipsilateral breast recurrences, 2 were in the same quadrant as the original primary tumor. Conclusion: In this preliminary report of the PRECISION trial, patients 50-75 years of age undergoing BCS and endocrine therapy for pT1N0 HR+ HER2-negative breast cancer with ROR score ≤ 40 had exceedingly low rates of LRR in the absence of adjuvant RT at a median follow-up of 26.9 months. Additional follow-up is required to determine whether these favorable results are durable.

Disclosure(s):

Lior Z. Braunstein, MD: No financial relationships to disclose

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12/6/2022

5:00 PM - 6:15 PM

OT1-12-03

Precision breast conserving surgery with the guidance of localization combined with multidetector CT 3-dimensional image reconstruction: a single center, prospective, cohort study

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Introduction: Precision breast conserving surgery (PBCS) requires doctors to precisely remove the tumor while preserving as much normal tissue as possible. The aims of this study were to determine whether wire-guided localization (WGL) combined with multidetector CT (MDCT) guided 3D reconstruction could guide PBCS.

Methods: From 2020 to 2022, 31 patients with unifocal breast cancer were enrolled for PBCS guided by WGL combined with MDCT guided 3D reconstruction. Surrounding WGL was performed under local anesthesia, followed by an immediate contrast enhanced MDCT scan. PBCS guided by MDCT guided 3D reconstruction was performed one day after the localization. Women who underwent palpation guided BCS were included as control, and logistic regression analysis was applied.

Results: PBCS were performed in 31 patients. The mean tumor size in US was 19.48±5.86mm (9-32mm). Compare with control group, a smaller specimen diameter was observed in PBCS group (P=0.005), and the rate of the largest margin greater than or equal to 20mm were significantly lower (P=0.004). The operation time of PBCS was shortened (P=0.046). Moreover, PBCS does not affect the reoperation rate (P=0.514) or the rate of positive margins (P=0.660). Conclusion: For patients with unifocal breast cancer, WGL combined with MDCT guided 3D reconstruction could guide PBCS without affecting the safety.

Table 1 Baseline characteristics of patients in PBCS_group and control group.

Variables	PBCS, N (%)	Control, N (%)	P value
Number	31	61	
Age, y			0.332
≤50	15 (48.4)	36 (59.0)	
>50	16 (51.6)	25 (41.0)	
Menstrual status			0.821
Premenopausal	16 (51.6)	33 (54.1)	
Postmenopausal	15 (48.4)	28 (45.9)	
BMI, kg/m ²			0.796
≤24	20 (64.5)	41 (67.2)	
>24	11 (35.5)	20 (32.8)	
Tumor side			0.161
Left	21 (67.7)	32 (52.5)	
Right	10 (32.3)	29 (47.5)	
Tumor location			0.641
Lateral-superior	16 (51.6)	26 (42.6)	
Lateral-inferior	5 (16.1)	10 (16.4)	
Interior-inferior	5 (16.1)	8 (13.1)	
Interior-superior	5 (16.1)	17 (27.9)	
Tumor size in US, mm			0.113
≤20	16 (51.6)	39 (63.9)	
>20	15 (48.4)	22 (36.1)	
Operation method			0.810
Sentinel lymph node biopsy	27 (87.1)	52 (85.2)	
Axillary lymph node dissection	4 (12.9)	9 (14.8)	
Node status			0.524
Negative	22 (71.0)	47 (77.0)	
Positive	9 (29.0)	14 (23.0)	
Molecular subtype			0.616
HR positive and HER2 negative	17 (54.8)	35 (57.4)	
Her2 positive	7 (22.6)	17 (27.9)	
Triple negative	7 (22.6)	9 (14.8)	

BMI, body mass index; US, ultrasound; HR, hormone receptor.

Table 2 Surgical outcomes of patients in PBCS group and control group.

Variables	PBCS, N (%)	Control, N(%)	P value	Odds ratio (95%CI)
Specimen diameter, mm				
>50	16 (51.6)	49 (80.3)		
≤50	15 (48.4)	12 (19.7)	0.005	3.828 (1.487-9.858)
Positive margins				
Yes	4 (12.9)	10 (16.4)		
No	27 (87.1)	51 (83.6)	0.660	1.324 (0.379-4.619)
Tumor diameter, mm				
>20	13 (41.9)	23 (37.7)		
≤20	18 (58.1)	38 (62.3)	0.694	0.838 (0.347-2.023)
Largest margin, mm				
≥20	13 (41.9)	45 (73.8)		
<20	18 (58.1)	16 (26.2)	0.004	3.894 (1.562-9.708)
Summation of margins, mm				
≤40	14 (45.2)	12 (19.7)	--	--
>40 和 ≤80	16 (51.6)	41 (67.2)	0.026	0.334 (0.128-0.877)
>80	1 (3.2)	8 (13.1)	0.048	0.107 (0.012-0.984)
Reoperation				
Yes	1 (3.2)	4 (6.6)		
No	30 (96.8)	57 (93.4)	0.514	2.105 (0.225-19.686)
Operation time, min				
>90	7 (22.6)	27 (44.3)		
≤90	24 (77.4)	34 (55.7)	0.046	2.723 (1.020-7.268)

Disclosure(s):

Yiqin Xia, MD student: No financial relationships to disclose
Da Cao, Postgraduate: No financial relationships to disclose
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12/6/2022

5:00 PM - 6:15 PM

OT1-12-04

MRO PMS study - Intraoperative Specimen Magnetic Resonance Imaging System for Intraoperative Margin Assessment for Invasive Breast Cancer Using the ClearCoast™ System in Breast Conserving Surgery

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Background Re-operation for involved margins in breast conserving surgery is associated with worse cosmetic outcome, increased medical costs, and patient anxiety. Therefore, obtaining negative margins during primary BCS is essential. In our prior non-interventional study, published in October 2021 (Thill M et al., J Surg Oncol 2021) the re-operation rate would have been reduced by 83% for invasive carcinoma, from 10% to 2%, and 50% for DCIS, from 30% to 15% re-operations, if results had not been blinded for the surgeon. The results suggested a potential reduction of the re-operation rate by up to 80% for patients undergoing BCS. Aim of the study Aim of our current study is to evaluate the interventional performance of the ClearCoast™ system (ClearCut Medical, Ltd.) in assessing surgical margins for IBC in breast conserving surgery (BCS) and reducing the re-excision rates. Material and Methods The ClearCoast™ system utilizes a diffusion-weighted-imaging (DWI) protocol to create 2D surface maps showing T2*, a MR parameter related to the tissue's apparent diffusion coefficient (ADC), with a depth penetration of 1mm. ADC is a highly accurate differentiator for irregular versus normal tissue. From May 2021 till to date a prospective, non- blinded post marketing study (N=93), evaluating the performance of the ClearCoast™ system is currently ongoing in the Breast Centre at the AGAPLESION MARKUS KRANKENHAUS, Frankfurt, Germany. After standard evaluation with ultrasound and/or X-ray with or without wire or clip marking, the specimens are intraoperatively scanned with the ClearCoast™ system, and positive margins will lead to a direct re-resection by decision of the surgeon applying a simple T2* threshold to

flag irregular tissue. The final histopathology results will be compared with the scan results on a margin per margin bases. In addition, the rates of recurrent surgery of the interventional group will be compared with those of a historical group on the bases of matched pairs. Primary endpoint of the study is the re-excision rates in both the interventional and the historical standard of care group. To date, 64 patients are enrolled in the trial, therefore, results of the trial may be presented at the SABCS 2022.

Disclosure(s):

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12/6/2022

5:00 PM - 6:15 PM

OT1-13-01

BIOSYM - A Feasibility Randomised Controlled Trial Comparing Biological Matrices with Synthetic Meshes in Women Undergoing One Stage Implant Based Breast Reconstruction. ClinicalTrials.gov Identifier: NCT05449691

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Research question: Is it feasible to conduct a multicentre randomised controlled trial (RCT) to test the long-term efficacy and safety of biological matrices compared with synthetic meshes in women undergoing one-stage mesh and implant breast reconstruction as standard care. Background: The use of biological and synthetic meshes in implant-based breast reconstruction has become standard care and is the most widely used procedure in the UK. However, there is limited evidence on patient outcomes and how safe each type of mesh is in the long-term to guide patient choices and surgeon decision-making. Aims: To assess patient and clinician acceptance, recruitment rate, and compliance with randomly allocated intervention. We will evaluate completeness of data on proposed future main study outcomes. The standard deviation (SD) of patient reported 'satisfaction with breasts' score on Breast Q will inform sample size calculations for the main study. To inform economic evaluation of main study, we will evaluate completeness of EQ-5D-5L and recommendation of an alternative preference-based QoL measure to be used in a definitive trial. Methods: Design: Pragmatic, feasibility, randomised controlled trial. Target population: Women undergoing mastectomy for breast cancer or risk reduction and immediate one-stage breast reconstruction using implant and mesh as standard care. Randomisation: Women will be randomised to biological matrix or synthetic mesh in a 1:1 ratio. Measurement of outcomes Complications: such as infection, wound breakdown, readmission, reoperation, unplanned surgery, skin flap necrosis, implant loss, seroma, pain, capsular contracture and haematoma will be recorded at 3- and 6-months post-surgery. Patient reported outcomes: Women will complete Breast Q and EQ-5D-5L questionnaires at randomisation, 3- and 6-months post-surgery. Sample size: By recruiting 60 (out of 120) we will be able to estimate a participation rate of 50% of women offered the trial to within a 95% confidence interval of +/-9% and a completion rate of 90% (54 of 60) within a 95% confidence interval of (80%, 95%). Additionally, 60 participants will be enough to estimate the SD for sample size calculation for the main study. Timelines for delivery: Recruitment start date:

01 September 2022. Anticipated Impact and Dissemination: The BIOSYM research question has been identified as a key research gap by Association of Breast Surgery (UK). If we can demonstrate feasibility, the definitive trial will provide high quality long-term data on patient outcomes and safety of each type of mesh. Results will be published in peer-reviewed high impact journals and, with PPI partners we will produce patient-facing summaries for a lay audience. The results will inform specialist and NICE guidelines.

Disclosure(s):

Amit Goyal, n/a: No financial relationships to disclose

Emanuele Garreffa, n/a: No financial relationships to disclose

Robert Newcombe, n/a: No financial relationships to disclose

Helena Harder, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

OT1-14-01

Efficiency and safety of palbociclib in patients with locally advanced or metastatic breast cancer: a multi-center real world study

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Endocrine therapy is the main treatment for premenopausal women with HR+/HER2- breast cancer. Palbociclib is an oral CDK4/6 inhibitor which preclinical evidence that ER+ and HER2-amplified breast cancer cell lines are most sensitive to CDK4/6 inhibition of proliferation and is used in vitro in combination with endocrine therapy showed better tumor suppressive effect. To evaluate the efficacy and safety of palbociclib in patients with locally advanced or metastatic breast cancer, we enrolled females with hormone receptor-positive breast cancer who treat with Palbociclib from July 2018 to March 2022. The study has so far included 267 patients in 4 centers. 32.83% patients were treated in first-line, 31.32% and 38.85% patients in second and third lines. 30.34% patients had hepatic metastasis. 35.47% patients were sensitive to previous endocrine therapy; 18.23% patients had primary resistance to endocrine therapy, while 46.31% patients had secondary resistance to endocrine therapy. The median PFS was 12.67 months (95% CI 11.51-13.92), and Median overall survival (OS) was not reached. Among all patients, the overall response rate (ORR) was 25.84%, and the disease control rate (DCR) was 78.62%. The main adverse events related to treatment were neutropenia (91.38%), white blood cell decreased (90.09%), anemia (43.78%), and thrombocytopenia (37.93%). The most common grade 3/4 adverse event was neutropenia (55.61%). 11.99% of patients had dose reductions. More patients still needed for further analyze.

Disclosure(s):

Yongmei Yin, MD: No financial relationships to disclose

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Wei Li, n/a: No financial relationships to disclose

Xinyu Wu, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

OT1-15-01

SWOG 1904: Cluster-randomized controlled trial of patient and provider decision support to increase chemoprevention informed choice among women with atypical hyperplasia or lobular carcinoma in situ (MiCHOICE)

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Background: Despite evidence of substantial breast cancer risk reduction, few high-risk women adopt chemopreventive medications such as selective estrogen receptor modulators (SERMs) or aromatase inhibitors (AIs). Women with benign breast disease, such as atypical hyperplasia (AH) or lobular carcinoma in situ (LCIS), have an increased risk of developing breast cancer and derive a greater benefit from antiestrogens compared to other high-risk women. Reasons for low uptake of chemoprevention include insufficient patient and clinician knowledge about antiestrogens, time constraints during the clinical encounter, and concerns about side effects. To address these barriers, we have developed patient and provider web-based decision support tools to improve informed choice about breast cancer chemoprevention among women with AH or LCIS. Study design: We are conducting a cluster-randomized controlled trial of clinical decision support to improve chemoprevention informed choice among women with AH or LCIS and their treating providers. Twenty-six U.S. sites through the SWOG Cancer Research Network were randomly assigned 1:1 to standard educational materials alone or in combination with the patient-centered decision aid (RealRisks) and provider decision support tool (BNAV). A total of 415 patients and 200 healthcare providers will be recruited from these sites. RealRisks consists of interactive modules to calculate personalized breast cancer risk and elicit preferences on chemoprevention. The modules are available in English and Spanish. BNAV is

comprised of self-directed case-based learning modules on breast cancer risk assessment and chemoprevention. Patients complete questionnaires at baseline, 6 and 12 months. Providers complete surveys at baseline and after their enrolled patient's 6-month clinical encounter. The primary endpoint is chemoprevention informed choice at 6 months, using a measure combining knowledge, attitude, and intention scales. Secondary endpoints include perceived breast cancer risk/worry, chemoprevention knowledge/intention, decision conflict/regret, shared decision-making, and chemoprevention uptake. For patients who begin chemoprevention, adherence and reasons for discontinuation are assessed annually for up to 5 years. Barriers and facilitators to implementing RealRisks and BNAV into clinic workflow will be assessed by conducting patient and provider interviews at baseline and mid-implementation. Eligibility criteria: Eligible patients include women, age 35-74 years, with AH or LCIS, no history of breast cancer, no prior use of SERMs or AIs, no bilateral mastectomies, English or Spanish-speaking, and access to the internet. Eligible providers include breast surgeons, medical oncologists, primary care providers, and physician extenders who see patients with AH or LCIS. Statistical methods: We have 90% power to detect a 15% increase in the frequency of chemoprevention informed choice with a 1-sided 0.025 level test, assuming an intraclass correlation (ICC) of 0.02 to account for clustering, roughly equal accrual at each site, 10% loss to follow-up, and ≤10% event rate in the control arm. Current/target accrual: The trial was activated on 9/1/2020. As of 7/7/2022, all 26 sites have been randomized, 157/200 providers and 184/415 patients have been enrolled. Discussion: Our hybrid effectiveness/implementation study seeks to evaluate the effectiveness of a multi-level intervention in promoting informed decision-making about breast cancer chemoprevention. Study results will provide valuable insights on how the decision support tools are integrated in diverse clinical settings.

Disclosure(s):

Katherine D. Crew, MD, MS: No financial relationships to disclose

Garnet Anderson, n/a: No financial relationships to disclose

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OT1-16-01

Trial In Progress: An Evaluation of FACIT-Fatigue in Patients with Locally Advanced or Metastatic Breast Cancer receiving Treatment with Taxane-based Chemotherapy

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Introduction: Cancer-related fatigue (CRF) is a common symptom in patients with metastatic breast cancer (MBC), who receive taxane-based chemotherapy, and is associated with poor outcomes. Current guidelines recommend regular screening for fatigue from the time of cancer diagnosis, during treatment, and after treatment is completed to identify CRF early, lessen its negative impact on quality of life, and prevent potential treatment interruptions. Fatigue is a subjective symptom and is assessed through patient questionnaires such as the FACIT-Fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue) survey. However, there is currently no gold standard or recommended survey to assess CRF. **Methods:** A prospective, non-interventional, multicenter trial is ongoing to validate the FACIT-Fatigue scale in patients with locally advanced or metastatic breast cancer who are eligible to receive taxane-based chemotherapy. Adult patients who have documented locally advanced or metastatic breast cancer (not amenable to surgical resection), and mild-to-moderate CRF indicated by a score of 1 to 6 on a scale from 0 to 10 (10 being most severe), who are candidates to receive cycle one of taxane chemotherapy will be included. Patients who are unable to take oral medications, have other cancer-related causes of fatigue, are using oral morphine ≥ 60 mg/day, or are participating in another clinical trial will be excluded. The primary objective is to evaluate the change in FACIT-Fatigue scores at baseline and at the end of the study (16 weeks). Secondary endpoints include evaluation of quality-of-life outcomes. A subgroup of patients will participate in a phone-based cognitive interview at the end of study visit or within 2 weeks of this visit to explore fatigue factors deemed important to patients. **Results:** The total planned sample size is estimated to be 60 patients to allow for a minimum clinically important difference (MCID) with a minimum precision of 1.9 points, and standard deviation of 3 points. The qualitative assessment will be conducted as part of a substudy inclusive of data from 30 patients. **Conclusions:** This study is currently ongoing to determine the MCID in FACIT-Fatigue scores in patients with locally advanced or MBC receiving treatment with taxane-based chemotherapy. Contact usmedinfo@dompe.com for information related to clinical trial sites and this study.

Disclosure(s):

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OT1-17-01

Protocol Description of Genetics and Inflammatory Markers to predict Chemotherapy-Induced Peripheral Neuropathy among Early Stage Breast Cancer Patients Receiving Taxane Therapy – GENIE Study

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Background Chemotherapy induced peripheral neuropathy (CIPN) is one of the most common dose-limiting side effects seen among patients with early stage breast cancer and received taxane-containing regimens. The primary clinical manifestation of CIPN is sensory neuropathy such as numbness, tingling and pain in hands and feet, which negatively affect the patient's

quality of life (QoL). Although in most patients, CIPN improves over time, in a subset of patients, it remains a substantial debilitating problem, significantly affecting QoL. To date, there are no effective prevention strategies- or sufficient treatment due to the limited understanding of CIPN pre-disposing factors or pathophysiology. We hypothesize that a multimodal integration of biomarkers with CIPN progression analysis will be required to understand the pathophysiology and to consistently predict patient susceptibility. Further, we hypothesize that this multimodal approach may be leveraged to identify targets for CIPN treatment and/or prevention. This abstract describes the study protocol used to explore this hypothesis. Objective This study is designed to 1) identify genetic, transcriptional, epigenetic, metabolic, inflammatory biomarkers predictive of CIPN development among patients with early stage breast cancer receiving a taxane containing therapy; 2) With these biomarkers, develop an algorithm to identify patients who are at risk of developing CIPN before or during taxane therapy. Methods This is a longitudinal, multicenter, observational study. Patients with early-stage breast cancer who are receiving a taxane-containing (paclitaxel, docetaxel or nab-paclitaxel) treatment regimen, without preexisting peripheral neuropathy are eligible. Estimated enrollment is 400 patients. Demographic and clinical data are collected after patients consent to participate. Molecular data and patient reported outcomes (PRO) are collected prior to initiation of taxane therapy, the 4th, 8th, and 12th week of taxane therapy, and at 3, 6, and 9 months after completion of taxane therapy. Blood samples are collected for molecular data which include genetic, transcriptional, epigenetic (DNA-methylation), and metabolic data. . PRO are assessed using (i) the European Organization for Research and Treatment of Cancer CIPN20 questionnaire, (ii) the Brief Pain Inventory, (iii) the Pain Catastrophizing Scale, and (iv) the PRO Measurement System for anxiety, depression and pain interference. Initial data analysis will characterize the association of biomarkers in each modality (e.g., genetic, epigenetic, etc.) with the presence or absence of CIPN, and machine learning will be used to build candidate biomarker signatures to predict CIPN before and during taxane treatment. Two distinct multi-modal prediction models will be constructed: 1) a pre-treatment model to predict risk of developing CIPN , and 2) an on-treatment model to predict the onset of CIPN. The goal is to develop a parsimonious, clinically translatable model for robust and accurate predictions of taxane-induced CIPN. Trial Status: Active, 135 subjects enrolled. Trial Centers: 1) Cleveland Clinic Foundation (8 regional sites in Ohio and 1 in Florida); 2) Huntsman Cancer Institute, University of Utah Research Funding: National Institute of Neurological Disorder and Stroke. Grant No.: 1R61NS113258-01A1

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COMPARATIVE ANALYSIS BETWEEN ACUPUNCTURE AND EXERCISE IN IMPROVING DERMAL SENSITIVITY DURING PACLITAXEL-CONTAINING CHEMOTHERAPY: A RANDOMIZED CLINICAL TRIAL

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OBJECTIVE: To compare skin sensitivity in patients diagnosed with breast cancer undergoing cycles of chemotherapy with taxanes, applied three different techniques, acupuncture needles, acupuncture with silicon tablets (Stiper) and kinesiotherapy. **DESIGN:** Randomized, controlled, open, parallel clinical trial. **Inclusion criteria:** women undergoing chemotherapy with taxanes from the 1st cycle onwards both neoadjuvant and adjuvant with stages I to III. **Excluded** were women with pre-existing diseases such as cancer in locoregional or distant activity, previous joint pain, rheumatologic diseases, and not undergoing chemotherapy containing Anthracyclines and/or Cisplatin, and those who had acupuncture in another service in the last three. **METHODS:** This study was carried out at the Oncomastology, Outpatient Clinic of the Mastology Discipline of the Gynecology Department of the Federal University of São Paulo (UNIFESP). 102 patients diagnosed with breast cancer. Excluded 39 patients, 63 volunteers were selected and randomized, allocated to three groups (Group S: Stiper n=26, Group A Acupuncture n=18: and Group C: Kinesiotherapy n=19) to undergo treatment once a week for ten consecutive weeks. Signed the Informed Consent Form and agreed to participate in the project (ICF). **INTERVENTION:** Division of the groups, GS - non-invasive acupuncture technique (silicon pads covered with acrylic blanket) are used for stimulation of acupuncture points on the meridians. GA: acupuncture applied the technique with sterile, disposable systemic needles, (measuring 0.25mm x 30mm) for stimulation of the acupuncture points on the meridians. GC Kinesiotherapy, a physiotherapy technique consisting of upper and lower limb exercises and lower limb proprioception training and sensitivity improvement with vibration. GS, GA, performed acupuncture on the acupoints (B11Dazhu, SI14 Jianwaishu, CV12 Zhongwan, GB34 Yanglingquan, SP6 Sanyinjiao, LR3 Taichong), frequency of 1 time per week, for 10 consecutive weeks, duration of 30 minutes per session. To evaluate Sensitivity, the

esthesiometer was used, consisting of microfilaments thickness and the force (in grams) needed to bend the filaments, the colors and values are: green (0.05 g), blue (0.2 g), violet (2.0 g), dark red (4.0 g), orange (10.0 g) and magenta red (300 g). The evaluation of quality of life FACT/GOG-Ntx before and after treatment. RESULTS: The qualitative demographic characteristics of patients at the chemotherapy. Neoadjuvant Chemotherapy was predominantly in the three groups: GS(88.5%), GA(83.3%) and GC(89.5%), $p=0.83$. Cancer type CINE (Non-special Invasive Carcinoma), GS(92.6%), GA (93.8%) and GC (94.4%), $p=0.58$. Diabetes Mellitus GS(84.6%), GA(77.8%) and GC(79.8%), $p=0.82$ and Systemic Hypertension GS(72%), GA(72.2%) and GC(52.6%), $p=0.32$. The C6D upper limb skin sensitivity assessment ($p < 0.04$ intergroup GS, GA and GC). T1D ($p < 0.03$ intergroup GS, GA and GC), corresponds to the forearm region. FACT/GOG-Ntx quality of life questionnaire in the domains (PWB, FWB and TaxS), Taxane Trial Outcome Index (TOI) comparing 1st session with 10th session $p < 0.02$, TaxS (Evaluates Symptoms of Chemotherapy Induced Peripheral Neuropathy) comparing 1st session with 10th session $p < 0.03$. Taxane total score) comparing 1st session with 10th session, $p < 0.03$. CONCLUSION: The C6 right hand and T1 right forearm sensitivity changes showed improvement in skin sensitivity after the intragroup intervention. FACT/GOG-Ntx questionnaire showed worsening of symptoms, physical, functional and peripheral neuropathy symptoms induced by chemotherapy compared to before and after. The cutaneous sensitivity of hands and feet remained stable and improved in the upper limbs, but chemotherapy had a negative impact on the quality of life, requiring further studies to evaluate the neuropathy of these patients. Keywords: Acupuncture, Chemotherapy, Quality of Life, Integrative and Complementary Practices. Table 1. Characteristics of skin sensitivity between groups Table 1. Characteristics of skin sensitivity between groups

Disclosure(s):

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A Single Arm Phase 2 Study of Peri-Operative Checkpoint-Mediated Immune Therapy and Cryoablation in Women with Hormone Receptor-Negative, HER2-Negative Early Stage/Resectable Breast Cancer

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Background: Local tumor destruction with cryoablation (cryo) induces inflammation and releases antigens that can activate tumor-specific immune responses. Pre-clinically, cryo with immune checkpoint inhibition (ICI)-augmented tumor-specific immune responses and prevented recurrence. Clinically, we established that peri-operative (peri-op) cryo with ipilimumab (ipi) +/- nivolumab (nivo) was not only safe in patients (pts) with operable, early stage breast cancer (ESBC) but also generated robust intra-tumoral and systemic immune responses. In this phase 2 study, we evaluate the disease specific impact of peri-op ICI in women with residual triple negative breast cancer (TNBC) after neoadjuvant chemotherapy (NAC), a subset at high risk of early relapse. Methods: Eligible pts are ≥ 18 y, with ER < 10%, PR < 10%, HER2 negative (per ASCO/CAP definition), ≥ 1.0 cm, residual operable disease after taxane-based NAC. Approximately 80 pts will be enrolled and treated with ipi/nivo/cryo followed by breast surgery and adjuvant nivo across multiple institutions. Pts undergo percutaneous, image-guided cryo with concurrent research core biopsy 7-10 days prior to surgery and will receive ipi (1mg/kg IV) with nivo (240mg IV) 1 to 5 days prior to cryo. After surgery, pts will receive 3 additional doses of nivo at 240mg IV Q2 weeks. Adjuvant capecitabine is recommended for all patients per local standard-of-care. Patients will be stratified by NAC platinum administration, NAC anthracycline administration, and clinical nodal status (positive versus negative). The primary endpoint is 3-year Event Free Survival (EFS). Secondary endpoints include Invasive Disease-Free Survival (IDFS), Distant Disease-Free Survival (DDFS), overall survival (OS) and safety. Exploratory correlative studies will be performed on tumor and serum to characterize the immunologic impact of the intervention and to explore predictors of efficacy and toxicity. Funding sources: Susan G. Komen, ASCO Conquer Cancer Foundation, Breast Cancer Research Foundation, Bristol-Myers Squibb, BTG International Ltd. NCT03546686

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12/6/2022

5:00 PM - 6:15 PM

OT1-20-01

SentiNot 2.0: Avoid unnecessary Sentinel Lymph Node Biopsies in women with DCIS.

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Background Approximately 15-30% of women with a preoperative diagnosis of ductal carcinoma in situ (DCIS) will be diagnosed with invasive cancer (IBC) on specimen pathology. Risk of upgrade, and impairment of lymphatic outflow after breast surgery, mainly mastectomy, are drivers for upfront sentinel lymph node dissection (SLND). In the SentiNot feasibility study, marking the SLN by superparamagnetic iron oxide nanoparticles (SPIO) injection during primary surgery minimized unnecessary SLNDs, allowing for delayed SLND (d-SLND) only in those with IBC up to 50 days after primary surgery. This policy resulted in that 78.3% study participants avoided upfront SLND. In the d-SLND setting, SPIO detection outperformed the isotope (98.5 vs 60.6%), regardless of type of breast procedure. Incremental healthcare costs were reduced by 8.5% (485 USD per patient) for the entire trial population (ref 1). Prospective Clinical Trial Design SentiNot 2.0 (ClinicalTrials.gov Identifier: NCT04722692), is currently

accruing data, powered to examine the detection rate of SPIO over isotope±blue dye during d-SLND. Trial candidates are: patients with a diagnosis of high-risk DCIS/pLCIS (mass-lesions, microinvasion, grade 3, grade 2 >20mm) regardless of type of breast surgery, and patients with planned breast surgery that precludes safe and accurate axillary mapping at a d-SLND (extensive oncoplastic breast conservation, tumors of the axillary tail and mastectomy). In d-SLND, study patients receive isotope±blue dye and within-patient-randomization is performed for which detection method to start with (SPIO-first vs. isotope-first). The trial is stratified for mastectomy and breast conservation. Secondary outcomes are nodal concordance (SPIO vs. isotope) at d-SLND, quality-of-life and health-economy outcomes. Present and Planned Accrual Total target accrual is 500 d-SLNDs. Insofar, 360 women have been included at six different sites in Sweden, Hong Kong, and the USA. Currently, data accrual and institution recruitment is active and expanding. For more information about the trial please refer to ClinicalTrials.gov Identifier: NCT04722692. For discussion regarding potential participation contact dr Andreas Karakatsanis (andreas.karakatsanis@surgsci.uu.se) .

Disclosure(s):

Eirini Pantiora, MD: No financial relationships to disclose

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OT1-20-02

Intralesional injection of anti-PD-1 (pembrolizumab) and OX40L/IL-23/IL-36 α mRNAs (mRNA-2752) results in regression of DCIS characterized by lymphocytic infiltrates.

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Background: High-grade DCIS with immune infiltrates may represent lesions that are able to be kept in check by the immune system, but still are at risk for progression to invasive disease. We and others have demonstrated that the presence of T cells, and in particular the spatial proximity of CD8+/PD-1+ T cells and PD-L1+ cells predicts response to chemotherapy and PD-1 inhibitors in the setting of invasive triple negative breast cancer. DCIS with high-risk features (e.g. large, palpable, high grade, HR-, or HER2+) often have T cell infiltrates. We hypothesized that it might be possible to potentiate the immune response in high-risk DCIS with immune checkpoint blockade. Since mortality for DCIS is extremely low, we proposed an intralesional pembrolizumab (pembro) treatment approach to avoid systemic adverse effects. In a phase 1

dose escalation study of single agent pembrolizumab we found 2 doses of 8 mg, administered intralesionally 2-3 wks apart, was tolerable, induced immunological changes within the DCIS lesions, but had little clinical benefit. Herein, we expanded the number of injections to 4 and also tested a combination with mRNA-2752 (Moderna), an mRNA-based therapeutic encoding a T cell co-stimulator OX40L, and pro-inflammatory cytokines IL-23 and IL-36 gamma, to determine if we could find a dose that was both tolerable and elicited anti-tumor responses.

Methods Women eligible for this study had DCIS with at least 2 of the following high-risk features: age < 45; high grade, extensive comedonecrosis; palpable mass; hormone receptor negative [HR-]; HER2+; size >5 cm, or microinvasion. A dose expansion cohort was performed using 4 doses of 8 mg pembro, 2-3 wks apart (n=5). We then combined pembro with mRNA-2752 (n=8 cases), initially at 8 and 4 mg, respectively. Dose reductions were implemented based on AEs. Patients received an MRI before and after 2 injections, spaced 2-3 wks apart. A total of 4 injections were allowed. Core biopsy or surgery was conducted after the last MRI.

Results We observed an increase in T cell density in the dose expansion cohort (pembro only), except when there was a paucity of T cells in the pre-treatment biopsy. However, only 1 patient in this cohort demonstrated a reduction in lesion size (clinically and on MRI). As of 22SEP22, 8 patients have received the combination of pembro and mRNA-2752; 7 are evaluable. Two patients with minimal T cell infiltrates at baseline (both HR+) failed to respond, based on imaging or pathology. 4/5 patients with moderate to high T cell infiltrates at baseline had partial (2) or complete responses (2) based on imaging (surgery pending), one of whom had absence of DCIS on post-therapy core biopsy and a clear MRI 4 months later. Correlative studies (immune cell densities, spatial proximities) will be presented at the meeting along with complete data (including post-treatment pathology) on the first 8 patients. Side effects were independent of response and included Gr1/2 fever, myalgias, and fatigue starting within 12 hours of injection (3-4 days), enlargement of regional nodes by day 2, and Gr 1/2 erythema and induration of the breast starting at 4 days and lasting 4-20 days. Earlier onset and persistence of symptoms with subsequent exposure required dose reductions for the majority of patients to maintain tolerability (avoid fevers over 39.4°C, intense erythema and swelling of the breast lasting > 4 days). No AEs were higher than grade 2.

Conclusion: The combination of intralesional pembro and mRNA-2752 demonstrated modulation of the tumor immune microenvironment and robust antitumor activity in high-risk DCIS (typically HR- or HER2+) with existing T cell infiltrates. This is an ongoing study; the optimal Phase 2 dose for the combination will be based on the totality of evolving safety and translational data.

Disclosure(s):

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OT1-21-01

Preoperative radiotherapy and systemic therapy following surgery in 'de novo' metastatic breast cancer (Protocol MF22-01; Intervention Systemic Treatment METastasis-ISTMET)

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Background Five to eight percent of breast cancer (BC) patients present with distant metastasis at diagnosis, known as 'de Novo' metastatic breast cancer (dnMBC). Recent data showed that approximately 40% of dnMBC patients undergo locoregional treatment (LRT). LRT treatment modalities for metastasis and primary tumor benefit a subset of patients with oligometastatic disease. Our study group has recently demonstrated two prospective studies regarding this topic with favorable outcomes. MF07-01 IMET study, one of the first clinical randomized trials, showed that the patients with the diagnosis of dnMBC undergoing LRT followed by systemic therapy had an additional 14% OS benefit by the end of the 10-year follow-up when compared with others who received only systemic therapy. A prospective multicenter registry study MF14-

01 BOMET also presented LRT prolonged survival and decreased locoregional recurrence in a prospective registry study with a median follow-up of 3 years. Timing of primary breast surgery either at diagnosis or after systemic treatment provided a survival benefit similar to systemic therapy alone in bone-only dnMBC patients. Although, the optimal timing of concurrent endocrine therapy, radiotherapy, and/or sequential surgery remains unclear. Hypothesis We hypothesize that in the era of modern radiotherapy and endocrine therapy, concurrent radiation and endocrine therapy will be non-inferior to sequential treatment modalities in terms of locoregional and systemic disease control in dnMBC. ER/PR (+), Her2 neu (-) oligometastatic dnMBC patients are potentially curable with multimodality treatments. Objectives The primary objective is to perform a Phase I study to evaluate the feasibility of this curative intent treatment approach for patients with oligometastatic disease. Secondary objectives are to present the treatment response evaluating with CTC and/or ctDNA, and IHC and marker changes with multimodality treatments Methods Postmenopausal ER/PR (+) and Her2 neu (-), oligometastatic dnMBC patients will be enrolled in the study. Inclusion criteria: Primary breast tumor amenable for complete surgical resection, patients in good physical condition for receiving protocol-driven locoregional and systemic treatments and radiotherapy; Bone-only oligometastatic disease (5 or less metastasis); Primary tumor biopsy, metastatic site biopsy (ER/PR, Her2, Ki67). Exclusion criteria: Primary tumor not amenable for complete resection; primary tumor with extended infection, bleeding, or necrosis; patients with poor physical condition which prevents the patient from receiving protocol-driven locoregional and systemic treatment; synchronous primary cancer at the contralateral breast; clinically involved contralateral axillary nodes; patients not suitable for adequate follow-up, and failure to give informed consent. Study Design: • RT to the primary tumor (Hypo fractionated) + AI concurrent, Collect CTC and/or ctDNA • Add CDK4/6i to AI 2-4 weeks after RT + (6 months) • RT to bone metastasis (if still visible), Collect CTC and/or ctDNA + (12 months) • Primary Breast Surgery, Collect CTC and/or ctDNA, ER/PR/Her 2 in the final specimen + • CDK4/6i +AI until progression and/or unmanageable toxicity Conclusion We hypothesize that in the era of modern radiotherapy and endocrine therapy, concurrent radiation and endocrine therapy will be non-inferior to sequential treatment modalities in terms of locoregional and systemic disease control in dnMBC. ER/PR (+), Her2 neu (-) oligometastatic dnMBC patients are potentially curable with multimodality treatments.

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OT1-22-01

Liquid biopsy and Ado-trastuzumab emtansine (T-DM1): drug-resistance traits in the blood of HER2-positive metastatic breast cancer patients

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Background: A previous study on 22 metastatic breast cancer (mBC) patients (Allegretti et al. Mol Cancer 2021) has associated drug resistance to Ado-trastuzumab emtansine (T-DM1) with two sets of genomic events: a) reversal of HER2 amplification, b) 'oncogenic replacement' of HER2 by alternative cancer drivers. To expand on this, we designed GIM21 (Gruppo Italiano Mammella) study. Materials and Methods: GIM21 is a multicentre, prospective study; tumor and

circulating total nucleic acids (tTNA and ctTNA) were obtained from primary and metastatic lesions (n=36 altogether), as well as plasma samples (n=501), the latter serially collected coincident with medical imaging re-evaluations. tCNAs/ctTNAs were sequenced by ultra-deep, largely overlapping 50-gene panels on Ion Torrent Gene Studio S5. Orthogonal dPCR validation was by dPCR (Quant Studio 3D). ctTNAs were correlated with clinical readouts and patient outcomes. Results: from September 2018 to January 2022, 50 HER2+ mBC patients receiving T-DM1 as second-line treatment. Median time to progression was 6.5 months (range 2.0-27.2). As previously shown, only a minority of patients (9/50 – 18%) retained residual HER2 amplification in blood at baseline, likely due to HER2 counterselection during previous therapy lines; all of them (9/9) underwent further neutralization during T-DM1 treatment, but an HER2-neutral blood status was reached in only 5 patients. In contrast, 2 HER2-neutral patients acquired HER2 amplification, suggesting either insufficient T-DM1 pressure or an unprecedented clonal escape mechanism. Overall, the circulating HER2 status did not correlate with progression free survival (PFS), further highlighting a loss of clinically relevant HER2 oncogenic dependence. At baseline, 24 circulating mutations were detected in 29/50 (58%) patients, 9 of which did not overlap with tissue mutations. Of note, carrying a given aberration in either blood or tissue resulted in outcome trends (p=0.16), but no clear association with therapeutic response. Rather, it was serial monitoring (appearance of any aberration in the blood) that predicted a dismal clinical outcome in 16/41 (39%) patients, with a median time to progression of 2.8 months (2.2-3.9). Unfortunately, liquid biopsy (LB) was confirmed to miss most patients developing brain (3/3 patients) or skin (2/3 patients) metastases. Most circulating alterations present at progression (40/60) were actionable (OncoKB level < 3B) in 34/41 (82.9%) patients, suggesting that LB may guide therapeutic strategies in post-T-DM1 settings. Conclusions: GIM21 trial showed that LB accurately predicts clinical outcome and reveals actionable drivers of T-DM1 escape. The final analysis are ongoing.

Disclosure(s):

Alessandra Fabi, MD: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Eisai: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Eli-Lilly: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Epionpharma: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); exact science: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Novartis: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Pfizer: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Pierre Fabre: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Roche: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Seagen: Consulting Fees

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12/6/2022

5:00 PM - 6:15 PM

OT1-23-01

Development of a hoRizontal data intEgration classifier for NOn-invasive early diAgnosis of breasT cancEr: the RENOVATE trial

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Background: The detection of breast lesions through self-examination or during screening tests is a frequent finding. Breast biopsy is required in case of radiologically suspect lesions, bestowing a high burden on both patients and national healthcare system, since only one every four biopsies is breast cancer (BC). To date, the assessment of circulating biomarkers failed to demonstrate clinical utility in the early diagnosis of BC, for its suboptimal accuracy and difficult transferability to clinical practice. The combination of novel cutting-edge methods for the assessment of circulating analytes in an integrated multiomic classifier may overcome such limitations, possibly allowing liquid biopsy to become a novel noninvasive procedure for the differential diagnosis of BC. Design: In the RENOVATE trial (NCT04781062), women with suspect (BI-RADS-4/5) breast lesions ≤ 2 cm (cT1) are asked, before biopsy, to donate ~ 35 mL of blood collected in four dedicated tubes and ~ 50 mL of urine at the Diagnostic Senology Unit of Ospedale Policlinico San Martino (Genoa, IT). Plasma cell-free DNA methylation and copy number alterations are assessed in a cohort of patients diagnosed with early BC and a matched set of patients with histologically proven benign lesions through cell-free methylated DNA immunoprecipitation and high throughput sequencing (cfMeDIPseq), as well as ultra-low

pass whole genome sequencing (ULP-WGS). Thanks to the volume and quality of our sample set, other experimental techniques will be tested as well. Results from cfMeDIP-seq and ULP-WGS, possibly in combination with other findings, will be integrated in a unique classifier for the noninvasive differential diagnosis of suspect breast lesions. Eligibility criteria: Patients with radiologically suspect breast lesions ≤ 2 cm (i.e. BIRADS 4/5) are eligible. Patients with previous history of cancer, or diagnosed with autoimmune or active allergic diseases, acute or chronic hepatic, renal, or cardiac diseases, or acute or chronic infectious diseases are excluded from the present trial. Specific aims: The primary aim of the present trial is to develop a noninvasive classifier for the differential diagnosis of suspect breast lesions detected through mammography and/or ultrasound. For such purpose we will assess the performance of plasma cfMeDIPseq, ULP-WGS, and other promising techniques for the differential diagnosis of BC. Such techniques will be integrated in a unique classifier in order to reach the maximum possible accuracy. Statistical methods: Sample size was calculated with a semi-parametric simulation-based approach from beta-distributions of PBMC datasets: assuming to test 20,000 CpG regions, with 300 differentially methylated target CpGs, a target maximal difference in DNA methylation of 0.2 between groups and an FDR of 0.05, $1 - \beta \sim 0.90$ would be achieved with an overall sample size of 150 samples split in a 1:2 ratio. Target accrual and present accrual: Minimum target accrual is set at 49 patients with BC and 98 patients with benign lesions. To date, we have collected plasma samples from 74 eligible patients with BC and 115 eligible patients with benign lesions. A validation cohort accounting for $\sim 30\%$ of our sample set will be recruited at Istituto Nazionale dei Tumori (Milan, IT). Contact information: For further information, please contact Gabriele Zoppoli at gabriele.zoppoli@unige.it.

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P1-01-01

The Role of Adjuvant Chemotherapy for Elderly Women with Triple-Negative Breast Cancer

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Purpose: There is little evidence determining whether elderly patients (from 70 to 90 years old) with triple-negative breast cancer (TNBC) could benefit from adjuvant chemotherapy (AC). The objective of this study was to explore the effect of AC in these population following surgery. **Methods:** A total of 4610 patients were identified in the Surveillance, Epidemiology, and End Results database (2010-2018). Inverse probability of treatment weighting (IPTW) was used to reduce the selection bias. IPTW-adjusted Kaplan-Meiers survival analysis and Cox proportional hazards models were performed to compare breast cancer specific survival (BCSS) and overall survival (OS) in the two different treatment groups. **Results:** All eligible patients were divided into two groups, the chemotherapy (n=1989) and the observation (n=2621) groups. The percentage of patients receiving AC versus observation increased significantly from 2010 to 2018 (estimated annual percentage change, 1.49%; 95%CI, 0.75-2.16%, p=0.002). The 5-year IPTW-adjusted rates of BCSS and OS in AC group were better than that in observation group (BCSS: 82.32% vs. 78.42%, p=0.010; OS: 75.54% vs. 64.65%, p< 0.001). In IPTW-adjusted Cox proportional hazards regression analysis, elderly patients could benefit from AC (BCSS: HR, 0.77, 95%CI, 0.62-0.94, p=0.012; OS: HR, 0.66, 95%CI, 0.57-0.78, p< 0.001). AC was associated with a significant outcome benefit across year at diagnosis, marital status, stage,

lymph node, surgery and radiation subgroups (all $p < 0.05$). Patients with T1ab could not benefit from AC. Conclusions: We show a BCSS and OS benefit from AC in old patients with TNBC. AC may remain a reasonable treatment approach in these specific patients. For the patients with T1ab, de-escalated treatment should be administered with caution. It requires further randomized controlled trial to ensure the AC effectiveness for elderly TNBC patients.

Disclosure(s):

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5:00 PM - 6:15 PM

P1-01-02

The impact of adjuvant chemotherapy on overall survival in hormone and node positive breast cancer patients with an Oncotype Dx score of 25 or less. A NCDB analysis.

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Background

The RxPONDER trial showed that in premenopausal breast cancer (BC) subjects who were hormone receptor positive (HR+), N1 lymph node status and had an OncotypeDx (RS) score \leq 25, the use of adjuvant chemotherapy (AC) along with endocrine therapy (ET) had better disease free and distant relapse free survival than ET alone. Using a large national database, we wanted to see if adding AC improved overall survival in a similar cohort of node positive BC patients.

Methods

The 2004-2018 National Cancer Database was used to include female BC patients aged 18-50 years. Inclusion criteria were N1-N3 lymph node status, M0 patients with any T stage, RS \leq 25, HR+ and HER2-. Patients who received neoadjuvant chemotherapy were excluded. Logistic regression was used to evaluate AC utility trends. Kaplan-Meier (KM) and multivariate (MV) propensity score (PS) weighted Cox model were used to compare survival between patients with and without AC use.

Results

8628 women were included of which only 3519 (40.8%) received AC (AC+). 5109 (59.2%) did not receive AC (AC-). AC+ had the following age distribution: (18-40 years: 23.73%, 41-50 years: 76.27%), while AC- had the following: (18-40 years: 15.15%, 41-50 years: 84.85%). RS score distribution are as follows: AC+(0-11: 17.56%, 12-25: 82.44%), AC-(0-11: 35.49%, 12-25: 64.51%). Most of the cohort received ET (AC+: 94.74%, AC-: 93.25%) and majority were N1 (AC+: 92.61%, AC-: 98.9%). Factors associated with AC use includes caucasian race [african american vs caucasian: 0.777(0.647,0.934), $p=0.0072$], higher stage [II vs I: 1.825(1.598,2.084), $p<0.0001$, III vs I: 3.199(1.593,6.426), $p=0.0011$] and higher grade [G3 vs G1: 2.261(1.886,2.711), G2 vs G1: 1.467(1.301,1.655), $p<0.0001$], radiation (RT) use [1.758(1.544,2.002), $p<0.0001$], younger age [40-50 vs 18-40: 0.684(0.542,0.863), $p=0.0013$], higher RS [12-25 vs 0-11: 2.325(2.065,2.618), $p<0.0001$], mastectomy [vs partial surgery:

1.668(1.469,1.894), $p < 0.0001$] and N2N3 nodal stage [N2N3 vs N1: 2.688(1.423,5.079), $p=0.0023$].

KM curves showed that AC+ had better survival at 10 years (93% vs 91%) (Table). Hazard Ratio (HR) comparison between the 2 groups favored AC+ [0.602(0.482,0.751), $p < 0.0001$] (Table). Subgroup analysis for overall mortality benefits from AC+, using MV adjusted HR showed favorable results in caucasian race [0.512(0.348,0.752)], both age groups of 18-40 years [0.429(0.217,0.847) and 40-50 years [0.585(0.394,0.869)], both poorly differentiated [0.404(0.186,0.874)] and well-differentiated [0.386(0.165, 0.903] grades and RS 12-25 [0.549(0.379,0.795)]. RS 0-11 did not reach significance [0.555(0.216,1.423)].

Discussion

Based on our analysis, AC use was noted in 40.8% of young, lymph node and HR+ BC patients with an RS score of 0-25. This group of patients had an overall survival advantage of around 40% with AC use, further supporting the findings of the RxPONDER trial. This benefit is of particular significance in patients with a RS of 12-25. The survival advantage was present in all patients less than 50 years, regardless of the age subgroup used in our analysis. Possible mechanisms leading to these outcomes include direct cytotoxic effects and menopausal induction with AC use. Limitations of our study include the use of non-population-based data and the possibility of confounding despite the use of PS matching. Moving forward, AC use along with hormone therapy may become standard practice in young HR + BC patients with lymph node involvement, regardless of the RS score.

Table. Survival difference between AC+ and AC-.

Survival Rate % at 10 years from KM estimate		
	AC+	AC-
Overall	93.0(89.8,95.2)	91.0(87.9,93.4)
18-40 years	86.0(72.6,93.1)	82.8(70.0,90.5)
41-50 years	94.7(91.9,96.5)	92.2(88.9,94.6)
HR estimates AC+ vs AC-		
MV cox model	0.543(0.388,0.759)	0.0004
PS weighted Cox model	0.602(0.482,0.751)	<0.0001

KM-Kaplan-Meier, AC-Adjuvant Chemotherapy, HR-Hazard Ratio, MV-Multivariate, PS-propensity score.

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5:00 PM - 6:15 PM

P1-01-03

The Impact of Comorbid HIV infection on Neoadjuvant and Adjuvant Chemotherapy Relative Dose Intensity in South African Breast Cancer Patients

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Introduction In the South African Breast Cancer and HIV Outcomes (SABCHO) study, early-stage breast cancer patients living with HIV, compared to their HIV-negative counterparts, demonstrated higher overall mortality and lower rates of pathologic complete response if treated with neoadjuvant chemotherapy. We aimed to determine if comorbid HIV also impacted receipt of timely and complete neoadjuvant and adjuvant chemotherapy. Methods We retrospectively identified Black, stage I-III SABCHO participants diagnosed with breast cancer from June 2015 to July 2019 and who received at least 2 doses of neoadjuvant or adjuvant chemotherapy at either Charlotte Maxeke Johannesburg Academic Hospital (Gauteng) or Grey's Hospital (KwaZulu-Natal). Data on the originally prescribed chemotherapy regimen and the dose and timing of all received chemotherapy was extracted from patients' medical records, as well as values from all complete blood counts and metabolic panels performed during treatment. Relative dose intensity (RDI) was calculated for each agent in the prescribed regimen with the mean RDI of all agents representing the RDI of the full regimen. We assessed

for associations between full regimen RDI and HIV status using a multivariable linear regression model that included demographic and clinical covariates also shown to impact RDI. We also compared rates of myelosuppression, alkaline phosphatase elevation, and creatinine elevation using linear regression. Using previously collected survival data, we compared overall mortality based on overall RDI above or below 0.85. Results We analyzed data from 325 eligible subjects, 166 of whom were living with HIV. No differences based on HIV status were appreciated in the prescribed chemotherapy regimens. For women without HIV median RDI was 0.87 (interquartile range (IQR) 0.77-0.94) and, in those living with HIV, it was 0.89 (IQR 0.77-0.95). HIV status showed no significant association with RDI on multivariable analysis, and the only patient characteristics associated with RDI were estrogen/progesterone receptor (ER/PR) and HER2 status. Patients living with HIV experienced more CTCAE v5.0 grade 3+ anemia and leukopenia than those without HIV (anemia: 10.8% vs 1.9%, $p=0.001$; leukopenia: 8.4% vs 1.9%, $p=0.008$) and were more likely to receive at least one dose of filgrastim (24.7% vs 10.7%, $p=0.001$). Receipt of RDI greater or less than 0.85 did not predict overall mortality in the full cohort or HIV status subgroups. A trend towards improved survival with RDI greater than 0.85 was seen among the 69 participants with ER/PR negative disease (hazard ratio: 0.60, 95% confidence interval: 0.30-1.21, $p = 0.15$). Conclusions Neoadjuvant and adjuvant chemotherapy RDI did not differ by HIV status among women in the SABCHO study, although women living with HIV experienced more myelotoxicity during treatment. Efforts to reduce chemotherapy dose reduction and delays should target all South African breast cancer patients.

Disclosure(s):

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P1-01-04

Comparing the Effects of TC and Anthracycline-based Chemotherapy in Women with Breast Cancer HER2 Negative Treated in the Adjuvant Setting – An individual Patient Meta-Analysis

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Background: Among women, breast cancer is the most common diagnosis of non-skin cancer and the fifth cause of oncological-related death worldwide. Adjuvant chemotherapy has been shown to extend overall survival (OS) and disease-free survival (DFS). Anthracyclines are cytotoxic regimens largely used in breast cancer, mainly in patients with risk factors or high burden of disease. The docetaxel and cyclophosphamide (TC) regimen is a Taxane-based treatment, and is an alternative option when anthracyclines are not indicated. However, anthracyclines have a myriad of adverse effects including alopecia, cardiac-related side effects and myelotoxicity. The question that remains is in which breast cancer population anthracycline chemotherapy should be omitted. Methods: A literature search was performed in Embase, Medline, and the Cochrane Libraries up to February 28 2022. We conducted an individual patient-level meta-analysis of 11,902 participants of 7 randomised controlled trials. The target population was adult women, with a histologically confirmed HER2 negative, stage I-III breast cancer who were treated with TC versus anthracycline-based chemotherapy in adjuvant setting under randomised-controlled trials. To analyse OS and DFS, we utilized the generic inverse variance method for time-to-event outcomes using hazard ratio (HR). A sensitivity analysis of risk of bias (ROB) was undertaken to examine the effects of high/moderate risk studies on each study endpoint. The assessment of certainty of evidence was conducted based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria. Results: With a median follow up of 60 months, the pooled analysis from 7 studies with available data on OS, and from 6 studies on DFS. From a total of 11,778 there was a total of 288 and 281 events of death in the TC and in the anthracycline-based chemotherapy groups, respectively. The analysis of OS revealed HR 1.01, 95% CI (0.86 – 1.19), $p = 0.88$; high certainty of evidence. From a total of 11,902 participants, there were 639 and 595 recurrence events in the TC and in the anthracycline-based chemotherapy groups, respectively. The analysis of DFS revealed HR 1.07, 95% CI 0.95-1.22, $p=0.26$; moderate certainty of evidence. No relevant absolute risk of death or recurrence events were found between the two treatments. In the quality of evidence assessment, the heterogeneity across all the studies is likely not more than what is due to chance ($i^2 < 14\%$). The risk of bias was not a serious concern, and the publication bias was undetected for the endpoints OS and DFS. Conclusion: In this study population, TC chemotherapy likely results little to no difference in OS or DFS compared to anthracyclines-based chemotherapies. Despite the large number of participants and minimum heterogeneity across all the studies, there was no evidence of significant benefit or harm between the treatments. Overall, there is a high to moderate quality of evidence that adjuvant TC chemotherapy does not increase OS or DFS when compared to anthracycline-based chemotherapy in patients with breast cancer HER2-negative. Albeit the choice between the two chemotherapies would need to be balanced considering the specific side-effects that each treatment is likely to cause.

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Adjuvant S-1 plus endocrine therapy for estrogen receptor-positive, HER2-negative, primary breast cancer: updated overall survival analysis from the POTENT trial

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Background: The Phase III POTENT trial demonstrated an improvement in invasive disease-free survival (IDFS) by the addition of S-1, an oral fluoropyrimidine, to adjuvant endocrine therapy in patients with ER-positive/HER2-negative early breast cancer. Because the trial was terminated at the interim analysis as the primary endpoint was met, the result of the overall survival (OS) remains immature. **Methods:** This multicenter observational study aimed to investigate the survival outcomes of patients who participated in the POTENT trial, in which patients with stage I to IIIB ER-positive, HER2-negative breast cancer without protocol-defined low-risk features received adjuvant endocrine therapy alone or with S-1 for 1 year. Of the full analysis set (FAS) of the POTENT trial (N=1930), patients who withdrew the consent or whose institutions terminated the contract were excluded from this study. The primary endpoint was OS. Secondary endpoints were IDFS and distant recurrence-free survival (DRFS). **Results:** A total of 337 patients (17%) in the POTENT study were excluded from this analysis (eight patients withdrew consent and 329 patients for institutions whose contract had been terminated). A total of 1593 patients were included in this study (803 in the endocrine therapy alone group and 790 in the endocrine therapy plus S-1 group). The median follow-up was 77.5 months (IQR: 68.8–86.0). The median duration of endocrine therapy was 71 and 69 months in the endocrine therapy alone and endocrine therapy plus S-1 groups, respectively. The patient characteristics were well balanced between the treatment groups, except for the number of lymph nodes involved. The endocrine therapy alone group included more patients with four or more positive nodes than the endocrine therapy plus S-1 group (12% vs. 9%, P=0.01). 58 (7%) patients in the endocrine therapy alone group and 51 (6%) in the endocrine therapy plus S-1 group died (HR 0.89, 95%CI: 0.61–1.30, P=0.54). The 5-year overall survival estimate was 94.7% (95%CI: 92.9–96.1%) in the endocrine therapy alone group and 95.6% (95%CI: 93.8–96.8%) in the endocrine therapy plus S-1 group. IDFS events were observed in 166 patients (21%) in the endocrine therapy alone group and in 135 patients (17%) in the endocrine therapy plus S-1 group (HR 0.80, 95%CI: 0.64–1.01). DRFS events occurred in 123 patients (15%) in the endocrine therapy alone group and in 91 patients (12%) in the endocrine therapy plus S-1 group (HR 0.74, 95%CI: 0.56–0.97). **Conclusions:** In this observational study, data from 337 patients (17%) were missing from the FAS of the POTENT trial. Both the endocrine therapy alone group and endocrine therapy plus S-1 groups showed favorable OS, and OS was similar between the treatment groups. The benefit of IDFS and DRFS by the addition of S-1 to endocrine therapy were maintained.

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12/6/2022

5:00 PM - 6:15 PM

P1-01-06

Differences in breast tumor response to neoadjuvant chemotherapy by race- Is obesity the key?

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Background:

Breast cancer treatment includes neoadjuvant chemotherapy (NAC), offered to patients with locally advanced breast cancer and who may benefit from down-staging before conservation therapy. NAC allows for evaluation of treatment response with pathologic complete response (pCR) acting as a marker of survival. Black women receive NAC more frequently as they often present with more advanced stage tumors and the triple negative subtype. Furthermore, Black women without pCR following NAC are at greater risk of mortality. Obesity is a prognostic factor for breast cancer. Non-Hispanic Black women have the greatest prevalence of obesity in most states. Patients with higher Body Mass Index (BMI) have previously been shown to have lower rates of chemotherapy response. Data on racial and ethnic differences in pCR rates are limited and whether obesity is a confounding factor requires investigation.

Methods:

Retrospective review of patients diagnosed with non-metastatic breast cancer who completed NAC and had surgery at Ohio State University James Comprehensive Cancer Center between January 1, 2005, and December 31, 2019, were analyzed. Clinical stage was calculated based on tumor size and nodal status. Operative treatment received was recorded to determine pathologic stage and chemotherapy response. The study endpoint, pCR, was assessed after definitive surgery. BMI categories were based on World Health Organization classification and obese defined as $\geq 30\text{kg/m}^2$. For the data analysis, we included self-reported Black and White women, excluding patients classified as "Other" race. Preliminary analyses included the distribution of sample descriptive characteristics. Differences by race and demographic characteristics were compared using Pearson's chi-square test for categorical variables and t-test or Wilcoxon rank-sum test for continuous variables. Univariate analysis and multivariable logistic regression for pCR by age, race, BMI, menopausal status, insurance status and employment status were performed.

Results:

A final sample of 882 met criteria (11.7% Black and 88.3% white women, 1% Hispanic ethnicity). Median age of diagnosis is 51, with median 147.4 months of follow-up. 64% of the sample had clinical stage 2 disease, 22% were triple negative, 62% Her-2 positive subtypes. For tumor characteristics 67% of Black women and 59% white women had high grade tumor. Black women also had more triple negative disease (30% vs. 21%), more advanced stage at presentation (27% vs. 21%). More white women were employed and had private insurance compared to Black women, who predominantly had public insurance. The median BMI was higher among Black women (31.5) than white women (28.6). 52% of white women vs. 47% Black had mastectomy over lumpectomy. 67% of white women had radiation vs. 61% of Black women. Overall, 33% of Black and white women had pCR, with 67% having no pCR. Race and BMI were not significant predictors of PCR rates on univariate or multivariable analysis. Age < 40 is the only variable associated with pCR (OR 1.645, [95 CI 1.117-2.420] p-value: 0.012).

Conclusions:

BMI was not a significant predictor of pCR in this limited retrospective review. However, further exploration with a larger sample evaluating differences in pCR by BMI can lead to a better understanding of the association between obesity and pCR. Though race was not significant in predicting pCR, there is also room for further research considering socioeconomic disparities and obesity rates by race.

Table 1. Predictors for pCR

Table 1. Multivariable logistic regression for pCR adjusted by age, race, BMI, menopause status, insurance status, employment status

Effect	Odds Ratio Estimates			P-values
	Point Estimate	95% Wald Confidence Limits		
Age: Age <40 vs Age >40	1.645	1.117	2.420	0.012
BMI: BMI <30 vs BMI >30	1.099	0.823	1.469	0.522
Race: White vs Black	1.024	0.644	1.628	0.921
Menopause: Postmenopausal vs Premenopausal	1.101	0.795	1.523	0.563
Insurance: Public vs Private	0.990	0.695	1.411	0.956
Insurance: Uninsured vs Private	1.354	0.656	2.798	0.413
Employment: Employed vs Unemployed	1.268	0.864	1.862	0.225

Univariate analysis for predictors of pCR performed for race and BMI.

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P1-01-07

Adjuvant and neoadjuvant chemotherapy for treatment of early and locally advanced breast cancer in the elderly population at a UK tertiary cancer centre

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Background: The prevalence of breast cancer in older adults (>65 years) is increasing, and these patients are often under-represented in clinical trials¹. It has been demonstrated that older patients are more likely to require dose alterations due to treatment-related toxicities². Increasing evidence suggests that with new-generation chemotherapy regimens, these patients can better tolerate optimal dose intensities^{3,4}. Here, we aim to assess the tolerability and toxicity of adjuvant and neoadjuvant chemotherapy in older patients diagnosed with early or locally advanced breast cancer at a UK tertiary cancer centre. Methods: Patients aged 65 years or over who were diagnosed with early or locally advanced breast cancer and received neoadjuvant or adjuvant chemotherapy between 2016 and 2021 at Royal Free Hospital NHS Trust in London, UK, were included in the analysis. Data was collected from the local patient database including patient demographics, performance status as defined by the Eastern Cooperative Oncology group, pathologic characteristics, chemotherapy and surgical treatment and disease progression and mortality. Statistical analysis was carried out using Pearson's chi-squared test to compare the underlying factors causing changes in dose intensities and treatment-related toxicities. Results: A total of 130 patients with early or locally advanced breast cancer met the inclusion criteria for analysis - 96 patients (mean age 74.5 years, range 68-86 years) and 34 patients (mean age 73.1 years, range 68-85 years) received adjuvant and neoadjuvant chemotherapy, respectively. In the adjuvant chemotherapy setting, 34.0% had ER+ breast cancer, 40.2% HER2+ and 25.8% triple negative (TNBC). Epirubicin/cyclophosphamide/paclitaxel (ECT) was the most frequently delivered chemotherapy regimen (42.7%), followed by paclitaxel plus trastuzumab (32.3%). 77.1% of patients had a dose alteration – 6.3% required a dose delay, 40.6% a dose reduction and 30.2% early discontinuation. Treatment-related toxicity (51.3%, $p=0.017$, $n=39$) was a significant factor leading to dose reduction, of which peripheral neuropathy was the major complaint (50.0%, $p=0.001$), as well as consideration of older age at the start of treatment (35.9%, $p=0.782$). Early

discontinuation of treatment was required in 30.2% (n=29), due to treatment-related toxicity (48.3%, p = 0.0001). Peripheral neuropathy was also the predominant toxicity within this cohort (57.1%, p=0.006). Other reasons for discontinuation were hospital admission (10.3%), adverse reaction to chemotherapy (13.8%) and acute infection (13.8%). Four patients (4.2%) had disease progression and there were no treatment-related deaths. In the neoadjuvant setting, 14.7% were ER+, 52.9% HER2+ and 32.4% TNBC.

Epirubicin/paclitaxel/cyclophosphamide/trastuzumab/pertuzumab (35.0%) and ECT (32.0%) were the most frequent chemotherapy regimens. Dose intensity was altered in 88.0% of patients – 6.0% dose delay, 50.0% dose reduction and 32.0% early discontinuation. Reasons for a dose reduction included toxicity (64.7%, p=0.0002), consideration of older age at the start of treatment (11.8%, p=0.208) and hospital admission (5.9%, p=0.069). Reported toxicities (n=11) were neutropenia (54.5%, p=0.02), peripheral neuropathy (18.2%), fatigue (9.1%) and mucositis (2.0%). Early discontinuation in chemotherapy (32.0%, n=11) occurred due to toxicity (90.9%, p=0.007) and hospital admission (9.1%). Partial pathological response to treatment was 70.6%, whilst 29.4% had a complete pathological response. Disease progression was seen in four patients (11.8%); however, no treatment-related deaths were observed.

Conclusion: This study shows that a large proportion of older patients with breast cancer require changes to their initial chemotherapy dose intensity, with neutropenia and peripheral neuropathy being significant toxicities in neoadjuvant and adjuvant treatment respectively.

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P1-02-01

Comparing the efficacy of aromatase inhibitors vs tamoxifen in hormone receptor-positive, human epidermal growth factor receptor 2-negative early breast cancer: a systematic review and trial-level meta-analysis

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Background: Five years of adjuvant endocrine therapy (ET) including aromatase inhibitors (AIs) and tamoxifen (TAM) is considered the standard of care in hormone receptor–positive, human epidermal growth factor–negative (HR+/HER2–) early breast cancer (eBC). Clinical practice guidelines recommend the use of an AI or TAM depending on menopausal status and clinical risk stratification. Although TAM is generally recommended and more commonly used in premenopausal women, there is mixed evidence for different clinical outcomes. Patient-level meta-analyses conducted by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) showed significantly lower rates of BC recurrence with AIs vs TAM. However, this was not specific to patients with HR+/HER2– eBC. This trial-level meta-analysis was conducted to compare AIs ± ovarian function suppression (OFS) vs TAM ± OFS in HR+/HER2–, pre- and postmenopausal patients with eBC. **Methods:** A systematic literature review (SLR) was conducted using key literature databases, ie, Embase, PubMed, and MEDLINE In-Process (from database inception to March 2022) and key conferences (2019-2021). Studies selected for the SLR were those that included either ≥80% of patients with HR+/HER2– eBC in the mixed patient population or subgroup data provided specifically for patients with HR+/HER2– eBC. Of these, randomized controlled trials (RCTs) investigating AI ± OFS vs TAM ± OFS and assessing disease-free survival (DFS) were included in the trial-level meta-analysis. This meta-analysis was conducted using the generic invariance method to obtain a pooled effect estimate (hazard ratio [HR]) together with its CI for DFS. This pooled estimate was calculated as a weighted average of the intervention effects estimated in the individual trials. Both fixed- and random-effect models (FEM, REM) were used to estimate the effect size. A base-case analysis was performed including all eligible trials. Three other scenario analyses were conducted: trials investigating only nonsteroidal AIs (NSAIs), assessing only premenopausal women, and assessing only postmenopausal women. Heterogeneity across the trials was assessed using I² statistic. **Results:** A total of 5 RCTs comparing AI ± OFS vs TAM ± OFS were eligible for the meta-analysis (SOFT, HOBOE, BIG 1-98, N-SAS BC 03, Li 2019; additional information on rationale for exclusion of specific trials will be reported). Two studies assessing NSAI vs TAM included postmenopausal women, while 3 studies assessing AIs + OFS vs TAM ± OFS included premenopausal women. A total of 6623 patients were followed up for 34-97.2 months across these five trials. Heterogeneity was found to be low (I² < 40%) across all scenarios. The base-case results (including all studies) using FEM significantly favored AIs ± OFS over TAM ± OFS, with a 29% reduction in risk of recurrence or death (pooled HR, 0.71 [95%CI, 0.64-0.80]). Similar results were observed with NSAIs ± OFS vs TAM ± OFS (HR, 0.73 [95% CI, 0.64-0.83]). Among premenopausal patients, the pooled HR for AIs + OFS vs TAM ± OFS was 0.66 (95% CI, 0.54-0.79). For postmenopausal women, the HR was 0.75 (95% CI, 0.65-0.87), favoring AIs over TAM. The findings for the base-case and different scenarios remained consistent when REM was used. **Conclusions:** This trial-level meta-analysis suggests significantly greater benefit with AIs than with TAM for HR+/HER2– eBC. Notably, AIs in combination with OFS are associated with a 34% reduction in risk of recurrence or death vs TAM ± OFS in premenopausal women; these results are aligned with the patient-level data findings of the EBCTCG. The findings indicate that AIs ± OFS are associated with a better DFS in the HR+/HER2– population, especially premenopausal women, than TAM ± OFS.

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P1-02-03

Real World Treatment Patterns of Adjuvant Endocrine Therapy and Ovarian Suppression in Premenopausal HR+/HER2+ Breast Cancer

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Background: Approximately 10% of breast cancers (BC) are hormone receptor positive (HR+) and HER2 positive (HER2+). Despite treatment advances in the modern era of HER2 targeted therapies for early-stage disease, there remains a risk for late relapses. However, the role of adjuvant endocrine therapy (ET) to reduce recurrence in this BC subtype is unclear. Oncologists employ clinical judgment given lack of consensus, resulting in differences in treatment patterns. The ideal endocrine agent including the role of adding ovarian suppression (OS) in premenopausal women is unknown. These patients are largely underrepresented in clinical trials such as the phase III SOFT and TEXT studies. Additionally, these trials were initiated prior to the widespread use of trastuzumab with chemotherapy, which is now standard of care for HER2+ disease. We aimed to describe real world patterns surrounding choice of adjuvant ET and clinicopathologic features which predicted treatment with OS in premenopausal women with HR+/HER2+ BC.

Methods: We performed a multi-institutional retrospective analysis of premenopausal women with non-metastatic HR+/HER2+ BC in the American Society of Clinical Oncology CancerlinQ® Discovery database from January 2010 to May 2020. Electronic health record data was obtained from 74 participating academic and community oncology sites. We collected clinical data on women less than 50 years who received chemotherapy, anti-HER2 therapy (trastuzumab with or without pertuzumab), and ET. Adjuvant OS was defined as receipt of at least 6 months of goserelin or leuprolide or surgical bilateral oophorectomy. Demographics, clinical characteristics, and treatment history was collected. Patients were categorized into 1 of 4 groups based on type of adjuvant ET prescribed at treatment initiation: aromatase inhibitor (AI) + OS, OS, tamoxifen + OS, or tamoxifen. Multivariable logistic regression was conducted to assess the association between clinicopathologic features and OS use.

Results: Out of 360,540 patients with invasive breast cancer in the database, 937 met inclusion criteria. Mean age was 41.7 (SD 5.9) years; 83% had stage 1 or 2 BC and 78% had node positive disease. The majority (n=818, 87%) were prescribed tamoxifen whereas only 4 (0.4%), 50 (5.3%), and 65 (6.9%) received OS, tamoxifen + OS, and AI + OS, respectively. Table 1 includes demographic and clinical characteristics of the cohort. No clinicopathologic features predicted OS use apart from age; patients ≥ 35 years were less likely to receive OS compared with those < 35 ($p < 0.001$) (table 2).

Conclusion: To our knowledge, this is the first real world study evaluating OS treatment in HR+/HER2+ BC. The use of OS was uncommon; this suggests a perception of its limited benefit when added to HER2-targeted therapy. Most patients received tamoxifen as the ET of choice. Age was the only factor to predict OS treatment; high risk features including node

positivity and higher stage was not associated with its use. This highlights the wide variability in real world practice surrounding the clinical indications for OS. Further investigation is warranted to characterize the utility of ET including addition of OS to prevent recurrence in premenopausal HR+/HER2+ BC. This will better inform a personalized approach to tailor therapy for optimal outcomes in this distinct BC subtype.

Table 1

	Aromatase Inhibitor + Ovarian Suppression (n=65)	Ovarian Suppression (n=4)	Tamoxifen + Ovarian Suppression (n=50)	Tamoxifen (n=818)	Overall cohort (n=937)
Age (years) Mean (SD)	38.4 (5.9)	41.8 (5.5)	38.9 (6.9)	42.2 (5.7)	41.7 (5.9)
Race (n, %)					
African American	3 (4.6%)	1 (25.0%)	6 (12.0%)	76 (9.3%)	86 (9.2%)
White	41 (63.1%)	0 (0.0%)	26 (52.0%)	521 (63.7%)	588 (62.8%)
Other	21 (32.3%)	3 (75.0%)	18 (36.0%)	221 (27.0%)	263 (28.1%)
Body Mass Index (n, %)					
<25 kg/m ²	20 (30.8%)	0 (0.0%)	12 (24.0%)	236 (28.9%)	268 (28.6%)
25-30 kg/m ²	15 (23.1%)	0 (0.0%)	8 (16.0%)	129 (15.8%)	152 (16.2%)
≥30 kg/m ²	5 (7.7%)	3 (75.0%)	9 (18.0%)	189 (23.1%)	206 (22.0%)
Unknown	25 (38.5%)	1 (25.0%)	21 (42.0%)	264 (32.3%)	311 (33.2%)
ER positive (n, %)	65 (100%)	3 (75.0%)	50 (100%)	793 (96.9%)	911 (97.2%)
PR positive (n, %)	55 (84.6%)	3 (75.0%)	44 (88.0%)	676 (82.6%)	778 (83.0%)
Clinical Stage (n, %)					
1	30 (46.2%)	0 (0.0%)	19 (38.0%)	314 (38.4%)	363 (38.7%)
2	28 (43.1%)	3 (75.0%)	17 (34.0%)	368 (45.0%)	416 (44.4%)
3	7 (10.8%)	1 (25.0%)	14 (28.0%)	136 (16.6%)	158 (16.9%)
Tumor Grade (n, %)					
1	1 (1.5%)	0 (0.0%)	0 (0.0%)	18 (2.2%)	19 (2.0%)
2	11 (16.9%)	1 (25.0%)	12 (24.0%)	172 (21.0%)	196 (20.9%)
3	24 (36.9%)	2 (50.0%)	18 (36.0%)	224 (27.4%)	268 (28.6%)
Unknown	29 (44.6%)	1 (25.0%)	20 (40.0%)	404 (49.4%)	454 (48.5%)
Nodal involvement (n, %)					
NO	11 (16.9%)	0 (0.0%)	10 (20.0%)	187 (22.9%)	208 (22.2%)
≥N1	54 (83.1%)	4 (100%)	40 (80.0%)	631 (77.1%)	729 (77.8%)
Anthracycline use (n, %)	8 (12.3%)	0 (0.0%)	13 (26.0%)	206 (25.2%)	227 (24.2%)

Table 1. Demographic and clinical characteristics of study participants by endocrine therapy treatment group

Table 2

Clinicopathologic variable	Odds ratio (95% CI)	P value
Age: ≥ 35 vs <35 years	0.43 (0.27, 0.68)	p<0.001
Race: White vs African American	0.92 (0.45, 1.90)	p=0.829
Clinical stage: 3 vs 1 and 2	1.13 (0.67, 1.90)	p=0.653
Tumor grade: 3 vs 1 and 2	1.36 (0.79, 2.33)	p=0.263
Nodal involvement: ≥N1 vs NO	1.27 (0.76, 2.14)	p=0.366
BMI ≥ 30 vs <25 kg/m ²	0.72 (0.38, 1.35)	p=0.308

Multivariable logistic regression model of clinicopathologic characteristics to predict use of ovarian suppression

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5:00 PM - 6:15 PM

P1-02-04

Real world adjuvant endocrine treatment in premenopausal breast cancer patients compared with the proposed algorithm using the Regan Composite Risk Score

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Background The Regan Composite Risk Score (RCRS) is a web-based prognostic and predictive calculator to guide the use of adjuvant exemestane plus ovarian function suppression (AI + OFS) versus tamoxifen plus ovarian function suppression (TAM + OFS) or tamoxifen alone (TAM) for premenopausal women with hormone receptor-positive HER2-negative early breast cancer (HR+/HER2- EBC). We compared our adjuvant endocrine therapy policy based on the tumor board with the treatment guided by the RCRS during 2 time periods, one before and one after the acquaintance of the Tamoxifen and Exemestane Trial (TEXT) and Suppression and Ovarian Function Trial (SOFT) data. This allowed us to see a possible evolution in therapy policy. **Methods** A retrospective cohort study of 563 premenopausal patients with HR+/HER2- and HER2+ EBC diagnosed at the University Hospital of Leuven during 2 periods, 2010-2012 (cohort 1) and 2015-2017 (cohort 2), was conducted. For each patient with HER2- EBC, the RCRS was calculated by entering the requested characteristics in the online available tool. The primary outcome was to investigate how frequent our therapy differed from the therapy guided by the RCRS based on the estimated 8-yr distant relapse free interval (DRFI) with an arbitrary cut-off set at 3 %. If the received therapy was ≥ 3 % less efficient in 8-year DRFI compared to the optimal therapy according to RCRS, the patient was considered undertreated. If the received therapy differed by less than 3 % in 8-year DRFI compared to the optimal therapy according to RCRS and yet the most intensive therapy (AI + OFS > TAM + OFS > TAM) was administered, the patient was considered overtreated. In the other cases, the patient was considered to have been treated concordant with the RCRS. **Secondarily**, nonadherence of the HER2- and HER2+ patients towards the endocrine treatments leading to therapy switch because of intolerance was recorded at 6, 12, 24 and 36 months. Analyses were performed using SAS software and the comparison of both cohorts was performed by the chi-squared test for categorical variables. **Results** According to the RCRS, 43.2 % (89/206) of the HER2-negative patients of cohort 1 were undertreated compared to 22.1 % (43/194) in cohort 2 (chi-squared test, p-value < 0.001). The number of overtreated patients also differed significantly between the two cohorts (chi-squared test, p-value = 0.003) with 2.9 % (6/206) in the first cohort and 10.3 % (20/194) in the second cohort. Finally, the number of patients treated concordant with the guidance derived from the RCRS was 53.9 % (111/206) in cohort 1 and 67.5 % (131/194) in cohort 2 (chi-squared test, p-value = 0.005). Treatment intolerance and switch was observed in 34.8 %, 16.7 % and 12.4 % of the patients receiving AI + OFS, TAM + OFS or TAM as initial therapy respectively; this was numerically higher for all treatments in cohort 2 vs cohort 1, although the observed difference was only significant for TAM. **Conclusion** In our center, a recent cohort of premenopausal women was more likely to be

treated with the adjuvant endocrine treatment concordant with the guidance derived from the RCRS when using an arbitrary cut-off of 3 % to define a relevant improvement in outcome.

Disclosure(s):

Charlotte Berteloot, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

P1-02-05

Endocrine-targeted therapies modify the gut microbiome affecting responsiveness in ER+ breast cancer

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Background: The microbiome consists of the totality of microorganisms (bacteria, fungi, protist, viruses, and phages) that live on and within the body. Studies implicate the gut bacterial microbiome as a risk factor for estrogen receptor-positive (ER+) breast cancer. While diet is the main contributor to the gut microbiome, medications also shift the bacterial microbiome. We currently do not know whether oral endocrine targeting therapies, such as aromatase inhibitors or tamoxifen shift the gut microbiome. Furthermore, we do not know whether gut microbiome populations can influence drug efficacy. Methods: Fecal samples from human donors were placed into ex-vivo colonic bioreactors for stabilization (n=3). Bioreactors were untreated or treated with letrozole or tamoxifen citrate for 48 hours. Samples were collected, DNA isolated, and metagenomic sequencing performed to determine direct drug-bug interactions. C57BL/6 mice were placed on a healthy control (HC; 21% kcal from fat derived from olive oil and fish oil) or a Western diet (45% kcal from fat derived from corn oil, lard, and milkfat) for 6 weeks. Mice within dietary patterns were randomized and administered control, tamoxifen (TAM; 37 ppm tamoxifen citrate), or an aromatase inhibitor (AI; 5 ppm letrozole) for 16 weeks. Metagenomics sequencing were performed on fecal DNA samples at study endpoint. Female BALB/c mice fed a HC or Western diet were injected with bone metastatic 4T1.2ER+ breast cancer cells. Mice were administered tamoxifen citrate, oral probiotics, or a combination of TAM + probiotics for 3-weeks. Tumor volume, tumor weight, and lung weight were recorded at the end of the study. Hindlimbs were analyzed for metastatic lesions. Results: Metagenomic sequencing from the ex-vivo colonic bioreactors treated with aromatase inhibitors or tamoxifen display differential shifts

in several β -glucuronidase-expressing and obesity-associated bacterial species suggesting AI and selective estrogen receptor modulators have varying effects in the gut microbiome that may influence estrogen bioavailability and metabolic parameters. C57BL/6 mice on HC or Western diet treated with AI or TAM also display differences in the microbiota and phage populations with TAM elevating *Lactobacillus johnsonii* and letrozole increasing *Lactococcus lactis* bacterial proportional abundance. In the tumor-bearing model, combination of oral *Lactobacillus* probiotics and TAM significantly reduced tumor weight when compared with the tumor weight in control, TAM, or probiotic treated mice fed a Western diet. Combination of probiotics and TAM also prevented the development of ER+ bone metastatic lesions. Conclusions: Our study indicates oral endocrine therapies differentially affect the gut microbiome and these drug-bug interactions are sensitive to dietary-influenced baseline microbiota populations, which may influence drug efficacy and metabolic outcomes. Furthermore, our preclinical studies suggest oral probiotic supplements may enhance tamoxifen efficacy to reduce tumor growth and metastatic development. Further clinical studies are needed on this topic.

Disclosure(s):

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P1-02-06

Improved survival with ovarian function suppression in premenopausal hormone receptor-positive breast cancer: a propensity score matching of ASTRRA-trial participants with single-center postmenopausal patients

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Background: Poor survival outcome in young women with hormone-sensitive breast cancer was reported. And previous studies have demonstrated that the addition of ovarian function suppression (OFS) significantly improved disease-free survival (DFS) in patients with premenopausal hormone receptor-positive breast cancer. In this study, we examined whether

ovarian function suppression treatment in premenopausal women is effective in survival comparable to postmenopausal status.

Methods: We evaluated 1,298 breast cancer patients included in the post-trial follow-up of the Addition of Ovarian Suppression to Tamoxifen in Young Women With Hormone-Sensitive Breast Cancer Who Remain Premenopausal or Regain Vaginal Bleeding After Chemotherapy (ASTRRA) trial who received either tamoxifen (TAM) only (n=647) or TAM + OFS (n=635), randomly assigned in a 1:1 ratio and postmenopausal patients in AMC (Asan Medical Center; Seoul, Korea) treated with aromatase inhibitor (AI) (n=603). All patients analyzed in this study underwent surgery between March 2009 and November 2011. The primary endpoint was disease-free survival (DFS) and the secondary endpoint was overall survival (OS). We use propensity-score matching by lymph node status, tumor size, tumor grade, histologic type of cancer, human epidermal growth factor receptor-2 (HER2) status, chemotherapy regimen, surgical modality, and radiotherapy in the overall cohort and in separate subgroups according to anti-hormonal therapy regimens.

Results: In the overall matched cohort, there was a significant difference between the postmenopausal AI group and premenopausal Tam only group in DFS (hazard ratio for the postmenopausal AI group, 0.654; 95% CI, 0.432 to 0.991) and OS was not significantly different between the premenopausal Tam only group and postmenopausal AI group (p=0.061). On the other hand, there was no significant difference between the postmenopausal AI group and premenopausal Tam+OFS group in disease free survival (hazard ratio for the postmenopausal AI group, 1.156; 95% confidence interval [CI], 0.735 to 1.820) or the overall survival (hazard ratio for the postmenopausal AI group, 1.04; 95% CI, 0.553 to 1.956).

Conclusion: This study's findings suggest that the poor prognosis of young women with hormone-sensitive breast cancer is improved by adding OFS to Tam and the effect is not inferior to that of using AI in post-menopausal women.

Outcomes in a Cohort of Patients Matched for Propensity Scores

	Propensity score matched set 1				Propensity score matched set 2			
	postmeno AI vs premeno Tam+OFS(Ref)				postmeno AI vs premeno Tam(Ref)			
	Hazard Ratio	95% CI	P value	Hazard Ratio	95% CI	P value		
Disease free survival (DFS)	1.156	0.735	1.820	0.530	0.654	0.432	0.991	0.045
Overall survival (OS)	1.040	0.553	1.956	0.902	0.489	0.231	1.033	0.061
Distant meta free survival (DMFS)	0.816	0.493	1.351	0.430	0.433	0.265	0.709	0.001
Free from distant meta	0.732	0.430	1.246	0.250	0.424	0.252	0.713	0.001
Recurrence free interval (RFI)	0.861	0.531	1.399	0.546	0.493	0.309	0.786	0.003
Loco-regional free survival (LRFS)	1.090	0.619	1.921	0.765	0.447	0.252	0.794	0.006

postmeno AI, postmenopausal patients who treated with aromatase inhibitor in Asan Medical Center; premeno Tam+OFS, premenopausal ASTRRA participants who treated with tamoxifen and ovarian function suppression; premeno Tam, premenopausal ASTRRA participants who treated with tamoxifen only

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CBD-oil: a potential solution in case of severe tamoxifen-related side effects

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Background Tamoxifen is frequently used in the adjuvant treatment of hormone sensitive breast cancer. Unfortunately, tamoxifen can lead to bothersome side effects resulting in non-adherence in 40% of patients. Patients searching for relief from these side effects are increasingly turning to cannabinoids such as CBD. However, since tamoxifen is mainly metabolised by CYP2D6, and CBD is suggested to be an inhibitor of CYP2D6, the use of CBD might affect tamoxifen pharmacokinetics (PK). Since the effect of CBD on both tamoxifen PK as tamoxifen-related side effects has never been investigated, the aims of this study were to determine the pharmacokinetic interaction between CBD and tamoxifen, and to subsequently investigate whether there is a beneficial influence of CBD on tamoxifen-related side effects.

Methods Patients had to be treated with tamoxifen for at least 3 months, have steady-state endoxifen levels >16 nM (conservative threshold) and experience tamoxifen-related side effects. PK sampling was done at initiation of CBD-oil and 28 days thereafter. Bio-equivalence could be concluded if the 90% confidence interval (CI) for the difference in endoxifen area under the curve (AUC) fell within the [-20%; +25%] interval (n = 15, two-sided α 0.05, β 0.20). In addition, endoxifen PK was analyzed for each CYP2D6 phenotype separately. The effect of CBD on side effects was evaluated with the FACT-ES questionnaire (n = 25, two-sided α 0.05, β 0.20). An improvement > 0.5 times standard deviation (SD) of baseline score was considered clinically relevant. Last, potential side effects of CBD were assessed. Results In this study 15 patients were included for PK analysis and 24 patients for side effect analysis. Endoxifen AUC decreased after CBD by 12.6% (90% CI -18.7%, -6,1%) but remained within bio-equivalence boundaries. The decrease seemed more pronounced in patients with intermediate (IM) CYP2D6 phenotype (-20.8%, 90% CI -26.4%, -14.8%, n = 8) compared to normal CYP2D6 phenotype (-2.2%, 90% CI -11.1%, 7.6%, n = 7). There was no difference in tamoxifen AUC (with or without CBD). On average, the endocrine sub-scale of the FACT-ES improved with a clinically relevant improvement of 8.3 points (95% CI 4.9 – 11.7) after using CBD (baseline SD = 12.8). CBD itself has a mild toxicity profile with few side effects in 10 of 24 patients. Side effects were headache (n=2), dry mouth (n=3), fatigue (n=3), gastroesophageal reflux (n=1), abdominal pain (n=1) and nausea (n=1) and all graded CTCAE 1. Conclusions As endoxifen levels with or without CBD remained within bio-equivalence boundaries and CBD-oil might have a positive effect on tamoxifen-related side effects, it could be considered in case of treatment-related side effects. However, caution is needed in patients with IM or poor metabolizer CYP2D6 phenotypes.

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P1-03-01

Eribulin versus S-1 as first- or second- line chemotherapy to assess Health-related Quality of Life and overall survival in HER2-negative metastatic breast cancer (RESQ study): a non-inferiority, randomized controlled trial

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Background Eribulin is a chemotherapeutic drug that prolongs overall survival (OS) in patients with HER2-negative metastatic breast cancer (MBC), mainly in third-line or later chemotherapy (ChT) [1]. However, health-related quality of life (HRQOL) and efficacy in patients who receive eribulin as first- or second-line therapy is not well known. In contrast, S-1, an oral 5-fluorouracil derivative, shows similar OS to taxanes as first-line ChT and better HRQOL, based on a large phase III trial conducted in Japan [2]. Here, we compared the effect on HRQOL and efficacy of eribulin and S-1 in MBC patients in a first- or second-line ChT setting. Methods We planned an open-label, multicenter, randomized controlled phase III study at 50 hospitals in Japan. We enrolled patients with HER2-negative MBC who had no or one previous ChT for MBC regardless of prior administration of anthracyclines and taxanes. Patients were randomly assigned (1:1) to either eribulin (1.4 mg/m² administered on days 1 and 8 of a 21-day) or S-1 (40–60 mg twice daily for 14 consecutive days, followed by a 7-day break). Randomization was stratified by institution, age, treatment line, hormone receptor status, and time from surgery to recurrence. HRQOL assessment was conducted using the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 questions (QLQ-C30) every six weeks until week 24, and then every nine weeks until week 42 after baseline assessment. The primary outcome measure was the global health status (GHS) score of EORTC QLQ-C30, with a prespecified non-inferiority margin of 10% for a difference in the proportion of patients experiencing deterioration at one year. Clinically meaningful deterioration was defined as a ≥ 10 -point decrease from baseline GHS score or death. Secondary outcomes were OS, progression-free survival (PFS), and adverse events. We estimated that the study needed 330 patients to obtain 80% power for non-inferiority. This trial was registered with the University Hospital Medical Information Network, Japan (protocol ID 000021398). Results Between June 2016 and October 2019, 302 patients were enrolled, with 152 assigned to eribulin and 148 to S-1. The full analysis set for HRQOL assessment included 134 and 136 patients, while that for efficacy consisted of 141 and 144 patients, respectively. Overall compliance with the questionnaire was 85.6%. Among the full analysis set for efficacy, 28 (19.9%) and 31 (21.5%) cases were triple negative, respectively. Eribulin and S-1 were administered as first-line ChT in 99 (70.2%) and 101 (70.1%) patients, respectively. Risk difference of GHS deterioration through one year for the eribulin versus S1 group was -0.66% (95% CI -12.47 to 11.16; P non-inferiority =0.077). Median time to first deterioration in GHS score was 5.64 months (95% CI 3.51–8.00) and 5.28 months (95% CI 3.28-7.80) (HR 1.07 [95% CI 0.79–1.45]; P =0.667); median OS was 35.0 months (95% CI 27.2-41.0) and 27.8 months (95% CI 24.6-33.5) (HR 0.69 [95% CI 0.50-0.95]; P=0.023); and median PFS was 6.07 months (95% CI 5.48-7.80) and 6.66 months (95% CI 5.48-7.77), respectively (HR 0.90 [95%

CI 0.68-1.18]; P=0.427). No previously unrecognized adverse events were observed. Conclusions We found a marginal non-inferiority in HRQOL for eribulin, albeit that the difference was not statistically significant owing to the smaller than planned sample size. Time to first clinically meaningful deterioration was almost identical between the two arms, whereas OS was significantly extended with eribulin. These findings indicate that eribulin in first- or second-line ChT is acceptable as a standard regimen in this patient population. [1] Lancet 2011; 377: 914–23 [2] Lancet Oncol 2016; 17: 90–98

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P1-03-02

**Efficacy of eribulin mesylate in HER2-low and HER2-0 metastatic breast cancer (MBC):
Results from an analysis of two phase 3 studies**

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Background: Breast cancer (BC) with low-level HER2 expression (HER2-low) is defined by an immunohistochemistry (IHC) score of 1+ or 2+ without HER2 gene amplification or excess HER2 gene copy number, as measured by in situ hybridization (ISH). This represents approximately half of patients with BC overall (estimated as 55% for hormone-receptor positive [HR+] BC and 38% for triple-negative breast cancer [TNBC]; Scott, ASCO, 2021). Some data suggest that patients with HER2-low BC may respond differently to treatment than those whose BC has no HER2 expression (HER2-0). In this post hoc unplanned analysis, we analyzed data from two pivotal phase 3 studies (Studies 305 and 301) comparing eribulin with other chemotherapeutic agents (treatment of physician's choice and capecitabine, respectively ["control"]) in patients with both HER2-low and HER2-0 MBC. Methods: Patients with MBC, 2–5 (Study 305) or < 2 (Study 301) prior lines of chemotherapy for advanced/metastatic disease, and who had received an anthracycline and a taxane, were analyzed. HER2-expression status was determined by IHC and/or ISH assays. Median progression-free survival (PFS) and overall survival (OS) were calculated using the Kaplan–Meier method adjusted by study; comparisons of PFS and OS between treatment groups were performed using stratified (by prior

capecitabine use, geographic region, and study) log-rank tests. Hazard ratios were estimated by a stratified Cox model. For each study, median PFS and OS were also calculated for HR+ and TNBC subgroups. Results: Baseline characteristics were generally balanced between treatment groups among patients with HER2-low (n=427) and HER2-0 (n=824) BC. Patients with HER2-low or HER2-0 BC showed trends toward benefit with eribulin treatment. In patients with HER2-low and HER2-0 BC, median OS was longer with eribulin vs control (15.1 vs 12.0 months and 15.2 vs 12.5 months, respectively); median PFS by independent imaging review (IIR) was also longer with eribulin vs control (4.0 vs 3.1 months and 3.9 vs 3.1 months, respectively). Objective response rate (ORR) by IIR was also higher with eribulin vs control in patients with HER2-low and HER2-0 BC (13.7% vs 9.2% and 10.2% vs 7.4%, respectively). In a separate analysis, median OS was longer with eribulin vs capecitabine in patients with TNBC and HER2-low and HER2-0 (15.4 vs 10.3 months and 14.4 vs 8.9 months, respectively). Conclusions: In this post hoc analysis, treatment with eribulin demonstrated trends toward improved OS, PFS, and ORR compared with chemotherapy controls in patients with HER2-low or HER2-0 MBC. Funding source: This trial was sponsored by Eisai Inc., Nutley, NJ, USA. Medical writing support was provided by Oxford PharmaGenesis Inc., Newtown, PA, USA, and was funded by Eisai Inc., Nutley, NJ, USA.

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P1-03-03

Real-World Treatment Patterns and Clinical Outcomes in Patients Treated with Eribulin After Prior PI3K Inhibitor Therapy for Metastatic Breast Cancer

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Background: Eribulin has been used in the treatment of metastatic breast cancer (MBC) following approval in 2010 in the United States (US). Recently, several new therapeutic classes have been approved for patients with MBC, including the phosphoinositide 3-kinase (PI3K) inhibitor alpelisib. This study aimed to assess the treatment patterns and clinical outcomes in patients with MBC treated with eribulin following alpelisib in US clinical practice. Methods: A retrospective, noninterventional medical chart review study was performed to obtain de-identified patient data via participating oncologists. Study population included adult female patients with a diagnosis of MBC who initiated eribulin therapy between March 1, 2019, and September 30, 2020, following prior therapy with alpelisib. Eribulin treatment parameters and patient characteristics were captured. Progression-free survival (PFS) and overall survival (OS) since eribulin initiation was assessed using Kaplan-Meier methods. Results: This interim analysis included 47 eligible patients (median age 62 years at eribulin initiation; 77% Caucasian). The majority (91.5%) of this cohort had HR+/HER2- MBC; 72.3% had a known PIK3CA mutation. Eribulin was classified as 2nd line, 3rd line, and 4th line or later in 34%, 47%, and 19% of patients, respectively, in regard to the line of therapy in the metastatic setting. At last follow-up, eribulin treatment was ongoing for 34% of patients. The median treatment duration was 5.2 months (q1, q3: 3.9, 7.1) among those who had discontinued eribulin, and 11.3 months (q1, q3: 10.0, 13.7) among those who were still on treatment. At last follow-up, 72.3% of patients were alive. The estimated PFS rate at 12 months was 57.1% (95% CI: 40.0-70.9). Median was not reached for OS after initiation of eribulin; the estimated OS rates at 12 and 24 months were 80.2% (95% CI: 65.3-89.2) and 61.8% (95% CI: 37.2-79.2), respectively. Conclusion: Among patients with MBC who initiated eribulin following prior treatment with a PI3K inhibitor, over 60% were estimated to survive for at least 2 years. Future studies to confirm these results are warranted.

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Visceral fat area as a predictive factor in metastatic HER2 negative breast cancer patients treated by first line chemotherapy with weekly paclitaxel and bevacizumab

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Background Obesity has previously been correlated with poorer survival in both early and metastatic breast cancer. Adipose tissues release proangiogenic factors such as Insulin-like Growth Factor and Vascular Endothelial Growth Factor that may ultimately promote tumor growth. CTscan can be used to measure the visceral fat area (VFA) and the subcutaneous fat area (SFA) on the same section. High VFA has been shown to independently predict poorer outcome in patients given first-line bevacizumab-based treatment for metastatic colorectal cancer and metastatic renal cell carcinoma. The prospective multicenter COMET trial included metastatic HER2 negative breast cancer patients receiving bevacizumab and paclitaxel as first-line chemotherapy. This study was designed to identify and validate reliable factors to predict benefit of bevacizumab and allow for a more personalized use of this antiangiogenic agent. Our aim was to evaluate the prognostic value of BMI (Body Mass Index), VFA and SFA in the COMET cohort and their impact on the quality of life. Patients and Methods Out of the 510 patients included in the COMET trial from 9/2012 to 3/2016, 480 received bevacizumab and paclitaxel as first-line treatment and 360 had available CTscan data. VFA and SFA were measured retrospectively on the CTscans performed before chemotherapy initiation, at the level of the umbilicus with the patient in the supine position. ImageJ software was used to measure pixels with densities in the -190 HU to -30 HU range in order to delineate the subcutaneous and visceral compartments and to compute the cross-sectional area of each in cm². These measurements were performed by a radiologist blinded to patients' characteristics and outcomes. For VFA and SFA, we used a threshold at the median value. VFA and SFA levels were tested for their association with progression-free survival (PFS) and overall survival (OS). The impact on quality of life was based on the Global Health Status, the Physical functioning, the Emotional functioning, Fatigue and Pain scores. Results The mean age at inclusion was 57 years (range: 28-83). At initial diagnosis, the main histological type was invasive ductal carcinoma (n = 247, 80.7%). Most patients had received prior neoadjuvant/adjuvant chemotherapy (n = 245, 68.1%) and a large majority (95.4%) had less than 3 metastatic sites. One hundred and forty patients (46.7%) had histological grade II and 41% had grade III tumors. The majority of the patients had positive hormone receptor tumor (n = 238, 79.3 %) and 62 (20.7%) had triple-negative tumor subtype. The median BMI was 24.7

(range : 17-46). After a median follow-up of 60.6 months (95%CI, 60-61.3), median PFS was 9.5 months (95CI, 8.6-10.3). There was no significant correlation between BMI ($p = 0.69$), VFA ($p = 0.24$) or SFA ($p = 0.58$) and PFS in the univariate analysis. The median OS was 29.6 months (95CI, 25.9-32.4). BMI, VFA and SFA were not correlated with OS. Out of the 360 patients, 328 had available data regarding the quality of life. There was no impact of the VFA or the SFA on the different quality of life scores. Conclusions In our prospective cohort of 360 patients with metastatic breast cancer receiving bevacizumab and paclitaxel as first-line treatment, high VFA or high SFA were not associated with a poorer survival. VFA and SFA had no impact on quality of life.

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P1-03-05

Overview of the management and factors associated with outcomes of metastatic breast cancer among elderly patients

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Background: Management of metastatic breast cancer (mBC) in elderly patients (pts) faces some challenges since some pts are frail or have functionality impairment, with higher risk of severe adverse events from oncologic therapy. We aimed to assess the treatment patterns for elderly pts with MBC and evaluate factors associated with outcomes in this population. **Methods:** This retrospective study evaluated pts 70 years and older with mBC treated in a tertiary cancer center from 2009 to 2022. Charlson index (ChI) was used to measure comorbidities. Endpoints were proportion and type of first-line systemic therapy, rates of treatment discontinuation due to toxicities, overall survival (OS) and prognostic factors. The Kaplan-Meier method was used for survival analyses. Hazard ratio (HR) and 95% confidence interval (95% CI) were calculated using Cox regression. **Results:** 460 pts with mBC were evaluated. Median age was 78 years (IQR 70-96). Most pts (n=331; 72%) had hormone receptor-positive HER2-negative (HR+HER2-) BC, while 11% (n=50) had HER2-positive (HER2+) BC and 14% (n=64) triple-negative (TN) BC. Most pts has de novo metastatic disease (n=316; 69%); ECOG-PS 3-4 (n=313, 68%), and ChI ≤ 7 (n=354; 77%). Forty-five pts (10%) did not receive systemic therapy for metastatic BC; this proportion was higher among TNBC (34%) than other subtypes (HR+HER2-: 5%; HER2+: 6%) ($P < 0.001$). The proportion not receiving systemic therapy was also higher among pts with ECOG-PS 3-4 (13%, $P < 0.001$), older than 90 years (19%; $P = 0.069$), and with ChI > 7 (15%; $P = 0.088$). Among 165 pts who received first-line endocrine therapy, 2% discontinued due to toxicity. Ninety pts received first-line chemotherapy and 18% discontinued due to toxicity. Breast cancer was the main cause of death (94%) in the cohort. Factors associated with increased risk of death were HER2+BC (HR 1.48, 95% CI 1.04 – 2.09; $P = 0.027$), TNBC (HR 1.52, 95% CI 1.05 – 2.20; $P = 0.025$), age group 80-90 years (HR 1.30, 95% CI 1.02-1.64; $P = 0.028$), ECOG-PS 3-4 (HR 2.34, 95% CI 1.73-3.15, $P < 0.001$), and not receiving systemic therapy (HR 4.48, 95% CI 2.88-6.98, $P < 0.001$). Median OS was 29 months for pts treated with systemic therapy, and 2.3 months for those who did not receive it ($P < 0.001$). **Conclusions:** Many factors influence the prognosis and the treatment decision for elderly pts with mBC. The rates of pts who do not receive systemic therapy are higher among TNBC, which points to the need for better tolerated therapies for this group.

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5:00 PM - 6:15 PM

P1-04-01

High HER2/CEP17 ratio is associated with better treatment outcomes in advanced HER2-positive breast cancer treated with pertuzumab, trastuzumab, and docetaxel regardless of HER2 2+ or 3+ results

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Background: Dual HER2 blockade with trastuzumab and pertuzumab combined with docetaxel (DHP) is the standard first-line treatment option for patients with HER2-positive metastatic breast cancer. However, HER2 positivity alone often fails to predict treatment outcome of HER2 targeted therapy. The magnitude of HER2 immunohistochemical staining (IHC) and HER2/CEP17 ratio from in situ hybridization (ISH) is a well-known predictive biomarker for HER2 targeted therapy. In the neo-adjuvant setting, patients with HER2 IHC 3+ have higher pathologic complete response (pCR) rate compared to HER2 IHC < 3+ with HER2 ISH positive. In addition, higher HER2/CEP17 ratio is associated with higher pCR rate in HER2-positive breast cancer patients treated with dual HER2 blockade regimens. However, there is no data whether there is an association between HER2/CEP17 ratio and treatment outcome of DHP regimen in patients with advanced of metastatic breast cancer especially among those with HER2 IHC 3+.

Methods: We performed a retrospective cohort study with patients with locally advanced or metastatic HER2-positive breast cancer who were treated with first-line palliative DHP regimen between August 2008 and January 2021 at Seoul National University Hospital. In the clinical setting, HER2 IHC 3+ is defined as HER2 positive and no further ISH testing is required. Additional ISH was performed in patients with HER2 IHC 3+ without archival HER2 ISH results. The association between HER2/CEP17 ratio and treatment outcome was assessed.

Results: In total, 165 patients were included with a median follow-up duration of 28.0 months. Among the 165 patients, 35 patients had archival ISH result and additional ISH was performed in 53 patients. The correlation between HER2/CEP17 ratio and treatment outcome was assessed in 88 patients. Cox proportional hazard analysis revealed that HER2/CEP17 ratio is correlated with PFS (HR 0.23, 95% CI 0.11-0.49, $p < 0.001$). When dichotomized by the median

HER2/CEP17 ratio of 4.17, patients with higher HER2/CEP17 ratio had significantly longer PFS (37.5 vs. 17.4 months, $p = 0.003$) and numerically higher ORR (54.5% vs. 34.1%, $p = 0.085$). Multivariate analysis revealed that HER2/CEP17 ratio is an independent prognostic factor for PFS (HR 0.72, $p = 0.001$). Of 88 patients with ISH results, 25 had HER2 IHC 1+ or 2+ and 63 had HER2 IHC 3+. HER2/CEP17 ratio was associated with PFS in both HER2 IHC 1+/2+ patients (HR 0.12, 95% CI 0.02-0.88, $p = 0.037$) and HER2 IHC 3+ patients (HR 0.18, 95% CI 0.07-0.49, $p = 0.001$). Patients with higher HER2/CEP17 ratio had longer PFS in both HER2 IHC 1+/2+ patients (28.6 vs. 12.9 months, $p = 0.003$) and HER2 IHC 3+ patients (Not reached vs. 18.3 months, $p = 0.005$) when dichotomized by the median HER2/CEP17 of 2.95 and 4.75, respectively.

Conclusion: This is the first study to report that higher HER2/CEP17 ratio is associated with longer PFS in HER2-positive advanced breast cancer patients treated with palliative first-line DHP. The strength of this study is that we identified prognostic role of ISH even in patients with HER2 IHC 3+. It would be helpful to perform ISH not only in patients whose HER2 IHC is ambiguous, but also in patients with HER2 IHC 3+ to make better prediction of treatment outcome.

Table 1. Patient characteristics

	Number of patients (%) (N = 165)
Female sex	165 (100.0%)
Age	
Median	52
Range	22 – 79
Disease status	
De novo metastatic disease	76 (46.1%)
Recurrence	89 (53.9%)
Metastatic site	
Locally advanced	23 (13.9%)
Bone only	27 (16.4%)
Visceral metastasis	115 (69.7%)
Specific metastatic sites	
Liver	51 (30.9%)
Lung	61 (37.0%)
Brain	9 (5.5%)
Hormone receptor status	
HR+ (ER+ or PR+)	75 (45.5%)
HR- (ER- and PR-)	90 (54.5%)
HER2 IHC	
1+	2 (1.2%)
2+	23 (13.9%)
3+	140 (84.8%)

Disclosure(s):

Jeongmin Seo, n/a: No financial relationships to disclose

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12/6/2022

5:00 PM - 6:15 PM

P1-04-02

Gut microbiome diversity correlates with tumor PD-L1 status in metastatic triple negative breast cancer (mTNBC): correlative analysis of gut microbiome and tumoral biomarkers

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Background: Greater gut microbiome diversity is observed in patients with a clinical response to immune checkpoint inhibitor (ICI) therapy in solid tumors and in preclinical models targeting the gut microbiome is a promising strategy to improve ICI efficacy. The investigation of the immunomodulatory effects of the gut microbiome and tumor biology is in its infancy and whether interindividual microbiome variations correlate with tumor biology in breast cancer is unknown. Here we report a correlative analysis of gut microbiome diversity with tumor biomarkers: PD-L1, tumor immune cell density, tumor infiltrating lymphocytes (TILs), MutSig3, and interferon (IFN) gene signatures in a cohort of mTNBC patients treated with olaparib and durvalumab of the Adaptive Multi-Drug Treatment of Evolving Cancers (AMTEC) trial (NCT03801369). Methods: AMTEC participants undergo a baseline biopsy (bx) and fecal sample collection, then start olaparib monotherapy on a 28-day cycle. Following the first cycle, an on-treatment (on-tx) bx and fecal sample are collected, then as part of enrollment to Arm 1, durvalumab is added to the treatment regimen. Ten patients with stool collections and tissue biopsies were used in this analysis, eight had paired pre- and on-tx collections. At interim-analysis, participants were categorized as responders (PR/SD) or non-responders (PD). Gut microbiome composition in fecal samples collected pre- and on-olaparib monotherapy was

assessed by 16S rRNA sequencing and alpha diversity was quantified by observed diversity, Fisher, Inverse Simpson, Pielou, and Shannon indices. Response, PDL1 expression (Positive CPS >1), multiplex immunohistochemistry (mIHC) immune cell density and immune cell signature, TILs, RNA signatures including interferon (INF) family signatures, and mutational significance (MutSig3) were correlated to alpha diversity by T-test. Results: Average baseline alpha diversity of the fecal microbiome did not vary based on response (6 non-responses and 4 responses). However, in the on-tx samples, Fisher (CB: mean = 21.81, std. dev. = 3.6; PD: mean = 17.04, std. dev. = 2.3; p=0.048) and Observed alpha diversity (CB: mean = 260, std. dev. = 38.8; PD: mean = 209, std. dev. = 25.8; p = 0.049) were higher in responders. Average baseline alpha diversity of the gut microbiome as measured across all examined indices was significantly lower in participants with PD-L1 expressing tumors ($p < 0.05$ for each, T-test). Among on-tx samples, there was a trend toward lower alpha diversity in PD-L1 expressing tumors, but PD-L1 expression did not correlate with clinical response. There was a notable trend toward greater alpha diversity in on-tx bx and high TILs. Alpha diversity did not differ by immune cell densities by mIHC (CD8+ T cell, B cell, and regulatory T cells), hypo-inflamed/pro-inflammatory signature, IFN gene signature, nor MutSig3 score. Conclusion: Our preliminary data reveal that higher alpha diversity following olaparib monotherapy correlated with response to therapy with combination olaparib and durvalumab and correlated with tumor PD-L1 status. Whether gut microbiome features represent a meaningful biomarker for ICI treatment of mTNBC warrants further study. Enrollment to stage 2 of AMTEC Arm 1 is ongoing.

Disclosure(s):

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12/6/2022

5:00 PM - 6:15 PM

P1-04-04

A multiomic approach to the identification of immune signatures of anti-PD1/PDL1 therapy responders in metastatic triple negative breast cancer: new implications in the role of helper T-cell and B-cell interplay

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Introduction Triple negative breast cancer (TNBC) is a heterogeneous breast cancer subtype which continues to portend a particularly poor prognosis compared to other breast cancer subtypes. Immune checkpoint inhibitor (ICI) therapies have emerged as promising options for locally advanced and metastatic TNBC. However, clinical trials have demonstrated mixed

results with respect to ICI response. Given varied outcomes and the potential for immune-related adverse events associated with ICIs, there is critical need for identification of accurate biomarkers of response and improved strategies to counteract ICI resistance and/or toxicity. Methods Advanced immunoprofiling of peripheral blood mononuclear cells (PBMCs) and plasma from 7 metastatic TNBC patients with variable responses to anti-PD1 or anti-PDL1 therapy was performed. Samples were analyzed from blood draws obtained: (i) prior to first administration, (ii) while receiving ICI treatment, and (iii) at the time of conformed clinical progression or response to therapy. Response was determined by standard radiological assessment. Immunoprofiling included high parameter flow cytometry, single cell transcriptomics (10x genomics) and secretome analysis (Isoplexis). Single cell RNA profiles from 63,984 cells were analyzed. Results High parameter flow cytometry identified higher circulating levels of a subpopulation of activated CD4+ T cells with a phenotype of CXCR3low CD62Llow CD45RAhigh and CD57high expression in responders versus non-responders. Higher effector function of CD4+ T cells was corroborated by significantly elevated plasma concentrations of IL-2 ($p=0.02$) and IL-5 ($p < 0.0001$) among responders. Single cell transcriptomic analysis revealed clusters of B and T cells with distinct activation patterns that were associated with radiographic response. Strikingly, genes involved in B cell activation and T cell-B cell conjugation such as CD81 were found to be highly upregulated among CD4+ T cells from responders. Conclusions Our results are consistent with previous reports describing an association of increased B cell activity in TNBC with improved overall survival. We identified a subpopulation of CD4+ T cells with effector functions consistent with type 2 helper T cells that may not only target cancer cells by direct cytotoxic function, but also promote increased B cell anti-tumor activity. Our study provides insight into specific mechanisms of immune cell interplay that may drive response to ICI therapy. These cell populations and their associated pathways may represent potential biomarkers of response and/or targets for resistance reversal.

Disclosure(s):

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5:00 PM - 6:15 PM

P1-04-05

Independent validation of the HER2DX genomic test in HER2-positive breast cancer treated with neoadjuvant paclitaxel, trastuzumab and pertuzumab (THP): a correlative analysis from the DAPHNe phase II clinical trial

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Background: HER2DX is a 27-gene prognostic (risk-score) and predictive (pathological complete response [pCR]-score) assay in early-stage HER2+ breast cancer (BC) based on clinical data and the expression of 4 gene signatures (immune, proliferation, luminal differentiation, and HER2 amplicon). Here we aim to evaluate, for the first time, the ability of HER2DX to predict pCR following neoadjuvant THP in HER2+ BC.

Methods: Standardized HER2DX was evaluated centrally on baseline pre-treatment FFPE

tumor biopsies from the DAPHNe phase II trial (Waks et al. NPJ Breast 2022; NCT03716180), in which patients (pts) with newly diagnosed stage II-III HER2+ BC were treated with neoadjuvant weekly paclitaxel x12 and HP every 3 weeks x4. Primary aim was to test the ability of HER2DX pCR-score to predict pCR (ypT0/isN0). Secondary objectives were to test the ability of HER2DX pCR-score to predict pCR independent of clinical-pathological variables and PAM50 subtype (HER2-enriched vs not) and to evaluate the association of HER2DX pCR-score with HER2DX risk-score. Five patients who received additional neoadjuvant chemotherapy after THP were excluded from this analysis. Logistic regression and receiver-operator curve (ROC) analysis were assessed. Statistical analyses were performed in R code 4.0.5.

Results: HER2DX was evaluated in 80 of 97 pts (82.5%) enrolled in the DAPHNe trial who received study treatment. Clinical T2-4 disease represented 81.3% of cases (n=65), clinical node-negative disease (cN0) represented 65.0% of cases (n=52), and 70.0% of tumors (n=56) were hormone receptor-positive. The overall pCR rate was 60.0% (95% confidence interval [CI] 49.3-70.7): 87.0% (95% CI 79.6-94.4) in hormone receptor-negative disease and 48.2% (95% CI 37.2-59.1) in hormone receptor-positive disease. The proportion of HER2DX low-, medium- and high-pCR groups was 38.8%, 27.5% and 33.7%, respectively. HER2DX pCR-score (as a continuous variable from 0 to 100) was significantly associated with pCR (odds ratio [OR]=1.05, p< 0.0001). In the overall population, the pCR rates in HER2DX pCR-high, pCR-med and pCR-low groups were 92.6%, 63.6% and 29.0% (pCR-high vs pCR-low OR=30.6, p< 0.0001), respectively. The AUC ROC of HER2DX pCR score (as a continuous variable) and pCR status was 0.835. In the ER-negative population, the pCR rates in HER2DX pCR-high, pCR-med and pCR-low groups were 94.7%, 66.7%, and 0%, respectively (Table 1). HER2DX pCR-score was significantly associated with pCR independent of hormone receptor status, HER2 immunohistochemistry (IHC) score, clinical stage, and PAM50 HER2-enriched subtype. The correlation between HER2DX pCR-score and HER2DX risk-score was weak (Pearson coefficient=-0.12), as previously described (Prat et al. EBiomedicine 2022). 51.3% of patients were categorized as HER2DX low-risk.

Conclusion: The 27-gene HER2DX genomic test predicts pCR following neoadjuvant THP in newly diagnosed stage II-III HER2+ BC. Patients with HER2DX pCR-low score and HER2DX high-risk score, representing 22.5% of pts, warrant further attention in order to optimize therapeutic strategies in this subset. The combination of HER2DX pCR-score and risk-score might guide therapeutic decisions by identifying patients who are ideal candidates for de-escalated or escalated systemic and locoregional treatments.

Table 1

HER2DX pCR score group / ER IHC status	N	%	pCR rate	HER2DX pCR score group / HER2DX risk of relapse group	N	%	pCR rate
High/ER+	8	10.0	87.50%	High/High	14	17.5	92.90%
High/ER-	19	23.7	94.70%	High/Low	13	16.3	92.30%
Med/ER+	16	20.0	62.50%	Med/High	7	8.7	57.10%
Med/ER-	6	7.5	66.70%	Med/Low	15	18.8	66.70%
Low/ER+	30	37.6	30.00%	Low/High	18	22.5	27.80%
Low/ER-	1	1.2	0.00%	Low/Low	13	16.2	30.80%

Disclosure(s):

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5:00 PM - 6:15 PM

P1-04-06

Characterization of recurrence risk after lumpectomy and radiotherapy in HER2-positive ductal carcinoma in situ of the breast, using 7-gene predictive biosignature: Implications for the NSABP-B43 trial results

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Background: HER2-positive versus HER2-negative ductal carcinoma in situ (DCIS) of the breast has been associated with an increased risk of local recurrence after breast-conserving surgery (BCS) and radiotherapy (RT). In recognition of this, the NASBP-B43 trial was designed to determine if two doses of trastuzumab would improve local control with BCS plus RT in HER2-positive DCIS. The trial demonstrated a non-statistically significant advantage with the addition of trastuzumab in reducing ipsilateral breast recurrence (IBR). The predictive 7-gene DCIS biosignature, DCISionRT with Residual Risk Subtype (PreludeDx™, Laguna Hills, CA) has been shown to classify DCIS patients into two distinct groups of patients with substantially different rates of IBR following BCS plus RT. Based upon these differences in outcome, we assessed the IBR rate in patients with HER2(+) DCIS treated with BCS and RT who were or were not in the Residual Risk Subtype group defined using DCISionRT, while accounting for the varying clinicopathologic profile of the patients.

Materials & Methods: DCISionRT was evaluated in a subset of 178 women with HER2(+) DCIS treated with BCS and RT as part of a multinational cohort of 926 patients from the United States, Sweden, and Australia, who were used in the validation studies for DCISionRT. Central pathology review and biosignature testing were performed at a CLIA-certified lab (Laguna Hills, CA). HER2(+) DCIS was defined as patients with a HER2(3+) immunohistochemistry >10% per ASCO/CAP guidelines. The IBR rate was calculated for the overall group of HER2(+) patients and those in the Residual Risk group. Individual patient outcome and biosignature results were analyzed using Kaplan Meier and Cox Proportional Hazard analyses.

Results: The biosignature classified 113 of the 178 (63%) HER2(+) women into the Residual Risk group (DS>2.8 with RRt). Patients in the Residual Risk group had a significantly greater IBR (HR=8.3; 95%CI: 1.1,50, p=.012) over 10-years, with a corresponding 10-year total IBR rate of 16.2% (95%CI: 9.7%, 26.5%) versus 1.6% (95%CI: 0.2%, 10.9%) for all other HER2(+) patients.

In univariate analysis, younger patients tended to have higher IBR rate after BCS plus RT, but only Residual Risk was significantly associated with IBR rate after BCS plus RT. Moreover, multivariable analysis demonstrated that the Residual Risk group was eight times more likely to recur after BCS and RT, while clinicopathologic factors (age, grade, tumor size) were not associated with higher IBR rates.

Conclusion: The DCISionRT Residual Risk group was predictive for 10-year IBR risk after BCS plus RT in women with HER2(+) DCIS. Approximately 40% of patients with HER2(+) DCIS

would be expected to achieve low rates of recurrence with BCS and RT, while about 60% of these women (classified in the Residual Risk group) would have higher recurrence rates and may benefit from further therapy, such as HER2-directed therapies. These findings suggest that if the results of the B43 trial were re-analyzed using the predictive 7-gene biosignature (DCISionRT with Residual Risk Subtype), better clarity could be gained on the true impact of trastuzumab on IBR rates in patients with HER2(+) DCIS and the patients most likely to benefit from this additional therapy.

Table 1: Univariate and Multivariable Cox Proportional Hazards Analyses

Factors	Multivariable		Univariate	
	HR 95% CI	p value	HR 95% CI	p value
Biosignature Residual Risk group (vs Low and Elevated Risk groups)	7.9 (1.0, 63)	.048	8.5 (1.1, 67)	.038
Extent >10 mm (vs ≤ 10 mm)	2.4 (0.8, 7.1)	.17	2.8 (0.7, 5.8)	.16
Grade 3 (vs Grade 1 and 2)	1.0 (0.2, 4.7)	.98	1.8 (0.4, 8.1)	.42
Age<50 (vs ≥age 50)	2.6 (0.9, 7.5)	.07	2.4 (0.9, 6.7)	.09

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P1-04-07

pCR Score: a novel prognostic method to estimate the predictive probability of pCR in early-stage breast cancer patients.

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Background: A gap in personalized medicine exists in the absence of a test to assess the probability of pathological complete response (pCR) for early-stage breast cancer patients. We have previously shown that our TumorScope platform, which utilizes pretreatment standard-of-care (SOC) diagnostic data to model in-vivo biologic interactions, can reliably predict a binary outcome of pCR for a given patient with any physician-chosen SOC neoadjuvant chemotherapeutic (NAC) regimen. To drive further utility, we now investigate a pCR score as a continuous outcome (0-100) to establish a prognostic system that evaluates the predictive probability that a patient will achieve pCR with any SOC NAC regimen. Furthermore, we sought to establish thresholds (low, low-mid, high-mid, high) and corroborate the score's utility in the context of 5-year EFS. Methods: The total cohort consisted of 1050 patients from seven institutions. The pCR Score was calibrated with a training cohort consisting of 665 patients of all breast cancer subtypes. We used a logistic regression model to calculate the probability of pCR for each individual patient based on NAC regimen, clinical and multiscale simulation predictors. For all breast cancer subtypes, the baseline model included the following clinical variables: age, race, grade, T stage, N stage. For hormone receptor-positive (HR+) and HER2+ subtypes, ER, PR and HER2 status were included. The TumorScope model included the clinical variables and simulation derived features including modeled tumor volume at start (V_s) and end (V_e) of therapy ($V_s + V_e$). We compared the TumorScope model (clinical variables + simulation variables) to the model consisting solely of clinical variables. We then calculated the prognostic ability of the pCR score to corroborate EFS in an independent testing cohort of 385 patients. Patients were stratified according to the likelihood of pCR into high, high-mid, low-mid or low probability and correlated to the 5-year event-free survival (EFS) for all patients and per breast cancer subtype. Results: TumorScope showed superiority in predicting pCR probability in all breast cancer subtypes calculated as the number of times that TumorScope outperformed the clinical model: HR+/HER2- (70% of 233 cases, $p=6 \times 10^{-8}$), HR+/HER2+ (79.6% of 162 cases, $p=8 \times 10^{-13}$), HR-/HER2+ (72.2% of 115 cases, $p=2 \times 10^{-6}$) and TNBC (96.4% of 253 cases, $p=3 \times 10^{-12}$). In the overall analysis, patient EFS at 5-year follow-up according to pCR score was as follows: low pCR score ($n=76$) 61% EFS, low-mid pCR score ($n=126$) 75% EFS, high-

mid pCR score (n=86) 82% EFS, and high pCR score (n=97) EFS 96%. EFS was also calculated for each breast cancer subtype stratified into high or low pCR score; high pCR score correlated with the best 5-year EFS and low score correlated with poor 5-year EFS in alignment with empiric expectations. Of the different subtypes, HR+/HER2+ with high pCR score had the best 5-year EFS (~85-90%) and TBNC with low pCR score had the worst EFS (55-60%). Conclusion: The TumorScope pCR (continuous) score system offers an enriched test output to further refine prognostic capability beyond a conventional binary (yes/no) result and permits risk-stratification of patients into predictive categories. Here, we validate the TumorScope pCR score as a reliable metric using a large, multicenter cohort. The TumorScope pCR score can be correlated with 5-year EFS in an easy-to-understand format, concurrent with currently available prognostic tests in the market. As the TumorScope model uses pre-treatment information for predictions, it may be a valuable tool to inform treatment-related outcomes in patients receiving NAC.

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P1-04-08

Independent Validation of a Novel, Non-invasive Approach to Predict Pathologic Complete Response (pCR) in a Blinded, Prospectively-Run Single Center Trial

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Background: As pathologic complete response (pCR) is correlated with higher rates of event free survival, accurately forecasting pCR advances our collective endeavors in precision oncology to discern and translate individual patient-specific data into risk stratification. We developed the TumorScope engine, a software platform that utilizes pretreatment diagnostic data to build a computational tumor model that simulates in vivo tumor characteristics and interactions, incorporating morphology, metabolism, vascularity, and nutrient and drug delivery. This non-invasive approach enables accurate forecasting of a patient's response to physician-chosen neoadjuvant chemotherapy-based treatment (NAC). Here we validate the prognostic capacity of this technology at a single site cancer center.

Methods: A blinded, prospective trial using retrospective data was conducted at UNC. The study cohort included patients aged 18 years or older diagnosed with any subtype of breast cancer who were treated with a NAC regimen and had a pre-treatment T1-weighted dynamic contrast enhanced (DCE) MRI available. Pre-treatment diagnostic and planned treatment data (demographics, drug regimen, receptor status (ER/PR/HER2), DCE MRI, and pathology) were input into the TumorScope engine to simulate predicted final tumor volumes (V_t) for each tumor and predict pCR or residual disease (RD); pCR predictions were compared to post-surgery pathologic assessments defined as ypT0/is/N0. Predicted pCR was set at pre-defined threshold of predicted V_t less than 0.01 cm^3 , or at least a 99.9% V_t reduction.

Results: One hundred and fifty subjects with 157 tumors were enrolled in the study. After excluding missing data (absent DCE-MRI), a total of 143 cases in 136 patients were included. The majority of patients self-identified as Caucasian (63%) or African American (23%). TumorScope had a pCR overall prediction accuracy of 92.3% (95% CI: 86.7 - 96.1%) with a sensitivity of 90.9 % (95% CI: 75.7 - 98.1 %) and specificity of 92.7% (95% CI: 86.2 – 96.8%). Based on our subgroup analysis, predictive accuracy remained reliable for HR+/HER2- (n=65; 95.4%), HR+/HER2+ (n=20; 85.0%), HR-/HER2+ (n=21; 85.7%) and TNBC (n=37; 94.6%) subtypes. Predictive performance remained stable across ethnic subtypes and tumor grade (see Table 1).

Conclusion: The TumorScope noninvasive method that incorporates imaging, pathologic, demographic and planned treatment data appears to accurately predict an individual patient's probability of pCR across clinical subtypes.

Table 1. TumorScope prediction performance.

	Overall n=143 (95% CI)	TNBC n=37 pCR rate=48% (95% CI)	HR-/HER2+ n=21 pCR rate=45% (95% CI)	HR+/HER2- n=65 pCR rate=3% (95% CI)	HR+/HER2+ n=20 pCR rate=20% (95% CI)
pCR	0.923	0.946	0.857	0.954	0.850
Accuracy	(0.867, 0.961)	(0.818, 0.993)	(0.637, 0.970)	(0.871, 0.990)	(0.621, 0.969)
pCR	0.909	0.944	0.900	1.000	0.750
Sensitivity	(0.757, 0.981)	(0.727, 0.999)	(0.555, 0.997)	(0.024, 1.000)	(0.194, 0.993)
pCR	0.927	0.947	0.818	0.953	0.875
Specificity	(0.862, 0.968)	(0.740, 0.999)	(0.482, 0.977)	(0.869, 0.990)	(0.617, 0.984)

Disclosure(s):

Cherie Kuzmiak, M.D.: No financial relationships to disclose

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P1-04-09

Correlating Predicted Adjuvant Therapy Benefit and Risk of Recurrence between Breast Cancer Index (BCI) and 21-gene Oncotype DX Recurrence Score (RS)

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Background: The 21-gene Recurrence Score (Oncotype DX) is a genomic assay that provides prognostic information for distant recurrence risk and is predictive of adjuvant chemotherapy benefit in hormone receptor (HR)-positive, HER-2 negative early-stage breast cancer (EBC). The Breast Cancer Index (BCI) is another molecular gene expression-based assay that evaluates the utility of extending adjuvant endocrine therapy (ET) from 5 to 10 years and

predicts risk of distant recurrence. In January 2021, the National Comprehensive Cancer Network (NCCN) Guidelines added BCI to guide duration of adjuvant ET as a category 2A recommendation. The goal of this study was to evaluate the association between BCI and RS in terms of their predicted benefit for adjuvant therapy and risk of distant recurrence. We also assessed the association of various anatomic and biologic tumor features with BCI. Methods: We performed a retrospective chart review of all patients with HR-positive EBC who had a BCI and Oncotype DX performed between 2007-2021. Demographics, tumor characteristics and BCI and RS results were extracted from the electronic medical record. Patients were categorized by BCI predictive of extended ET (formerly BCI high) versus not (formerly BCI low) and RS of low (0-10), intermediate (11-25) and high (26-100). Numerical values for distant recurrence risk were recorded for both BCI and Oncotype DX tests. Multivariable regression models were used to assess the relationship between BCI and Oncotype DX as well as factors associated with each. Results: We identified 153 women with HR-positive EBC with both RS and BCI performed. The median age of the population was 57 years and 25% were premenopausal. 32% (n=49) had a BCI result predictive of benefit from extended adjuvant ET. When comparing patients with BCI predictive of extended ET versus those with BCI not predictive of extended ET, there was no association between BCI and RS based on multivariate logistic regression models, $p=0.7$. A similar distribution of RS was observed between patients who had a BCI result predictive of benefit from extended ET versus not predictive. Among 49 patients with a BCI predictive of extended ET, 35% had high RS, 63% intermediate RS and 2% low RS. Among 104 patients with a BCI not predictive of extended ET, 24%, 73% and 3% had high, intermediate, and low RS, respectively. Multivariate regression models revealed an association between poorly differentiated tumors and BCI result predictive of extended ET, $p=0.002$. No associations were observed between BCI and menopausal status, ER%, PR%, tumor size or lymph node positivity. Regarding risk of recurrence, there was an association between BCI and Oncotype DX in terms of their predicted numerical risk of recurrence, $p<0.001$. Higher percentage of PR positivity, poorly differentiated tumors, and lymph node positivity were associated with a higher risk of recurrence on the BCI. Conclusions: In our patient population selected to have Oncotype DX and BCI performed, we found no association between the two genomic assays in terms of their predictive benefit. However, there was an association between Oncotype DX and BCI in terms of their prognostic ability. Given the increased use of BCI since its inclusion in national guidelines, it is important to understand its relationship with other genomic assays especially when used to guide clinical decisions and estimate prognosis.

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P1-04-10

Association of stromal tumor infiltrating lymphocytes (sTILs) in pretreatment biopsies in different molecular subtypes of HER2+/ER+ breast cancer: Assessment of NRG Oncology/NSABP B-52

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Background: The primary aim of the NRG Oncology/NSABP B-52 clinical trial was to test if estrogen deprivation (ED) administered concomitantly with neoadjuvant docetaxel, carboplatin, trastuzumab, and pertuzumab (TCHP), would improve the pCR rate in patients with HER2+/ER+ early breast cancer. A numerical increase in the pCR rate was observed with ED (46.1% v 40.9%), but the difference was not statistically significant. The purposes of this study were to assess the association of sTILs in pretreatment biopsies with pCR in the total population and within the molecular subtypes of breast cancer and to assess changes in sTILs between pre- and on-treatment biopsies. The secondary endpoints of recurrence-free interval (RFI) and overall survival (OS) are currently being analyzed and will be presented along with association of these endpoints with sTILs in pretreatment biopsies in the total cohort and within molecular subtypes. Methods: Scoring of sTILs on routine H&E slides from pre-treatment biopsies with sufficient tumor from 249 of the 315 patients (79%) entered in B-52 were performed by one of two pathologists (SKM, RSM). Both pathologists scored sTILs on a subset of 64 patients to document concordance. Wilcoxon two-sided test, box and whisker plots, and forest plots were used to assess associations with pCR. Molecular subtypes were determined utilizing RNA-seq data and AIMS subtyping method. On-treatment biopsies were available in 46 patients and were scored and compared to paired baseline samples. Results: Good concordance between pathologists was established with an inter-pathologist difference of <20% difference between scores in 92% of cases. sTILs in pre-treatment samples were associated with pCR across both arms of the trial (p=0.0074) and in the TCHP+ED arm (p=0.033), but not in the TCHP arm (p=0.093). The distribution of intrinsic subtypes was 34% luminal B, 29% luminal A, 28% HER2E, 5.8% normal, and 2.7% basal, with no significant differences between the arms. Presence of sTILs showed a trend for association with pCR in HER2E pre-treatment samples (p=0.054) but not in non-HER2E (p=0.75). Similarly, sTILs were associated with pCR in non-luminal tumors (p=0.055) but not in luminal tumors (p=0.44). Stratification by treatment

arm and menopausal status suggested sTILs are associated with pCR in premenopausal women treated with TCHP (OR: 1.04, 95% CI=1.00-1.09). Interestingly, decreases in the sTIL scores with treatment were associated with pCR in the TCHP+ED arm (p=0.01) but not in the TCHP arm. Analysis of RFI and OS on B-52 is ongoing and will be presented along with associations of sTILs with intrinsic subtypes for RFI and OS. Conclusions: Although a positive correlation between sTILs and pCR was observed, the clinical utility appears limited because of the extensive overlap in the TIL scores between pCR and non-pCR tumors. Significance for a positive association of sTILs with pCR was detected in HER2E but not in luminal tumors. This may be due to the molecular differences of the subtypes, or the make-up of the TILs, or both. The association of a decrease in sTILs with TCHP+ED treatment needs further investigation. The small number of samples is a limitation of the study; however, the B-52 protocol specified that the collection of the B-52 samples was for the purpose of exploratory analysis. Our results highlight the molecular heterogeneity of the HER+/ER+ patient population and suggests that different treatment strategies may be required in future treatment regimens for this patient population. Support: NSABP Foundation; BCRF; 3U10CA180868-03S2, -180822; UG1CA189867; Genentech.

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Tumor Infiltrating Lymphocytes in initial HER2-Low breast cancer

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Rationale Human Epidermal Growth Factor Receptor 2 (HER2)-positive breast cancer (BC) represents a distinct subgroup of patients (pts) that derives significant benefits from anti-HER2 therapy. More recently, patients with metastatic BC that were previously considered HER2-Negative but with low positivity by immunohistochemistry (IHC) and a negative in situ hybridization (ISH) (HER2 1+, or 2+ with negative ISH) derived benefit from treatment with trastuzumab-deruxtecan (T-Dxd), an antibody-drug conjugate that targets HER2 receptor. This novel subgroup, termed HER2-Low (H-Low), represents nearly 60% of BCs. Tumor infiltrating-lymphocytes (TILs) are a biomarker that can be easily analyzed without additional stains, and that tend to be higher in tumors with more aggressive features. High levels of TILs can predict better outcomes in triple-negative (TN) and HER2-Positive (H-Pos) tumors. To date, there is no information about TILs levels in H-Low tumors. Objectives This work aims to determine TILs levels in HER2-Low tumors and their correlation with clinicopathologic features. Methods We retrospectively analyzed tissue from breast surgical products in a tertiary hospital in Sao Paulo, Brazil, from January 2021 to March 2022. Inclusion criteria were stage I to III invasive BC and available data for TILs, HER2, estrogen receptor (ER), progesterone receptor (PR) by IHC, and ISH, when applicable. Exclusion criteria was neoadjuvant therapy. We extracted clinical, histopathologic, and IHC parameters. HER2 subtypes were defined as follows: HER2-Negative (H-Neg) when HER2 0+ in IHC; H-Low when IHC 1+, or 2+ with ISH negative; and H-Pos when IHC 3+ or 2+ with ISH positive. TILs were defined as absent (0), low (1 to 9%), intermediate (10 to 39%) and high (>40%). Ki-67 levels were divided as low (up to 19%) and high ($\geq 20\%$). Results We included 202 eligible pts. 128 were H-Neg, 51 were H-Low (35 IHC 1+ and 16 IHC 2+ with ISH negative), and 23 were H-Pos. Four pts were TN in H-Neg and none in H-Low group. The mean ages for H-Neg, H-Low and H-Pos were 57, 51, and 57 years, respectively. ER and PR were negative in 3.1% and 11.7% of H-Neg, 0 and 7.8% of H-Low, and 52.4% and 56.5% of H-Pos. Ki-67 levels were high in 27.3% of H-Neg, 31.4% of H-Low and 82.6% of H-Pos. Nodal stages and multifocality were similar. Ductal histology had 89 (69.5%), 45 (88.2%), and 21 (91.3%) cases for H-Neg, H-Low, and H-Pos. Lobular carcinoma was found in 30 (23.4%) in H-Neg, 4 (7.8%) in H-Low, and none in the H-Pos group. Nuclear grade (NG) 2 was seen in 64.8% of H-Neg and 62% of H-Low. Nuclear grade 3 seen was in 82.6% of H-Pos. Histologic grade 1 was present in H-Neg and H-Low, with 29.7% and 25.5%; grade 2 was seen in 56.3% and 56.9%, respectively. In H-Pos grade 3 was found in 47.8%. Angiolymphatic invasion and perineural invasion were present in 26.6%, 35.3%, and 17.4%; and 26.6%, 35.3%,

and 13% of H-Neg, H-Low and H-Pos respectively. TILs in H-Neg, H-Low, and H-Pos were, respectively, absent in 16.4%, 17.6%, and 8.7%; low in 69.5%, 52.9% and 34.8%; intermediate in 11.7%, 25.5% and 47.8%; and high in 2.3%, 3.9% and 8.7%. We divided samples into TILs levels to look at the distribution of HER2 subtypes. Absent, low, intermediate, and high TILs had respectively 32, 124, 39, and 7 cases. There were more H-Neg in low TILs and H-Pos in high TILs, with, respectively, 65.6% and 6.3% of absent; 71.8% and 6.5% of low; 38.5% and 28.2% of intermediate; and 42.9% and 28.6% of high TILs. Conversely, H-Low showed stability among the groups, with 28.1%, 21.8%, 33.3%, and 28.6% in absent, low, intermediate, and high TILs, respectively. Complete data and statistical analysis will be presented at the meeting. Conclusion TILs in H-Low are similar to H-Neg. Both had lower TILs compared to H-Pos pts. In our study, only 25% were defined as H-Low, which demonstrates that a better comprehension about prevalence or pathology concordance between HER2 IHC 0 and 1+ is warranted. TILs may not play a role as a biomarker in H-Low tumors.

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5:00 PM - 6:15 PM

P1-04-12

Systemic immune response to a Phase I/II trial of Durvalumab concomitant with neoadjuvant chemotherapy in early stage TNBC

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Background Peripheral blood cells and secreted products are important regulators of the systemic immune response. Circulating cytokines have been shown to predict severity of immune-related toxicity in melanoma patients that received combination anti-PD-1-based immunotherapy. In this study, we evaluated 38 serum cytokines and the peripheral blood t cell receptor (TCR) immune repertoire of 66 patients with TNBC for associations with pCR, treatment phase (PRE; POST), and immune related treatment emergent adverse events (TEAEs). Methods Serum and peripheral blood buffy coats were collected at pre-treatment (week 0) and at post-treatment (~ week 24). MILLIPLEX MAP Human Cytokine/Chemokine Magnetic Bead Panel was run in duplicate and read on the Luminex platform. Genomic DNA was isolated using QIAGEN Kits per manufacturer's instructions. TCR immune repertoire profiling was performed using the Immunoseq at Adaptive Biotechnologies. Statistical analysis was performed in R. P-values < 0.05 for serum cytokines and P-values < 0.05 for TCR were considered significant. Results Pielou's diversity index showed no difference between patient groups for TCR (P>0.319). Baseline samples had increased sCD40L, EGF, and IL-10 in patients with RD compared to pCR (P< 0.05). Baseline samples had decreased FGF2 and IFN gamma in patients with immune related TEAEs compared to those with no immune related TEAEs (P< 0.05). Comparison of Pre- vs Post-treatment revealed that EGF, MIP1 alpha, IL-1 alpha, IL-8, and MDC were increased in patients with pCR compared to those with RD. Comparison of Pre- vs. Post- also revealed increased levels of cytokines (EGF, IL-7, IFN gamma, GM-CSF) in samples in patients with immune related TEAEs (P< 0.05) compared to those patients without immune-related TEAEs. It also revealed that there was an increase in a subset of cytokines (IL-7, IL-4, MCP3, and IL-1 alpha) in patients that presented with serious immune related TEAEs (P< 0.05) compared to those patients without serious immune-related TEAEs. Conclusions There are subsets of circulating inflammatory cytokines that may be associated with treatment emergent adverse events in patients with TNBC treated with Durvalumab concomitant with standard of care chemotherapy.

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P1-04-14

Predicting the likelihood of response in PDL-1 positive metastatic triple negative breast cancer treated with an immune checkpoint inhibitor

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Background: Patients with metastatic triple negative breast cancer (mTNBC) have a poor prognosis with median survival of 18 months or less. While the combination of immune checkpoint inhibitors (ICIs) and chemotherapy has shown promise in mTNBC, biomarkers beyond PDL-1 are needed to better predict which individuals will benefit from this treatment approach. In this study, we assessed the ability of spatial characteristics in predicting clinical best response in patients with PDL-1 positive mTNBC treated with an ICI and chemotherapy. Methods: Women with advanced unresectable or mTNBC treated with an ICI plus chemotherapy at Emory University between 2019 and 2021 with available biopsy specimens were retrospectively evaluated. Different cell types (tumor, stroma, immune cells) were identified by morphology on H&E staining. A cellular network was created by connecting each cell centroid to its adjacent centroids within a 30- μ m distance. The resulting spatial neighborhood network was used to assess tumor density and quantify immune infiltration. The immune infiltration score was defined as the number of immune to tumor cell neighbors divided by the total number of immune cell neighbors in a region of 75- μ m. A final immunoscore was calculated for each patient by averaging the immune infiltration scores in regions with high tumor cell density. Tumor infiltrating lymphocytes (TILs) were manually quantified. Responders were defined as those with a complete response (CR), partial response (PR), or stable disease (SD), while those with progressive disease (PD) were categorized as non-responders. A continuous response score was developed from tumor measurements of a target lesion on

serial imaging. Pearson's correlation coefficients were used to assess the relationship between continuous response scores and tumor characteristics. Responders and non-responders were compared using Mann-Whitney U tests. Results: Fifteen women with PDL-1 positive mTNBC treated with ICI plus chemotherapy and available tissue were included. All patients had relapsed disease, and 10 patients (67%) received an ICI and chemotherapy as first line treatment for mTNBC. Eight patients (53%) received atezolizumab and nab-paclitaxel while the remaining 7 (47%) patients received pembrolizumab with an approved chemotherapeutic agent. Seven patients (47%) experienced a PR, 3 (20%) with a CR, and 1 (7%) had SD. Four patients (27%) had PD with no clinical benefit. Higher immunoscores (-0.17, $p=0.6$) and TILs (-0.21, $p=0.5$) were numerically associated with continuous response scores. However, there were no significant differences in immunoscores (0.28 vs 0.26, $p=0.6$) or TIL counts (2 vs 5, $p=0.6$) between responders (N=11) and non-responders (N=4). Interestingly, patients with response to treatment had lower tumor densities compared to non-responders (7.5 vs 17.3, $p=0.02$). Conclusions: Spatial analysis of tumor density and immune infiltration, including immunoscore shows evidence of correlation with response. Tumor density was the only parameter significantly associated with response. The study identified novel tumor characteristics that need to be considered in the prediction of response to ICIs plus chemotherapy in mTNBC. The current findings are hypothesis generating and need validation in additional tissue samples to determine the role of tumor density as a predictor of response to ICI.

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P1-04-15

Clinical application of 21-gene breast-cancer assay (Oncotype DX) in early hormone-receptor–positive, human epidermal growth factor receptor 2 (HER2)–negative breast cancer with Lymph-Node-Positive Disease

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The 21-gene breast-cancer assay (Oncotype DX) has become widely available since 2011 and it is incorporated in treatment guidelines for early hormone-receptor–positive, human epidermal growth factor receptor 2 (HER2)–negative breast cancer. The Rxponder trial shows the role of adjuvant chemotherapy in node positive patients with a RS score less than 25, but in patients under 50 years of age benefit from adjuvant chemotherapy treatment regardless of the Oncotype. We analyzed our results of the Oncotype Dx in 317 node positive hormone-receptor–positive, HER2-negative early breast cancer patients, performed as a clinical practice since 2015 to 2020. The aims to current study are to examine the clinical significance of the oncotype Dx results in this specific population. The median age was 59 years with 102 patients (32%) less than 50 years. Median Oncotype DX score was 18 (1–68), RS< 25 in 247 (78%) and RS>25 in 70 (22%) patients. Median initial tumor size was 20 mm and the expression of classical biological variables was: median estrogen and progesterone receptors by immunohistochemistry 276 and 139 respectively and median Ki67 index was 23%. 145 patients received chemotherapy treatment (45,7%), (RS < 25:32%, RS>25: 94%) with a 63% of the

patients in the group less than 50 years of age in contrast to 36% in patients with more than 50 years. Patients with more than 50 years have less RS score (median 18) than patients less than 50 years (median 21). With a median of follow up of 45 month with achieved a total of 29 recurrence (9,1%), RS< 25: 8% and RS>25 13%. The estimated median disease free survival of patients with RS< 25 was 111 in contrast to 97 in patients with RS>25 (log rangk : p:0,035) and without differences according with age of the patients. In axillary node positive patients, Oncotype Dx could avoided chemotherapy in 55% of patients, with a index of recurrence of 9%. Patients with a RS score greater than 25 have a higher rate of recurrence (13%) despite the fact that the majority (94%) received treatment with chemotherapy. Improve adjuvant treatment is needed in patients with a score greater than 25.

Disclosure(s):

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A nomogram based on clinicopathologic factors and pretreatment systemic inflammation response index to predict pathological complete response of neoadjuvant systemic therapy in HER2-positive breast cancer: A dual-center study

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Purpose:

Multiple pretreatment systemic inflammatory markers (SIMs) have been reported as predictors of pathological complete response (pCR) after neoadjuvant systemic therapy (NST) in patients with breast cancer (BC). However, the most significant SIM remains to be conclusively identified, and variations among different molecular subtypes remain unknown. The objective of the study was to identify the most significant SIM in patients with human epidermal growth factor receptor 2 (HER2) positive BC, and to construct a pCR-predictive nomogram combining it with other clinicopathological factors.

Methods:

We retrospectively reviewed the findings for 240 patients with stage I–III HER2-positive BC who underwent NST and subsequent surgery at Kaohsiung and Taichung Veterans General Hospital from 2011 to 2021. Clinicopathological factors were analyzed by stepwise logistic regression with forward selection. The data were used to construct a nomogram plot for determining the probability of pCR.

Results:

Among the pretreatment SIMs, only SIRI was significantly related to pCR, with an optimal cutoff value of $1.27 \times 10^9/L$. Stepwise logistic analyses indicated that clinical N stage, HER2 immunohistochemistry (IHC) score, hormone receptor status, targeted therapy regimen, and SIRI were independent predictors of pCR, with an area under the curve (AUC) of 0.722. The Hosmer–Lemeshow test and calibration curve revealed that the predictive ability was a good fit to actual observations. A nomogram was constructed based on the logistic model.

Conclusions:

Pretreatment SIRI < 1.27 is predictive of pCR in HER2-positive BC. Our nomogram could efficiently predict pCR and facilitate clinical decision-making before neoadjuvant treatment.

Univariable and multivariable analyses for predictive factors of pathological complete response of neoadjuvant systemic therapy in HER2-positive breast cancer

Variables	Univariable analysis		Multivariable analysis	
	OR (95%CI)	p value	OR (95%CI)	p value
Age, years	0.99 (0.96-1.01)	0.272		
BMI, kg/m ²				
<25	1			
≥25	0.68 (0.39-1.16)	0.156		
Clinical T stage				
cT1-2	1			
cT3-4	0.44 (0.22-0.86)	0.017		
Clinical N stage				
cN0	1		1	
cN1-3	0.29 (0.16-0.53)	<0.001	0.25 (0.13-0.48)	<0.001
HER2				
IHC 2+, FISH+	1		1	
IHC 3+	4.52 (1.64-12.47)	0.004	4.60 (1.54-13.78)	0.006
Hormone receptor				
ER- or PR-	1		1	
ER+/PR+	0.56 (0.33-0.95)	0.031	0.50 (0.28-0.91)	0.023
Ki-67				
<20%	1			
≥20%	0.75 (0.27-2.09)	0.580		
Unknown	0.78 (0.16-3.80)	0.756		
Histologic type				
Invasive ductal carcinoma	1			
Others	0.63 (0.23-1.67)	0.349		
Histologic grade				
1-2	1			
3	0.83 (0.49-1.41)	0.496		
Unknown	1.27 (0.42-3.88)	0.677		
Chemotherapy regimen				
Taxane	1			
Taxane+Anthracycline	0.98 (0.55-1.75)	0.941		
NST duration				
<12 weeks	1.55 (0.43-5.65)	0.504		
≥12 weeks	1			
Targeted therapy				
Trastuzumab	1		1	
Trastuzumab+Pertuzumab	1.60 (0.94-2.73)	0.087	1.85 (1.03-3.32)	0.040
ALC, 10 ⁹ /L	0.92 (0.58-1.44)	0.704		
NLR	0.90 (0.77-1.05)	0.181		
PLR	0.997 (0.994-1.001)	0.135		
LMR	1.10 (0.97-1.25)	0.121		
SIRI, 10 ⁹ /L	0.69 (0.49-0.98)	0.038		
<1.27	1		1	
≥1.27	0.54 (0.31-0.93)	0.026	0.55 (0.30-0.996)	0.048

Multivariable analysis was based on forward stepwise logistic regression (likelihood ratio) analysis
OR, odds ratio; CI, confidence interval; BMI, body mass index; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; FISH, fluorescence in situ hybridization; ER, estrogen receptor; PR, progesterone receptor; NST, neoadjuvant systemic therapy; ALC, absolute lymphocyte count; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; LMR, lymphocyte-monocyte ratio; SIRI, systemic inflammation response index

Disclosure(s):

Hong Yu Wu, M.D.: No financial relationships to disclose
Yen-Dun Tzeng, M.D.: No financial relationships to disclose
Jie Ru Yang, M.D.: No financial relationships to disclose
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: Clinical and pathological differences between HER2 Low and other cancer subtypes in breast cancer patients

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Background: HER2 is a tyrosine kinase receptor belonging to the human epidermal receptor family and is considered an important proto-oncogene in the biology of breast carcinoma. HER2 overexpression is determined by a +3 score on the immunohistochemistry (IHC) assay. In addition, tumors with IHC results of +1 or +2 with ISH negative were defined as HER2-low. Recent studies have shown that the clinicopathological characteristics of HER2-low tumors, pointing out potential differences regarding hormone receptor status and new treatment possibilities in this patients. Objective: To assess the frequency and clinicopathological differences between cancer subtypes, as well as the survival of these patients. Methods: All patients with breast cancer diagnosed between 1987 and 2021 included in the Pérola Byington Hospital database were eligible. Patients were excluded if they had bilateral disease, had participated in clinical studies, or had incomplete data. The primary endpoint was overall survival stratified by cancer subtype, secondary endpoints were clinicopathological differences between cancer subtypes and death probability. Both the t-test and the chi-square test were used to analyze the association of each variable between the groups. Multivariate analysis was used to calculate odds ratios (OR) and 95% confidence intervals (CI) for the death outcome. Cox regression was used for survival analysis, with the Log-rank method and the results were presented in a survival graph using the Kaplan-Meier method. The R software version 4.1.1 was used to perform all analyzes, with a p-value < 0.05 being considered statistically significant. Results: 11,234 patients were included: 4,541 (40.42%) had Luminal cancer subtype, 2,955 (26.30%) HER2 Low, 2,242 (19.96%) triple negative, and 1,496 (13.32%) HER2 overexpression. Age, self-reported ethnicity, BMI, presence of comorbidities, clinical stage, nuclear grade, histological grade, family history, radiotherapy, chemotherapy, surgery, local, and systemic recurrence, and death showed statistically significant differences between cancer subtypes (table 1). In the multivariate regression (adjusted for the other evaluated

characteristics), patients with HER2 overexpression cancer subtype showed a 44.8% greater probability of death than patients with HER2 Low (OR 1.448, 95%CI 1.046-2.004, p=0.026), while the patient with triple-negative cancer had a 26.1% lower probability of evolving to death when compared to the HER2 Low patient (OR 0.739, 95%CI 0.562-0.969, p=0.0229). The luminal subtype showed no statistically significant difference when compared to the patient with HER2 Low. Overall survival showed a statistically significant difference between cancer subtypes, with a median of 12 years for Luminal HR 0.816 (0.73-0.913), 15 years for HER2 overexpression HR 1.154 (1.003-, 327), and no statistical difference for triple negative HR 0.978 (0.859-1.114) compared to 12 years for HER2 Low. Conclusion: This study in breast cancer patients demonstrates significant differences between cancer subtypes, with a higher probability of progression to death for patients with HER2 overexpression, while patients with Luminal subtype had a lower probability, when compared with HER2 Low. More studies are needed to clarify the impact of these differences between cancer subtypes on response to therapy.

Association between cancer subtype and other variables (n=11,234).

Characteristics	General	HER2 Low	HER2 overexpression	Luminal	Triple-negative	p-value
N (%)	11234 (100%)	2955 (26.3%)	1496 (13.32%)	4541 (40.42%)	2242 (19.96%)	
Age at diagnosis	55.7 (13.2)	56 (13.2)	52.6 (12.5)	57.2 (13.2)	54.4 (13.2)	<0.001
Age category						
<40 years	1180 (10.5%)	293 (9.9%)	226 (15.1%)	376 (8.3%)	285 (12.7%)	<0.001
40-50 years	3038 (27.1%)	786 (26.6%)	436 (29.1%)	1185 (26.2%)	631 (28.2%)	
>50 years	6997 (62.4%)	1874 (63.5%)	834 (55.7%)	2964 (65.5%)	1325 (59.1%)	
Self-declared ethnicity						
Undeclared	471 (4.2%)	137 (4.6%)	76 (5.1%)	143 (3.1%)	115 (5.1%)	<0.001
White	6123 (54.5%)	1634 (55.3%)	811 (54.2%)	2546 (56.1%)	1132 (50.5%)	
Yellow	128 (1.1%)	36 (1.2%)	15 (1%)	57 (1.3%)	20 (0.9%)	
Brown	3576 (31.8%)	908 (30.7%)	469 (31.4%)	1433 (31.6%)	766 (34.2%)	
Black	936 (8.3%)	240 (8.1%)	125 (8.4%)	362 (8%)	209 (9.3%)	
BMI						
Malnutrition	153 (1.8%)	44 (2%)	22 (1.9%)	56 (1.6%)	31 (1.9%)	0.026
Norma	2541 (30.2%)	694 (31.2%)	372 (32.1%)	990 (28.8%)	485 (30.3%)	
Overweight	3110 (36.9%)	804 (36.1%)	452 (39%)	1254 (36.5%)	600 (37.5%)	
Obesity	2621 (31.1%)	684 (30.7%)	313 (27%)	1140 (33.1%)	484 (30.2%)	
Comorbidities						
No	5909 (52.6%)	1497 (50.7%)	878 (58.7%)	2248 (49.5%)	1286 (57.4%)	<0.001
Yes	5325 (47.4%)	1458 (49.3%)	618 (41.3%)	2293 (50.5%)	956 (42.6%)	
Clinical stage						
I	2470 (24%)	673 (24.2%)	249 (18.4%)	1206 (28%)	342 (18.3%)	<0.001
II	4049 (39.3%)	1146 (41.2%)	502 (37%)	1724 (40.1%)	677 (36.3%)	
III	3007 (29.2%)	802 (28.8%)	495 (36.5%)	1017 (23.6%)	693 (37.2%)	
IV	778 (7.5%)	161 (5.8%)	109 (8.1%)	355 (8.2%)	153 (8.2%)	
Histological type						
Ductal in situ	774 (6.9%)	220 (7.4%)	92 (6.1%)	288 (6.3%)	174 (7.8%)	0.084
Ductal	9497 (84.5%)	2481 (84%)	1264 (84.5%)	3872 (85.3%)	1880 (83.9%)	
Lobular	530 (4.7%)	138 (4.7%)	73 (4.9%)	227 (5%)	92 (4.1%)	
Others	433 (3.9%)	116 (3.9%)	67 (4.5%)	154 (3.4%)	96 (4.3%)	
Nuclear grade						
1	2747 (24.5%)	580 (19.6%)	255 (17%)	1145 (25.2%)	767 (34.2%)	<0.001
2	5760 (51.3%)	1683 (57%)	735 (49.1%)	2693 (59.3%)	649 (28.9%)	
3	2727 (24.3%)	692 (23.4%)	506 (33.8%)	703 (15.5%)	826 (36.8%)	
Histological grade						
1	4676 (41.6%)	998 (33.8%)	510 (34.1%)	1973 (43.4%)	1195 (53.3%)	<0.001
2	5029 (44.8%)	1554 (52.6%)	727 (48.6%)	2196 (48.4%)	552 (24.6%)	
3	1529 (13.6%)	403 (13.6%)	259 (17.3%)	372 (8.2%)	495 (22.1%)	
Family history						
No	9056 (80.6%)	2415 (81.7%)	1250 (83.6%)	3586 (79%)	1805 (80.5%)	<0.001
Yes	2178 (19.4%)	540 (18.3%)	246 (16.4%)	955 (21%)	437 (19.5%)	
Radiotherapy						
No	5011 (44.6%)	1224 (41.4%)	720 (48.1%)	1855 (40.9%)	1212 (54.1%)	<0.001
Yes	6223 (55.4%)	1731 (58.6%)	776 (51.9%)	2686 (59.1%)	1030 (45.9%)	
Hormone therapy						
No	4688 (41.7%)	924 (31.3%)	910 (60.8%)	909 (20%)	1945 (86.8%)	<0.001

Disclosure(s):

ANDRE MATTAR, MD, PhD: No financial relationships to disclose

Andressa Amorim, MD: No financial relationships to disclose

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5:00 PM - 6:15 PM

P1-04-18

Identification of UGT2B family genes as potential biomarkers of response to neoadjuvant therapy in HER2+ breast cancer.

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INTRODUCTION Human Epidermal Growth Factor Receptor (HER2) is overexpressed and/or amplified in 15-20% of breast cancer at time of first diagnosis and is associated with an aggressive clinical progression disease. Management of HER2+ early breast cancer, include a combination of sequential chemotherapy and HER2-targeted therapy, which is currently the gold standard of care. Achieving pathological complete response (pCR) to after neoadjuvant

therapy has been proposed as a prognostic marker for the prediction of disease-free survival (DFS). Although there are different criteria to define pCR, in general pathological complete response is the absence of residual disease in breast and lymph nodes in the pathology analysis of the surgical piece resection (ypTo/is ypN0). However, there is a compelling need to identify molecular biomarkers that will help determine which patients will benefit from neoadjuvant therapy. Considering that the UGT2B family plays an important role in drug metabolism, our aim is to analyze its role as potential predictive biomarkers of pCR to neoadjuvant therapy in breast cancer. **METHODS** We included 18 female patients diagnosed as early breast cancer HER2+ at the time of neoadjuvant treatment. Tissue samples were obtained from the surgical resection performed at Virgen del Rocío Hospital (Seville, Spain) and were formalin-fixed paraffin-embedded (FFPE) to subsequently carry out the pertinent analyses of the study. All patients were treated with chemotherapy plus anti-HER2-targeted therapy and were stratified according to response to neoadjuvant treatment. We defined two groups: responder (R; RCB-0; n=14) and non-responder (NR; RCB-II/III; n=4). Total RNA from FFPE tissue was extracted using the RecoverAll Total Nucleic Acid Isolation commercial kit (Ambion, Austin, TX, USA) following the manufacturer's instructions. RNA concentration was measured using the NanoDrop ND-1000 spectrophotometer (Nanodrop Tech, DE, USA). A total of 18 samples were labeled and hybridized with a Clariom D pico Array microarray (Affymetrix, Santa Clara, CA, USA) following the manufacturer's instructions. Differences in expressed genes according to response were identified using the Mann-Whitney U test where p-values < 0.05 were considered significant and ROC curve was used to determine predictor value of complete response for each member of UGT2 family. Differential expression between the two groups was analyzed using the statistical packages SPSS version 28 and R 4.1.1.1. Statistical significance was established for p-values < 0.05 and fold change ≥ 2 **RESULTS** We found 954 differentially expressed transcripts: 311 downregulated transcripts (lower expression in R) and 643 upregulated transcripts (higher expression in R). Our data showed a significant upregulation in 5 genes of the UGT2B family in non-responder patients (p-value < 0.05). 3 genes of the UGT2b family showed an acceptable ability to discriminate responders and non-responders to neoadjuvant treatment of HER2-positive in the ROC (receiver operating characteristic curve) analysis. **CONCLUSIONS** We identified a set of transcript differentially expressed (FC > 2; adjusted p-value < 0.05) in patients with residual disease (nR) when compared with tissue samples in patients that achieve pCR (R). UGT2B family genes are consistently upregulated in non-responder patients. UGT2B genes encode enzymes involved in glucuronidation. They are phase II drug-metabolizing enzymes with steroids removal capabilities in the liver and various steroid target tissues. An increased rate of glucuronidation is been associated with a loss of potency for the target drugs. These genes would be used as predictive biomarkers of pCR to neoadjuvant therapy in breast cancer.

Disclosure(s):

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Maria A Dominguez-Cejudo, PhD: No financial relationships to disclose

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12/6/2022

5:00 PM - 6:15 PM

P1-05-02

Reducing Delays of Breast Cancer Care Using An Innovative Digital Health Platform

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Background: For breast cancer patients, prolonged time from core needle biopsy to initiation of treatment is associated with an incremental decrease in overall survival. This overall survival reduction disproportionately affects patients with stage I and II breast cancer (hazard ratio: 1.09-1.16, $p < 0.001$), the subgroup of breast cancer patients for which a survival reduction would be least expected due to its early stage and least accepted due to its large population size and potential increased cost of healthcare. Materials and Methods: We conducted an IRB-approved quality improvement initiative among patients with Medicare Advantage at a large integrated healthcare organization in Nevada to assess the ability of an innovative digital health platform to reduce the time interval between positive core needle biopsy to initiation of breast cancer treatment compared to a historical cohort of Medicare Advantage patients diagnosed and treated at the same facility over the preceding 6-month period. The study was restricted to women evaluated at a single contracted breast imaging center for inconclusive (BI-RADS 0) and suspicious (BI-RADS 4 & 5) mammograms, ultrasound, and/or breast MRI. Time to treatment (TTT) calculations were limited to the subset of patients diagnosed with in situ and invasive breast cancer by core needle biopsy. The primary goal was to reduce the historical TTT by greater than 50%. A secondary goal was to reduce TTT to < 30 days, well below the interval where overall survival would be adversely affected. Results: Between September 2021 and April 2022, 552 patients with BI-RADS 0, 4, and 5 breast imaging were enrolled in the quality improvement initiative and managed on the XpediteMD digital health platform. 208 patients were designated as BI-RADS 4 or 5 (i.e., suspicious imaging findings), all of whom ultimately underwent a diagnostic core needle biopsy. Of these, 75 patients were found to have invasive or in situ breast cancer and were subsequently referred to surgery or medical oncology where treatment was initiated. Among these patients, average TTT was 32 days with use of the digital health platform compared to 74 days in the historical cohort, a statistically significant 57% reduction in TTT, exceeding the 50% TTT goal. Although the study did not meet the target goal of average TTT < 30 days from needle biopsy to initiation of treatment, failure to achieve this goal was largely attributable to 3 patients who elected to delay cancer therapy for personal or health reasons. Excluding these 3 patients would have yielded an average TTT of 28.75 days, which is within our < 30 -day goal. Conclusions: This quality improvement initiative demonstrated the successful deployment of a novel digital health platform which achieved a 57% reduction in the time interval from a positive core needle biopsy to performance of breast cancer surgery or initiation of systemic therapy. By reducing TTT to 32 days, the initiative

eliminated any delay in initiation of cancer therapy that could have compromised patients' overall survival.

Disclosure(s):

Dennis R. Holmes, MD: XpeditMD: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

Riya Pulicharam, MD: XpeditMD, Inc.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

12/6/2022

5:00 PM - 6:15 PM

P1-05-03

Prevalence of BRCA1/2 mutations in an underrepresented population of women with breast cancer: Observations from the City of Hope INSPIRE study

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Table 1. Incidence of BRCA 1 and 2 mutations by Race and Ethnicity
BRCA1 BRCA2 BRCA1 or 2 VUS/Negative Native American 0 1 1 6 Asian 2 3 5 150 Black/African American 3 2 5 48 Native Hawaiian or Pacific Islander 0 0 0 5 Other 1 1 1* 26 White 25 17 42 688 Unknown 0 0 0 20 Declined 1 0 1 24 TOTAL 32 24 55 967 * Patient had both BRCA1 and BRCA2 mutations

Disclosure(s):

Joanne Mortimer, MD: Astra Zeneca: Research gift (Terminated, December 13, 2020), Research gift (Terminated, December 13, 2020)

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5:00 PM - 6:15 PM

P1-05-04

Physician Practice Patterns of Breast Imaging After Treatment: Survey of Real-World Practice

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Introduction: Mammography is the cornerstone of breast cancer screening, diagnosis, and surveillance. After definitive treatment for breast cancer, mammograms are continued for surveillance. The current recommendations regarding surveillance after definitive treatment (surgery and radiation) lack consensus amongst various societies. There are no clear guidelines in regards to the type of mammogram recommended: diagnostic or screening mammogram or if a diagnostic mammogram is used, when to return to routine screening protocols. Current practice patterns are driven by physician's preference. We conducted a survey to evaluate physicians' preferences in ordering breast imaging post- breast cancer diagnosis and treatment. Methods: This survey was approved by University of Arizona institutional review board. This survey was conducted through American Society of Clinical Oncology (ASCO) voluntary opt-in Research Survey Pool (RSP). ASCO sent out this survey to 1000 randomly selected members between 10/19/2021-11/22/2021. Weekly reminders to participate were sent through the ASCO RSP for 5 weeks. Participants clicked the link to the survey platform where upon consent they completed the survey. Results: The survey was completed by 244 healthcare professionals through the ASCO RSP. Most respondents were physicians (n=228), primarily medical oncologists (n=174) and practiced in an academic environment in the United States (n=132). After definitive treatment, majority (58%) ordered first

imaging at 6 months post-surgery/radiation, and it was primarily a diagnostic mammogram (68%). Interestingly, for patients at age 80 or above, screening mammogram was used for surveillance after definitive treatment by most respondents (59%). After first post-surgery/radiation mammogram there is an almost even split (50%) on continuing with diagnostic versus screening mammograms for follow up. Of those who order diagnostic mammograms, majority (38%) do it for 3-5 years with an additional 30% continuing it beyond 5 years. Almost 65% of respondents reported they do not stop screening mammograms at any age for patients with a history of early-stage breast cancer as long as they are healthy. Conclusions: The practice patterns of healthcare professionals as it relates to the type and frequency of breast imaging varies significantly. Despite having the same imaging quality there is a significant difference in the cost of screening and diagnostic mammograms. In addition, in clinical practice, most routine screening care is covered by insurances without co-pays or out of pocket costs for patients. Diagnostic imaging does not fall under routine screening care and frequently requires out of pocket expenses for patients. As insurance companies start to decline certain imaging modalities used for cancer detection due to lack of data supporting the use of these expensive studies, specific imaging guidelines for follow up in post-treatment setting for patients with breast cancer are needed.

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Meredith Whittaker, MD: No financial relationships to disclose

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5:00 PM - 6:15 PM

P1-05-06

Establishment of the breast ultrasound support system using deep-learning system.

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Although the categorization of ultrasound using the Breast Imaging Reporting and Data System (BI-RADS) has become widespread worldwide, the problem of inter-observer variability remains. To maintain uniformity in diagnostic accuracy, we have developed a novel artificial intelligence (AI) system in which AI can distinguish whether a static image obtained using a breast ultrasound represents BI-RADS3 or lower, or BI-RADS4a or higher, to determine the medical management that should be performed on a patient whose breast ultrasound shows abnormalities. To establish and validate the AI system, a training dataset consisting of 4,028 images containing 5,014 lesions and a test dataset consisting of 3,166 images containing 3,656 lesions were collected and annotated. We selected a setting that maximized the area under the curve (AUC) and minimized the difference in sensitivity and specificity by adjusting the internal parameters of the AI system, achieving an AUC, sensitivity, and specificity of 0.95, 90.0%, and 88.5%, respectively. Furthermore, based on 30 images extracted from the test data, the

diagnostic accuracy of 20 clinicians and the AI system was compared, and the AI system was found to be significantly superior to the clinicians (McNemar test, $p < 0.001$). Then, we conducted a trial to introduce the system for use in clinical practice. Physicians reviewed the images and determined whether they were BI-RADS3 or lower, or BI-RADS4a or higher. Next, the classification was performed again for the same images concerning the AI diagnosis. At this time, the initial judgment was allowed to be overturned. We checked whether there was any difference in the diagnostic accuracy, sensitivity, and specificity before and after reviewing to the AI diagnosis. Reviews by 24 physicians were evaluated: 4 Japanese Breast Cancer Society breast specialists, 5 non-specialists and physicians with experience treating more than 40 cases of breast cancer, and 15 non-specialists and physicians with no experience treating more than 40 cases of breast cancer. The average rate of accuracy before confirming the AI diagnosis increased to 73.1% after confirming the AI diagnosis ($p=0.00548$), compared to 69.3% on average before the AI diagnosis. Compared to practice experience, the accuracy increased from an average of 77.1% to 79.6% for the 9 physicians who were breast specialists or who had treated 40 or more cases of breast cancer. For the 15 physicians with less than 40 breast cancer cases, the average rate of accuracy increased from 64.7% to 69.2%. Furthermore, sensitivity increased significantly to an average of 99.7% after reviewing of the AI diagnosis from an average of 88.8% prior to reviewing the AI-diagnosis. ($p < 0.01$). Specificity increased from an average of 62.4% to 63.8% ($p=0.433$) after reviewing AI diagnosis. We showed that our AI system, when applied to clinical practice and used by physicians, contributes to the improvement of diagnostic accuracy. Our results indicated that our AI diagnostic system was sufficiently accurate to be used in the clinical practice.

Disclosure(s):

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5:00 PM - 6:15 PM

P1-05-07

Detection of progression or regression of breast cancer by circulating tumor DNA (ctDNA)

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Background:

Circulating tumor DNA (ctDNA) are short DNA sequences shed by tumor cells into the systemic circulation. Studies have shown potential utility of the test to predict relapse or recurrence following treatment in solid tumors, but sensitivity and specificity have varied widely, ranging from 19-100% and 80-100% respectively, in breast cancer specifically. Moreover, literature describing the utility of monitoring dynamic changes in ctDNA trends is limited. We aim to evaluate the correlation between ctDNA test, both single test as well as dynamic trends in value over time, with imaging findings.

Methods:

We retrospectively analyzed the medical records of all adult patients diagnosed with breast cancer who underwent ctDNA testing at the hematology-oncology clinic at William Beaumont - Royal Oak and Troy Hospitals, Michigan, from August 2017 to June 2022. Patients who had ctDNA testing done but did not have imaging to correlate it with were excluded from the study. We calculated the sensitivity and specificity of a single positive ctDNA test to detect disease progression or residual disease on imaging. In patients with multiple ctDNA tests, we calculated the sensitivity and specificity of dynamic trends in ctDNA values to detect progression, regression, or absence of disease on imaging. Moreover, we calculated the lead time for positive ctDNA results to detect disease progression compared to imaging.

Results:

Nineteen patients were included in the study, with 34 total ctDNA test results, each utilized as a separate data point to compare with corresponding imaging findings (Table 1). Ten out of the 19 patients had multiple(≥ 2) ctDNA test results reported, with a total of 15 pairs of ctDNA values and each pair was analyzed separately as up trending (N=7), down trending (N=4), or persistent negative (N=4) to compare with a corresponding pair of imaging findings (Table 2). The median age at diagnosis was 55 years, and 94.7% were female. At diagnosis, majority of

patients (68.4%) had either stage III or IV disease. Our primary endpoint, the correlation of single positive ctDNA result with imaging showing either progression or residual disease, showed a sensitivity and specificity of 100% and 93.3%, respectively. Secondly, serial ctDNA trend analysis in ten patients revealed both sensitivity and specificity of 100% for up-trending ctDNA values to detect progression, down-trending to detect regression, and persistent negative results to detect absence of disease on imaging, respectively. The positive ctDNA results detected disease progression with a median lead time of 44.5 days compared to imaging.

Conclusion:

Given the high sensitivity and specificity to detect disease progression and regression in breast cancer patients by single ctDNA results and dynamic ctDNA trends in our study, we conclude that this may be a valid way to reliably monitor for changes in disease status before they become evident in imaging studies. Further clinical studies are required to prove the utility of ctDNA to detect changes in disease status and to guide therapeutic interventions in breast cancer.

Correlation of single ctDNA result with imaging findings

Table 1: Correlation of single ctDNA result with imaging finding

CtDNA result	Imaging finding		
	Progression/residual disease	No progression/residual disease	Total
Positive	19	1	20
Negative	0	14	14
Total	19	15	34

Correlation of dynamic trends in ctDNA values with imaging findings

Table 2: Correlation of dynamic trends of serial ctDNA values with imaging finding

CtDNA values	Imaging/biopsy finding			
	Progression	Regression	Absence of disease	Total
Up-trending	7	0	0	7
Down-trending	0	4	0	4
Persistent negative	0	0	4	4
Total	7	4	4	15

Disclosure(s):

Ujjwal Karki, MBBS: No financial relationships to disclose
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5:00 PM - 6:15 PM

P1-05-08

Assessment and Diagnosis of Breast Pathology in Young Women: What Can We Learn?

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Introduction: Women 30 years-old or older that present with a breast complaint typically receive a standard work-up, which includes a diagnostic mammogram □ ultrasound. Because women under 30 years-old have extremely dense breast tissue, the initial imaging work-up begins with ultrasound. The American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) describes and categorizes imaging findings using a standardized language to convey to non-radiologist physicians and patients the risk associated with a described breast lesion. Interpretation of the results can be problematic in young women (< 18 y.o) that may undergo imaging at a pediatric facility, often without on-site breast imaging specialists and standard breast imaging protocols in place, including the usage of the BI-RADS lexicon. Appropriateness of biopsy and surgical management require careful consideration especially in a setting where the pathology is often benign. We describe our 5-year experience of 482 young women undergoing breast imaging at a single institution to identify key features characteristic of young women with malignant lesions.

Methods: A retrospective cohort study was conducted on all patients between the ages of 9-29 years old that presented to a breast imaging center for evaluation of a breast complaint from January 2017 through December 2021. Patients were identified via an Epic SlicerDicer query based on age and breast imaging procedure. A retrospective chart review was conducted on this cohort to capture demographic information (Table 1), medical history and family history. Information related to radiographic evaluation, biopsy procedures, and post-operative pathology

was also recorded.

Results: Four hundred-eight two patients with mean age of 23.8 ± 3.7 years were seen for a breast complaint at the imaging center, of which 462 underwent breast ultrasound (96.7%). A BI-RADS classification was assigned in 418 reports (87%). Fifty-eight patients (12%) had imaging at an outside facility before coming to our dedicated breast imaging center. The mean maximal dimension at presentation was 1.3 ± 1.6 cm. A BI-RADS classification of ≥4 was assigned to 46 patients (9.6%). A core needle biopsy (CNB) was performed in 63 patients (13.1%). Seventy-seven patients (16%) underwent surgery. Of the patients undergoing surgery, 38 (49.4%) had a CNB prior to surgery and the mean pre-operative maximal dimension on ultrasound was 3.1 ± 1.6. Reason for excision included: mass size (30.3%), symptoms (27.6%), biopsy result (21.1%) and growth (19.7%). Eight patients (12.7%) were found to have a malignancy on CNB. Fibroadenoma (64.5%) was the most common pathology after surgery. A phyllodes tumor was identified in 8 patients, of which 6 were benign (7.9%) and 2 were classified as borderline (2.6%); there were no malignant phyllodes in the cohort. The mean size for phyllodes lesions were 3.8 ± 1.8 cm. Six of 8 patients had a malignant lesion on final surgical pathology (7.9%); the other 2 patients achieved a pathologic complete response (pCR). Details regarding malignant lesions can be found in Table 2.

Conclusions:

While the American College of Radiology helps provide guidance for appropriate imaging evaluation in young women, there are no treatment algorithms that address the appropriateness of surgical treatment in this age group where the diagnosis is often benign. Radiologist and surgeons that specialize in breast disease may be asked to provide guidance on management decisions for a population they may rarely see (patients < 18 years-old), just as pediatrician or pediatric surgeons may feel pressure to making management plans for complaints they rarely encounter (breast). The value of using standardized imaging and treatment protocols with dedicated breast radiologist and surgeons may offer the best comprehensive approach to this unique subset of patients and deserves further evaluation.

Table 1. Demographic and medical history

	Total n=482
Age at primary imaging (years)	21 [17-24]
BMI (kg/m ²)	24.0 [21-28.7]
Ethnicity	
Hispanic or Latino	152 (31.5%)
Not Hispanic or Latino	254 (52.7%)
Race	
Asian	16 (3.3%)
Black or African American	102 (21.2%)
White	260 (53.9%)
Payor	
Medicaid/Medicare	186 (38.8%)
Private	274 (57.2%)
History of malignancy	21 (4.4%)
History of chest radiation	4 (0.8%)
Family history of breast cancer	135 (28.2%)
Positive personal history of <u>genetic abnormalities</u> associated with breast cancer	8 (1.7%)

Values are n (%) or median [interquartile range]; BMI, body mass index

Table 2. Characteristics of masses in young women

	Non-malignant n =476	Malignant n=8	<i>p value</i> ^{αβ}
Age (years)	24 [21-27]	27.5 [26.3-29]	0.01
History of malignancy	20 (4.2%)	1 (12.5%)	0.3
History of chest radiation	4 (0.8%)	0 (0%)	--
Family history of breast cancer	132 (28.0%)	3 (37.5%)	0.5
Positive personal history of genetic abnormalities associated with breast cancer	8 (1.7%)	0 (0%)	--
Size on imaging (cm)	0.8 [0-2.20]	2.3 [1.4-3.5]	0.004
BI-RADS classification (4,5,6)	40 (8.4%)	6 (75%)	<0.00001

Values are n (%) or median [interquartile range].; *including juvenile fibroadenoma; **benign cyst, ductal ectasia, normal breast tissue, and papilloma; □independent t-test was used to compare means for continuous variables; □Pearson's chi-squared test was used for categorical data; BMI, body mass index; NS, not significant

Disclosure(s):

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Brian A. Menegaz, BS, CCRP: Syneos Health: Salary (Ongoing)

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12/6/2022

5:00 PM - 6:15 PM

P1-05-09

Targeting treatment to tumor response: demonstration of response monitoring with subsequent impact on treatment choices in real time utilizing a novel technology.

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Breast cancers, both early and advanced, are heterogeneous causing differential responses to targeted therapy. Explosion in targeted treatment choices requires real time assessment of tumor characteristics in patients initially and over time. A dynamic detection system, not a static pathology specimen, is required for continuous profiling while treatment changes; hence, the interest in circulating tumor cells (CTCs). Our novel QCDx br™ system analyzes all nucleated cells from a blood sample aliquot, morphologically intact and immobilized in hydrogel, after multiplex, immunofluorescent (IF) staining. We characterize increased numbers of CTCs (nucleated, CD45-negative cells) as single cells, in clusters and in connection with circulating inflammatory cells, stained with two, separate IF marker cocktails, denoting (1) epithelial (EpCAM, Cytokeratin CK), mesenchymal (Vimentin VIM) phenotypes and (2) therapeutic HER2, ER and TROP2 targets which are the basis for targeted therapy in breast cancer. In the ongoing, prospective CLINBREAC trial, we enrolled to date 9 neoadjuvant (early stage, ES) and 21 metastatic (late stage, LS) breast cancer patients, collecting 7.5 ml of blood at 3-month intervals or at change of therapy. We are now out over 2 years with the earliest ES and LS patients showing changes in CTCs with disease progression and in response to treatment, often pre-dating changes seen in follow up biopsies. Detection of HER2+ CTCs was of particular interest in patients with HER2 low cancers (1+ or 2+). Results presented here, contain the more complete datasets from 8 ES and 11 LS patients. QCDx br™ detected CTCs in all 19 Stage I-IV patients that could exceed 100 CTCs/2500 nucleated cells in LS and 50 CTCs/2500 nucleated cells in ES patients. The table shows count averages of CTCs/2500 nucleated cells detected by different IF markers. Of note, CTCs showed combinations of IF markers (hybrid cells). For example, CTCs expressed both VIM and CK indicating epithelial to

mesenchymal transition (EMT) phenotype, which may signify higher metastatic potential. ER+ CTC were seen in LS, not ES patients. All ES patients including those with HER2 low tumors, showed HER2+ CTCs. Of note, not included in the table are two, triple-positive patients with oligo-metastatic disease now 4 and 10 years out from diagnosis without evidence of disease and on maintenance HER2 and ER-directed therapy. No CTCs are seen at their first data point. We were unable to detect CTCs in 13 healthy volunteers. In ES patients, CTC numbers did not associate with tumor size, nodal involvement, ER or HER2 status. For example, one TNBC patient with a T3 tumor and positive nodes had some of the lowest numbers of CTCs. The more complete quantification of the LS patients is in process. As development of QCDx br™ continues, multiplex IF staining of 12+ markers per CTC and identification of single CTC mutational changes is expected. This powerful technology enables targeted treatment decisions with specific drugs resulting in maximal responses.

Average CTC counts/2500 nucleated cells detected by phenotypic and therapeutic IF cocktails

Patients	Phenotypic Panel				Therapeutic Panel			
	CTC	EpCAM	VIM	CK	CTC	HER2	ER	TROP2
Early	27	7	14	15	14	8	1	7
Late	85	17	52	42	81	34	18	38

Disclosure(s):

Susan Tannenbaum, M.D.: No financial relationships to disclose

Emily Hsu, M.D.: No financial relationships to disclose

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Triantafyllos Tafas, PhD: QCDx LLC: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

12/6/2022

5:00 PM - 6:15 PM

P1-05-10

Referral pathways for breast cancer diagnosis and treatment in Mexico: a physicians' survey

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Background: Clinical stage at diagnosis is one of the most relevant prognostic factors for breast cancer (BC). In Mexico, more than half of BC patients are diagnosed at stage III-IV due to delays in referral, diagnosis, and treatment. The median time between symptom presentation and treatment initiation is 7 months; with the longest delay occurring between the first consultation and treatment start. The cause of this delay is not well defined. Our objective is to investigate if physicians in Mexico are aware of referral pathways in their respective institutions for patients with clinical suspicion and confirmation of BC.

Methods: Physicians were asked to answer an anonymous and voluntary survey that included 20 questions aimed at collecting general sociodemographic data, their plan of action when BC is suspected or diagnosed, and the perception of delays and barriers in breast cancer care. The survey was promoted on exclusive social networks of Mexican health professionals.

Results: In total, 802 surveys were collected. Of these, 98% were physicians, with the highest proportion (50%) being gynecologists, family, and general practitioners. The average age was 41 years, and 36% reported practicing in the public sector, 35% in the private sector, and 29% in both sectors. When faced with clinical signs and symptoms suggestive of BC, 41% of physicians in the public sector would request a breast imaging study and refer to another specialist. In contrast, 39% of specialists in the private sector preferred to request a breast imaging study and reevaluate the results.

Specialties to which physicians refer patients when suspicious in public and private sectors were gynecology 41% and 29%, surgical oncology 24% and 36%, and medical oncology 17% and 19%, respectively. In the case of a confirmed BC diagnosis, physicians preferred to refer patients to oncologic surgery in 40% and 45%, medical oncology in 40% and 32%, and gynecology in 9% and 10%, respectively. Of the healthcare professionals that were surveyed, 36% in the public sector and 67% in the private sector ignored the existence of referral pathways for BC clinical suspicion and confirmation in their institution.

Regarding the time interval from the onset of symptoms to treatment initiation, 64% of the private practice physicians estimated a waiting time of < 30 days. In contrast, only 22% considered this time interval in the public sector, 30% answered between 31-90 days, and 17% replied > 90 days.

Most respondents from the private sector considered factors associated with the patient as the main cause for this delay. Respondents from the public sector added to this opinion that factors related to the public health services were a contributor to the delays (Table1). Lack of knowledge about the referral pathways was significantly associated with perceiving greater

delays in care ($p < 0.001$).

Conclusion: The results of this study indicate that there is no consensus among healthcare professionals in Mexico about an action plan when breast cancer is suspected or diagnosed. Although a proportion of the respondents acknowledge the presence of established referral pathways, long waiting times and delays persist between the first evaluation and the start of treatment. Associated factors include the saturation and limited resources of public health services. The development of a universal program and its promotion among all health professionals is imperative to improve BC care in Mexico.

Table 1. Factors associated of delay in the care of clinical suspicion and confirmation of BC

Table 1. Factors associated of delay in the care of clinical suspicion and confirmation of BC		
	Public sector (%)	Private sector (%)
Absence of a defined diagnostic algorithm	62 (12.1)	52 (10.4)
Factors associated with the patient (fear, apathy, lack of knowledge, financial, difficulty of transportation, etc.)	217 (42.5)	323 (64.9)
Lack of medical specialists in several areas (pathology, oncologists, radio-oncologists)	174 (34.1)	25 (5.0)
Lack of well-established referral paths	108 (21.1)	62 (12.4)
Saturation of services to establish a diagnosis (outpatient clinic, laboratory, imaging)	322 (63.1)	39 (6.4)
Saturation to start treatment (delayed surgery times or insufficient chemotherapy infusion centers)	209 (40.9)	32 (6.4)

Disclosure(s):

Daniela Vazquez-Juarez, n/a: No financial relationships to disclose

Raul Andrade-Moreno, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

P1-05-11

Improving the Performance of Early Breast Cancer Diagnosis by a Model Combining Breast Ultrasound with Methylation Markers in Non-Invasive Circulating Tumor DNA

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Background Breast cancer is one of the most common cancers worldwide with the highest incidence among females in 2020 [1]. The application of breast ultrasound benefits the diagnosis of breast cancer at the early stage, but also leads to over-diagnosis. Patients with breast nodules detected by ultrasound at BI-RADS 4a or higher are usually advised to have a fine needle biopsy or surgery, although the PPVs of BI-RADS 4a and 4b categories are low (6% and 25%, respectively) [2]. Methods In this study, AnchorIRIS™ assay was used for analyzing the methylated status of cfDNA. Target enrichment was performed using an AnchorDx breast cancer-specific methylation panel consisting of 129,794 methylated markers. One hundred and twelve pairs of breast tissue and plasma samples (Malignant: Benign= 56: 56) and 40 leukocyte samples (Malignant: Benign = 20: 20) were used to identify reliable breast cancer-specific methylation markers with low noise background. Finally, a methylation model trained on 307 plasma samples (train set: test set = 214: 93) was selected for differentiating benign from malignant nodules, which was validated by two independent sets (Validation-1: Malignant: Benign = 42:46; Validation-2: Malignant: Benign = 62: 46). Results This methylation model exhibited a powerful performance on differentiating benign from malignant nodules with an AUC of 0.837 (95% CI: 0.757-0.918) in the test set, and maintained a stable predictive power with AUCs of 0.820 and 0.801 in two independent validation sets, respectively. In addition, this

methylation model can reflect the difference in methylation signals between metastatic and non-metastatic cancers three years in advance. In contrast to ultrasound, the prediction rate of breast cancer is more accurate across the different age groups using the methylation model, especially for younger women less than 40 years old. Under the ultrasound BI-RADS 4 category, the accuracy (ACC) of the methylation model (IndVal-1, 73.02%; IndVal-2, 78.31%) is on average 22% higher than ultrasound (IndVal-1, 55.56%; IndVal-2, 51.81%). In both of the independent validation sets, the overall accuracy (78.7%) and specificity (SP) (58.7%) at the sensitivities above 95% of the combined model is greater than applying either ultrasound (ACC: 65%; SP: 26.1%) or the methylation model (ACC: 70.6%; SP: 52.2%) alone. Conclusion This methylation model has great potential for the diagnosis of early-stage breast cancer. It improves the diagnostic accuracy of the indeterminate breast nodules, which may assist in decreasing the unnecessary biopsies or surgeries of patients with benign lesions. The methylation model also has the potential in predicting metastatic and non-metastatic breast cancers that is valuable for patient surveillance and risk prediction. References: [1]. Siegel RL, Miller KD, Jemal A: Cancer statistics, 2020. CA Cancer J Clin 70:7-30, 2020 [2]. Spinelli Varella MA, Teixeira da Cruz J, Rauber A, et al: Role of BI-RADS Ultrasound Subcategories 4A to 4C in Predicting Breast Cancer. Clin Breast Cancer 18:e507-e511, 2018

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12/6/2022

5:00 PM - 6:15 PM

P1-05-12

Evaluation of the benefit of the tumor marker cancer antigen 15–3 (CA 15-3) in different subtypes of metastatic breast cancer

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Background: Cancer antigen 15-3 (CA 15-3) is the most commonly used tumor marker in patients with breast cancer (BC). However, the usefulness of CA 15-3 is still controversial and there is lack of evidence for its role in metastatic BC. We performed a retrospective analysis of the value of CA 15-3 for monitoring and diagnosis in subgroups of metastatic BC. Method: This retrospective study included three cohorts of a total of 196 patients with advanced or metastatic BC treated during the years 2015-2020. Patients' data, such as subtype, hormone receptor status, and CA 15-3 values, were retrieved from a treatment database to find out how well the CA 15-3 levels followed the disease progression or remission over time. An increase or decrease of CA 15-3 less than 10% indicated stable disease and changes larger than 10% indicated progress or response of therapy. The patients were then categorized into one of six groups based on the proportion of correct CA 15-3 values in each patient during the course of the disease. A proportion of correct values of 95% or higher placed the patient in category 5, between 90% and 95% category 4, 75% to 90% were category 3, 50% to 75% category 2, and below 50% category 1. Patients without any elevated CA 15-3 values and with no evidence of association with a trend of CA 15-3 and disease progression were categorized as 0. Patients in categories 3, 4, and 5 were classified with approved CA 15-3 conformity and categories 4 and 5 with excellent conformity. Results: The median number of samples per patient was 27 (range 5-102) and at diagnosis of metastatic disease, 79%, 66% and 60% of patients had elevated CA 15-3 in the luminal, HER2-positive, and TNBC groups, respectively. Overall, 72.4%, 95% confidence intervals (CI) (66.2-78.7) of the patients had an approved conformity of CA 15-3 to monitor the course of the disease. The benefit of CA 15-3 differed significantly between the subtypes, luminal BC had an approved conformity for 94%, 95% CI (88.6-99.1) of the patients, HER2 BC 63%, 95% CI (52.1-73.5) and for TNBC 46% (95% CI 29.9-62.0) of patients. In patients with Luminal A, the conformity was excellent in 84% of patients compared to 60% of patients with Luminal B. Estrogen receptor status (ER) was the single most important factor for the value of CA 15-3, with an approved conformity of 91%, 95% CI (85.6-95.7) of ER-positive patients and 37%, 95% CI (25.3-48.2) of all ER-negative patients. Elevated baseline levels of CA 15-3 in the diagnosis of metastatic BC increased the benefit of the marker to approved levels in 62.5% of the ER-negative patients, but ER-positive patients mostly had approved conformity, despite negative CA 15-3 at baseline. Visceral or bone metastases further improved

the utility of CA 15-3 and soft tissue or solitary CNS metastases decreased it. Conclusion: The benefit of serum marker CA 15-3 in monitoring patients with metastatic BC depends mainly on whether the tumor expresses ER or not. ER-positive patients were excellently monitored in most cases and elevated CA 15-3 values at baseline indicated potential utility in ER-negative patients.

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P1-05-13

Clinical impact of whole-body magnetic resonance imaging on subsequent management in luminal/HER2-negative breast cancer patients

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Background: Routine imaging can be inaccurate, especially in metastatic breast cancer (MBC) with bone-only disease or mainly bone disease. This analysis investigates how the use of whole-body magnetic resonance imaging (WB-MRI), in addition to routine computed tomography (CT) and bone scintigraphy (BS), can influence treatment decisions in patients with known MBC. Methods: In a prospective observational study, in our Institute, we performed WB-MRI as baseline and follow-up examination in addition to routine imaging (CT, BS) in luminal/HER2-negative BC patients with prevalence of bone disease potentially candidate to CDK 4/6 inhibitors. All examinations were interpreted by two experienced radiology specialists. Using the results of the examination, a multidisciplinary oncology committee (MOC) reported on the treatment strategy. A positive impact on clinical management was considered if the examination determined a modification in the treatment strategy compared to the MOC decision before WB-MRI. Results: Thirty consecutive luminal breast cancer patients in a metastatic setting at standard imaging were recruited. All these patients underwent CT and BS followed by WB-MRI study. At standard imaging, fourteen patients (46.7%) presented with bone-only disease, while eight patients (26.6%) did not show bone lesions. In 18 of 30 cases (60%) WB-MRI led to a modification of the therapeutic approach. Due to the detection of new metastatic lesions or progression of known metastatic sites, reported on WB-MRI alone, the therapeutic decision changed in 6 (20%) and 3 (10%) patients, respectively. In one patient (3%) the therapeutic decision changed because of both findings. Nine patients (30%) started a new therapeutic line due to evidence of progressive disease on WB-MRI, while 4 patients (13.3%) underwent radiotherapy and 1 patient received orthopaedic counselling for high risk WB-MRI-assessed bone lesions. In 8 patients (26.6%) the disease was re-classified as early breast cancer based on WB-MRI assessment. Conclusions: WB-MRI could play a role in the clinical assessment of luminal MBC. Further studies are needed to better address the potential use of WB-MRI in the assessment and monitoring of bone only/bone predominant luminal MBC and/or in equivocal cases.

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P1-05-14

ctDNA IN BREAST MILK FOR EARLY DETECTION OF PREGNANCY ASSOCIATED BREAST CANCER

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The potential of cell-free tumor DNA (ctDNA) for early tumor detection in asymptomatic patients is yet to be established. In the case of pregnancy associated breast cancer (BC), early detection is of special interest, since it is an entity of special aggressiveness due to a delay in diagnosis, along with the negative effect of mammary gland involution when BC is diagnosed during the postpartum period (PPBC). Indeed, PPBC has double metastatic risk and worst prognosis. With a potential applicability for cancer screening during breastfeeding, here we explored the presence of ctDNA in breast milk (BM) from women with BC associated to pregnancy. Matched samples from breast tumor, plasma and BM from a cohort of 14 women diagnosed during pregnancy or breastfeeding were analysed by droplet digital PCR and a targeted next generation sequencing panel (NGS). Thirteen patients had early-stage disease (11% Stage I, 61% Stage II and 28% Stage III) whilst one was diagnosed at advanced stage. BM harboured ctDNA, since mutations present in the tumor tissue were detected in 86% of the cases by ddPCR and in 71,4% by NGS (difference owing to technique sensitivity). Matched plasma samples had detectable ctDNA levels in only 8% of the cases. In one of the patients, a BM sample collected 18 months prior to BC diagnosis revealed the presence of a pathogenic PIK3CA mutation later detected in the surgically removed tumor. With the ultimate goal of applying the NGS in BM as a technique for early detection of BC in the postpartum period, we have collected samples from healthy volunteers and patients at high risk of developing BC (defined as women becoming pregnant at >40 years or carriers of germ-line pathogenic variants associated with BC -ie: BRCA1, BRCA2, PALB2, RAD51C/D). The application of NGS in BM as a technique for early detection of BC in the postpartum period, identified in a high-risk woman (criteria of enrolment was the age, 46yo) an AKT1 pathogenic mutation in the right-sided BM anticipating by 6 months the radiological diagnosis of a Luminal A tumor, stage pT1bN0M0. In summary, our data provides evidence that ctDNA in BM is highly prevalent even at initial tumor stages, and could be exploited for early breast cancer screening during breastfeeding.

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5:00 PM - 6:15 PM

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DCE-MRI for early prediction of excellent response versus chemoresistance in triple negative breast cancer

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PURPOSE

Triple-negative breast cancer (TNBC) is a heterogeneous disease with variable response to neoadjuvant therapy (NAT). Pathologic complete response (pCR) has become a prognostic marker for overall and disease-free survival. The aim of this study was to determine if dynamic contrast-enhanced (DCE)-MRI after 2 and/or 4 cycles of NAT can identify patients with a high likelihood of achieving pCR, triaging them to standard of care (SOC), or, when appropriate, to de-escalation trials. Conversely, we aimed to identify chemoresistant tumors that are unlikely to achieve pCR and may benefit from escalated targeted trials.

METHOD AND MATERIALS

309 patients with stage I-III TNBC underwent DCE-MRI (temporal resolution: 9-12 sec) at baseline (BL), 2 cycles (C2), and 4 cycles (C4) of SOC doxorubicin/cyclophosphamide (AC) NAT as part of a prospective IRB-approved study (NCT02276443). Tumor volumes of the index lesion were calculated using 3 axis measurements during the early phase of the DCE-MRI (60s). Percent tumor volume reduction (TVR) between BL, C2, and C4 was calculated. Patients were randomly assigned to a training or a validation cohort in a 1:1 ratio. pCR was assessed at surgery after completion of SOC NAT. Correlation between pCR and TVR was evaluated using

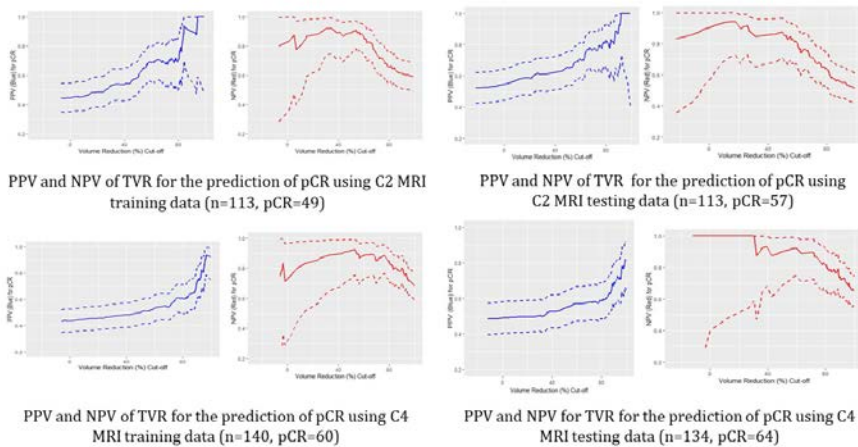
ROC analysis.

RESULTS

Of 309 TNBC patients, 136 (44%) achieved pCR. Following 2 cycles of NAT, TVR >80% was predictive of pCR (chemosensitivity), while TVR ≤ 55% was predictive of non-pCR (chemoresistance) with PPV 80%, NPV 89%, AUC 0.811 (0.73~0.893, p< 0.0001) in the training cohort, and PPV 82% , NPV 85%, AUC 0.815 (CI:0.736~0.894, p< 0.0001) in the validation cohort. Following 4 cycles of NAT, TVR >90% was predictive of pCR, while TVR ≤80% was predictive of non-pCR with PPV 80%, NPV 84%, AUC 0.827 (0.756~0.898, p< 0.0001) in the training cohort and with PPV 73%, NPV 82%, AUC 0.785 (CI:0.709~0.862, p< 0.001) in the validation cohort. Using this model, the pCR status was correctly classified in 50% of TNBC patients using C2 DCE-MRI in the training cohort, and 54% in the validation cohort. Only 8% were misclassified in the training cohort, and 10% in the validation cohort. Using C4 DCE-MRI, the pCR status of 61% and 57% of TNBC was correctly classified in the validation and the testing cohorts, respectively. 12% were misclassified in the validation cohort, and 21% in the testing cohort.

CONCLUSION

DCE-MRI after 2 and 4 cycles of AC-based NAT correctly predicted the pCR status of 54% and 57% of TNBC patients, respectively, as either excellent responders or nonresponders with high AUC 0.811 and 0.827. This may allow patients to be triaged to SOC NAT with option of de-escalation or early targeted therapies for non-responders.



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5:00 PM - 6:15 PM

P1-05-16

Bioimpedance Spectroscopy Monitoring Reduces Long-term Clinical Lymphedema Risk

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Background: A prospective surveillance model (PSM) of care can reduce the risk of breast cancer related lymphedema (BCRL). Bioimpedance spectroscopy (BIS) devices can identify sub-clinical BCRL (sBCRL). A recent randomized controlled trial (RCT) demonstrated the benefit of a PSM model of care using BIS over tape measure (TM) but it did not look at the long-term risk following intervention. This work reports the actuarial risk of clinical lymphedema for those who have triggered an intervention for sBCRL by either BIS or TM. **Materials and Methods:** 879 women with breast cancer were randomized to lymphedema screening with either BIS (n=442) or TM (n=437). Following consent, patients underwent baseline pre-surgical measurements with BIS (L-Dex U400, ImpediMed) and volume (circumference) measurements (Gulick II tape) and randomized after surgery. Both the TM and BIS arms underwent planned post-operative assessments at 3, 6, 12, 18, 24, 30, and 36 months as well at the end of any intervention. Patients with a BIS change from baseline of ≥ 6.5 L-Dex units or TM volume change ≥ 5 and $< 10\%$ above pre-surgical baselines "triggered" for sBCRL form the basis of this study. Triggered patients underwent 4-weeks of wearing a class two (23–32 mmHg) compression sleeve and gauntlet for 12 hours per day. TM volume change $\geq 10\%$ was considered clinical BCRL (cBCRL) for all patients who triggered by either BIS or TM. The cumulative incidence of cBCRL was calculated via the Kaplan-Meier method and compared by the Log-rank test. **Results:** 209 (23.8%) women triggered an intervention and completed treatment for sBCRL (BIS: 89 (20.1%), TM: 120 (27.5%)). The median follow up for the women who triggered was 32.2 months (IQR 17.0 – 33.9) with 30 women (14.4%) women developing cBCRL (BIS: 7 (7.9%), TM: 23 (19.2%)). There was a significant difference in risk between the groups over the follow up interval (log rank test $p = 0.021$) with the cumulative risk in the BIS group being lower compared to the TM group (Hazard Ratio = 0.38, 95%CI 0.19 – 0.79). The 2-year actuarial risk of cBCRL for triggered patients undergoing lymphedema screening by BIS was 5.0% versus 15.7% for TM screening ($p = 0.021$, HR = 0.30). The corresponding 3-year rates of cBCRL were 10.3% and 21.2%, ($p = 0.031$, HR = 0.40) respectively. **Conclusions:** BIS monitoring for sBCRL with subsequent intervention provides significantly lower risks of cBCRL. The lower triggering rates with BIS highlight its better discrimination of true sBCRL compared to TM and support its use for post-treatment surveillance to detect sBCRL and initiate early intervention. These data suggest that monitoring for sBCRL with BIS and subsequent intervention does not just delay the inevitable progression to cBCRL, but rather prevents it over the duration of the study.

Disclosure(s):

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5:00 PM - 6:15 PM

P1-05-17

Radiomic models based on dynamic contrast-enhanced magnetic resonance imaging predict the immunophenotype reflecting spatial distribution of CD8+ tumor-infiltrating lymphocytes in breast cancer

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Purpose: This study aimed to develop noninvasive magnetic resonance imaging (MRI)-based radiomic models to predict immunophenotypes of breast cancer. Methods: A total of 182 breast cancer patients who underwent upfront surgery were analyzed, divided into training (n = 137) and validation (n = 45) cohorts. Dynamic contrast-enhanced (DCE)-MRI was acquired, and immunophenotype was determined on the surgical tumor sections: immune-inflamed (high degree of CD8+ T cells infiltrated), -excluded (CD8+ T cells accumulated at invasive margin but not efficiently infiltrated in tumor bed), and -desert (CD8+ T cells absent within tumor and at margins). Based on 833 radiomic features extracted after manual delineation, the least absolute shrinkage and selection operator method was used to build radiomic models. Results: Our radiomic models from the whole tumor sections showed moderate performance in predicting the immune-inflamed versus non-inflamed tumors, showing the highest AUC values, of 0.659 and 0.671 for training and validation cohorts, respectively. Combining the models, much improved predictability was observed, with AUC values of 0.973 and 0.985 for training and validation cohorts, respectively. Other radiomic features from tumor periphery data discriminated immune-excluded versus immune-desert status, with AUC values of 0.993 and 0.984 for training and validation cohorts, respectively. The combined models were also applicable to predicting immunophenotype for different molecular subtypes, with AUC values \geq 0.867. Conclusions: By integrating the immunohistochemistry profiles, we established MRI-derived radiomic models to predict the detailed immunophenotype of breast cancer. This study suggests the feasibility of noninvasive assessment of tumor immune status in real-world clinics.

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P1-05-18

Orphan non-coding RNAs for early detection of breast cancer with liquid biopsy

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Background

Early detection of breast cancer is crucial for optimal patient outcomes but cannot always be accomplished based on symptoms or screening mammography. Biomarker-based screening could aid early detection of breast cancer by improving sensitivity and specificity. Exai Bio has developed a novel liquid biopsy technology that detects and analyzes small non-coding RNAs that are cancer specific, termed orphan non-coding RNAs (oncRNAs). Previous work in patients with diagnosed breast cancer demonstrated that changes in oncRNAs in serum reflected treatment response and event-free survival. In this study, we developed an assay that measures oncRNAs in serum to detect breast cancer across the range of tumor stages and sizes.

Methods

Previously, a library of ~260,000 oncRNAs from 32 different cancers was compiled based on smRNA sequences found in tumor tissues and largely absent in tumor-adjacent normal tissues from The Cancer Genome Atlas (TCGA). To refine this library for applications in serum, we sequenced smRNA in 31 control serum samples. These smRNA sequences were filtered from the larger library, reducing its size to 250,332 oncRNAs. The diagnostic performance of these oncRNAs was then assessed in an independent cohort of archived serum samples from 96 female patients with clinically diagnosed, untreated breast cancer and 95 age- and sex-matched individuals with no known history of cancer. We sequenced smRNAs at an average depth of 17.7 million 50-bp single-end reads per sample. Of the 250,332 oncRNAs in our library, 171,981 (68.7%) were detected in our independent study cohort. An ensemble of logistic regression models was trained with 5-fold cross-validation, using only those oncRNAs yielding an odds ratio >1 and observed in >6% of samples within each training set.

Results

The cohort of 96 breast cancer patients and 95 matched controls had mean ages of 59.4 and 56.3 years, respectively. Area under the receiver operating characteristic curve (AUC) for detecting breast cancer was 0.94 (95% CI, 0.85–0.96). Sensitivities for detecting breast cancer at 95% specificity ranged from 0.75 to 0.87 among the four breast cancer stages, including a sensitivity of 0.81 for tumor stage I (Table 1); and from 0.67 to 0.87 among the four main TNM T categories (Table 2). Sensitivities at 95% specificity were relatively high for small tumors, at 0.75 (95% CI, 0.40–0.97) for T1b (>5mm to ≤10mm; n = 9) and 0.80 (0.68–0.94) for T1c (>10mm to ≤20mm; n = 37).

Conclusions

We have demonstrated the potential value of an oncRNA-based liquid biopsy assay by showing that oncRNAs can be used to detect breast cancer in serum samples with high sensitivity, and that detection requires fewer reads than are needed with other platforms. Moreover, we found that this oncRNA-based assay performed well in detecting early-stage breast cancer and small tumors. This suggests that an oncRNA-based liquid biopsy assay may be beneficial for early detection of breast cancer.

Table 1. Model sensitivity by tumor stage

Tumor Stage	N	Sensitivity (95% CI)
I	45	0.81 (0.71–0.94)
II	19	0.75 (0.54–0.94)
III	19	0.80 (0.60–0.97)
IV	13	0.87 (0.64–1.00)

For the indicated numbers of cases (N), sensitivity and Pearson-Clopper 95% confidence intervals are reported for tumor detection by the oncRNA-based model at 95% specificity by tumor stage, as defined by the AJCC 7th Edition breast cancer staging system.

Table 2. Model sensitivity by tumor size

TNM T Category	N	Sensitivity (95% CI)
T1	48	0.80 (0.70–0.93)
T2	30	0.87 (0.73–0.98)
T3	8	0.78 (0.47–1.00)
T4	10	0.67 (0.35–0.93)

For the indicated numbers of cases (N), sensitivity and Pearson-Clopper 95% confidence intervals are reported for tumor detection by the oncRNA-based model at 95% specificity by TNM T category, as defined by the AJCC 7th Edition breast cancer staging system.

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5:00 PM - 6:15 PM

P1-05-19

Impact of the COVID-19 pandemic on the diagnostic pathway of breast cancer in the Netherlands: a population-based study

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Objective: The COVID-19 pandemic has had an impact on health care. In the Netherlands, hospital capacity for non-covid care was limited and population screening temporarily halted. The aim of this study was to investigate the impact of the pandemic on the diagnostic pathway of breast cancer.

Methods: In this study, 48,425 breast cancer patients with a primary breast tumour were selected from the Netherlands Cancer Registry and the Dutch Hospital Data. Patients diagnosed in period January 2020 to July 2021 were divided into six periods, based on the number of hospitalizations due to the COVID-19 pandemic and compared to the same periods in 2017-2019. A t-test was performed to compare the number of diagnosed patients per period. Patient characteristics were compared using chi-squared test. The impact on the procedures performed was analysed using logistic regression. The median time between diagnosis and therapy and the median time between first diagnostic procedure and therapy was analysed using Cox Proportional Hazards Regression. All results were corrected for age, stage and region.

Results: During the first peak of the pandemic in 2020, significantly fewer patients (-48,2%) have been diagnosed with breast cancer. This decrease is mainly seen in lower stage tumours. Mammography and echography were performed significantly less per patient during the first recovery in 2020 (OR=0.83 and OR=0.85 respectively) compared to 2017-2019. PET-CT was performed significantly more often during the first peak and first recovery in 2020 (OR=1.94 and OR=1.39 respectively). The median time between diagnosis and start of therapy significantly decreased in 2020, during the first peak by 3 days (HR=1.26), during first recovery and second peak by 1 day (HR=1.04 and HR=1.16 respectively). The median time between first diagnostic procedure and start of therapy significantly decreased in 2020, during the first peak by 4 days (HR=1.25), during the first recovery by 1 day (HR=1.04) and during the second peak by 2 days (HR=1.13).

Conclusion: The decreased number of diagnosis was related to the temporary halt of the screening. Diagnostics for early stage tumours was limited and for PET-CT was performed more often reflecting the change in proportion of higher stage. A reduced time of the diagnostic pathway is the result of less hospitalized patients with cancer and the effort on keeping the

oncology care in place.

Table 1: Overview results diagnostic pathway of breast cancer

Table 1: Overview results diagnostic pathway of breast cancer

Period distribution	Period	A	B	C	D	E	F
	Description	Pre-COVID	Peak 1	Recovery 1	Peak 2	Peak 3	Recovery 2
	From (week-yr.)	1-2020	12-2020	21-2020	42-2020	1-2021	21-2021
	To (week-yr.)	11-2020	20-2020	41-2020	53-2020	20-2021	30-2021
Procedure performed Odds ratio	Mammography	1.09	1.10	0.83**	1.11	1.02	1.07
	Echography	1.17	0.89	0.85*	0.92	0.90	1.07
	PET-CT	0.98	1.94**	1.39**	1.20	1.21	1.04
	CT	0.69**	1.35	1.12	1.25	0.83*	0.68*
Time to therapy Hazards Ratio	Diagnosis to therapy	0.82**	1.26**	1.04*	1.16**	0.9**	0.88**
	First procedure to therapy	0.8**	1.25**	1.04*	1.13**	0.89**	0.85**

* significant difference between periods $p < 0.05$

** significant difference between periods $p < 0.01$

* significant difference between periods $p < 0.05$

** significant difference between periods $p < 0.01$

Disclosure(s):

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P1-05-20

COVID-19 Lockdown Resulting in Advanced Cancer and Worse Histology at Presentation in Hispanics

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Background In breast cancer, prognosis is marked by histology and stage at diagnosis. Patients presenting with HER-2 positive or triple negative breast (TNBC) often have a worse prognosis. Early detection of breast cancer is mainly based on yearly screening mammograms, which were disrupted during the lockdown stages of the COVID-19 pandemic. In general, underserved populations, especially the Hispanic population often lack access to preventive care due to lack of funding causing delays in access to timely care. The COVID-19 pandemic caused many patients to miss their annual mammogram screening due to lockdown causing subsequent presentation of more advanced cancer. We, therefore, hypothesized that more patients were diagnosed with advanced cancer after lockdown and worse histology in the Hispanic population compared to the non-Hispanic population of San Antonio, Texas. Methods We identified 3 cohorts retrospectively using chart review: Pre-covid-19 era was defined

between 2018 to March 2020. Lockdown is defined as a period between April 2020 to December 2020 followed by the post-vaccine era from January 1st 2021 to 2022. Pearson's Chi-squared and logistic regression tests were used to determine the relationship between time, histology at diagnosis and ethnicity. Results More Hispanic patients were found to present with HER2+ disease (OR: 1.65. p-value .047) compared to non-Hispanic women. When looking at presentation of HER2+ disease in the pre-covid-19 era, there was a 15.11% increase in the presentation of HER2+ disease in the post-vaccine era. When looking at the presentation of TNBC disease in women, there was not a significant correlation seen in the lockdown or post-vaccine period in Hispanic compared non-Hispanic women. Other factors such as funding status were associated with TNBC at presentation independently of ethnicity. In the lockdown era, the number of newly diagnosed breast cancer patients reached an all-time low and during the post-vaccine era, the patient numbers are back to the pre-covid era. Conclusion Ethnicity in part played a role in the number of patients presenting with more aggressive histology such as TNBC and Her 2 positive breast cancer in the post-vaccine era. These findings may be secondary to fact that certain ethnic groups are more likely to miss preventive screenings and the covid 19 pandemic lockdown exacerbated this problem. Diagnosis of advance cancer can further deter patients from seeking care due to socioeconomic factors and possibly increase mortality in these populations. These findings suggest that there seems to be a correlation between race and presentation of more aggressive histology caused by the effects of the pandemic in cancer care affecting minorities.

Disclosure(s):

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P1-05-21

Change in breast cancer detection method, stage at diagnosis and treatment during the COVID-19 Pandemic: 2019-2021

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Objective: Identify changes in breast cancer detection method, stage at diagnosis and treatment prior to, during and after stay-at-home orders and restricted health care access due to COVID-19.

Methods: Statistical comparison of detection method (patient (PtD), mammography (MamD) or other), Anatomic TNM Stage 8 (0-IV) and invasive BC treatment change over time by three time periods (time 1: 2019+Q1 2020; time 2: Q2-Q4 2020; time 3: 2021) using chi-square analysis in an institutional retrospective cohort of first primary breast cancer (BC) patients (n=1799), years 2019-2021.

Results: In the years prior to the study, 2016-2019, there was no difference in detection method or stage at diagnosis by year with 682 to 733 newly diagnosed BC annually (p=.462). In 2020 (n=535) and 2021 (n=582) annual diagnosed cases dropped 22% and 15% from 2019 levels. Compared to time 1, time 2 MamD BC dropped significantly (64% to 58%) with a subsequent increase in MamD BC to 70% in time 3 (p < .001) creating a U-shaped curve for MamD over time. PtD BC increased in time 2 from 30% to 36% but declined in time 3 to 25% (p < .001). Concurrently, stage at diagnosis shifted from time 1 to time 2 with stage 0 and I declining [stage 0: 21% to 16%, stage I: 40% to 38%] and stage II and IV increasing [stage II: 28% to 33%, stage IV: 2% to 4% stage IV] (p<.001). Subsequently in 2021 stage shifted again with an increase in stage 0 to 22% and stage I to 45% and a decline in stage II (33% to 24%), III (9% to 7%) and IV (4% to 2%) (p<.001). Combining stage 0 and I, the percentage of lower stage BC declined from 61% to 54% and increased to 67% in time 3 (2021) when health services became more readily accessible.

There was no change in type of surgery for invasive breast cancer (stage I-III, n=1386) with equivalent numbers of breast conserving surgery (58%), subcutaneous mastectomy (24%) and mastectomy (18%) over the time period. Chemotherapy treatment rates for invasive BC did not change (38%). Radiation therapy increased from 66% (time 1: 2019+Q1 2020) to 73% (time 2: Q2-Q4 2020) then back to 64% in time 3: 2021 (p=.007) independent of surgery type but

concordant with an increase in stage IA and stage IIB BC among invasive breast cancer cases in time 2: Q2-Q4 2020 (p<.001). Likewise, neoadjuvant therapy increased and then declined from 33% to 38% to 29% from time 1 to time 3 (p<.001).

Conclusions: Number of diagnosed BC cases fell after the first quarter of 2020 during the time of COVID-19 related shut downs and decreased access to health services. During the Q2-Q4 2020 time period mammography detected BC declined with a relative increase in patient detected breast cancer. When mammography detection declined, BC stage at diagnosis shifted to higher stage concurrent with increased rates of radiation and neoadjuvant therapy. In 2021, the relative increase in mammography detected BC indicates a return to more normal screening patterns with a catch up for screening lost in the prior year due to access limitations. In the third time period: 2021, with the return to prior levels of mammography detected breast cancer, stage shifted back to pre-pandemic expected distribution and the excess treatment with radiation and neoadjuvant therapy declined to previously observed levels. Although the changes in detection method, stage and treatment did not persist they were statistically significant and could represent a need for re-establishing pre-pandemic screening behavior.

Detection Method by COVID Pandemic Diagnosis Time Periods: 2019-2021 (N=1799)

Table. Detection Method by COVID Pandemic Diagnosis Time Periods: 2019-2021				
	PtD	MamD	Other	
(n=1799)	(n= 538)	(n = 1156)	(n = 105)	p value
	N (%)	N (%)	N (%)	
Time 1: 2019/Q1 2020	219 (30%)	467 (64%)	50 (7%)	<.001
Time 2: Q2-Q4 2020	172 (36%)	279 (58%)	30 (6%)	
Time 3: 2021	147 (25%)	410 (70%)	25 (4%)	

Disclosure(s):

Judith A. Malmgren, PhD: No financial relationships to disclose

Mary Atwood, CTR, CTR: No financial relationships to disclose

Henry Kaplan, MD: No financial relationships to disclose

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P1-05-22

The Impact of the COVID-19 Pandemic on Breast Cancer Diagnoses in San Antonio, TX

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Introduction

Breast cancer is the most frequently diagnosed cancer and the second leading cause of cancer death in women in the United States. The significant advances in care over the last decades are largely attributable to early detection and treatment. The pre-COVID-19 pandemic 5-year survival rate of breast cancer was in the range of 90%, however, there has been public concern that the pandemic has led to delayed diagnosis. The objective of this study was to determine if patients diagnosed during the pandemic had more advanced breast cancer at presentation compared to those diagnosed prior.

Methods

This is a retrospective study of patients with an ICD code for Breast Cancer seen within the University of Texas Health San Antonio MD Anderson Cancer Center between 1/1/2018 and

12/31/2021. Data abstractors collected information on gender, age, race, ethnicity, funding, screening mammogram dates, date of cancer diagnosis, stage at diagnosis, and treatment. Those diagnosed before 1/1/2018 or that received initial treatment outside our institution were excluded from the analysis. Pearson's Chi-squared and logistic regression tests were used to determine the relationship between time and stage at diagnosis. The timeline was divided into three periods: from 01/01/2018 to 03/31/2020 as the pre-COVID era, from 04/01/2020 to 12/31/2020 as the lockdown period, and from 01/01/2021 to the present as the post-vaccine era.

Results

A total of 696 patients with breast cancer were included. There was a significant statistical difference between the cancer stage at diagnosis in the pre-COVID-19 era compared to the lockdown period and the post-vaccine era ($p= 0.003$, table 1). Therefore, patients diagnosed after the beginning of lockdown were more likely to have more advanced cancer as time progressed. The odds ratio for Tis stage was 0.38 (95% CI: 0.23-0.60; $P < 0.001$) in the post-vaccine era compared to the pre-COVID era. The OR for Tis stage was not statistically significant (OR, 0.68; 95% CI: 0.42-1.10; $P < 0.12$) when comparing the lockdown period to the pre-COVID era.

Conclusion

Patients diagnosed with breast cancer in the COVID-19 pandemic were more likely to present with more advanced disease at diagnosis compared to those diagnosed in the pre-COVID-19 era confirming our hypothesis. The OR of presenting with Tis disease when diagnosed during the post-vaccine compared to the pre-COVID-19 era was 0.38, however, this was not seen when comparing the lockdown period to the pre-pandemic era. We believe this difference was not significant because delays in cancer care may take months to years to take full effect.

Breast cancer stage at diagnosis per period

Table 1 – Breast cancer stage at diagnosis per period

Stage	Pre-COVID-19, N = 264 ^f	Lockdown, N = 171 ^f	Post-vaccine, N = 261 ^f	p-value ^g
Tis	69 (26%)	33 (19%)	31 (12%)	0.003
T1 or T2. N0 or N1	133 (50%)	105 (62%)	177 (68%)	
N2 or N3 disease	10 (3.8%)	4 (2.4%)	10 (3.8%)	
Clinical or pathologic T3 or T4 with any N	24 (9.1%)	16 (9.4%)	22 (8.5%)	
Metastatic presentation at Unknown	28 (11%)	12 (7.1%)	20 (7.7%)	
	0	1	1	
n (%)				

^f n (%)
^g Pearson's Chi-squared test

Disclosure(s):

Gabriel Roman Souza, MD: No financial relationships to disclose

Tamarah Aldawoodi, MD: No financial relationships to disclose

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P1-05-23

**OPTIMIZING THE DIAGNOSIS OF LEPTOMENINGEAL METASTASES IN BREAST
CANCER PATIENTS BY CIRCULATING TUMOR CELLS AND CIRCULATING TUMOR DNA**

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Introduction: Leptomeningeal metastases (LM) occur in approximately 5% of patients with breast cancer, negatively impacting their prognosis. Reliable diagnosis of LM is challenging, but timely diagnosis could lead to more treatment options and consequently a better prognosis. Circulating tumor DNA (ctDNA) and circulating tumor cells (CTCs) in cerebrospinal fluid (CSF) are potential methods to improve the diagnosis of LM. In this prospective study we compared cytology (current gold standard for CSF analysis in diagnosing LM) with CTC enumeration and ctDNA detection in CSF for diagnosing LM in patients with breast cancer. Methods: In a

prospective study in patients with clinical suspicion of LM who were planned to undergo a diagnostic lumbar puncture (LP) for CSF cytology the presence of CTCs/ctDNA in CSF was compared to the presence of tumor cells in CSF by cytology. CTC enumeration was performed using the FDA approved CellSearch System (Menarini). The detection of ctDNA was performed using the mFAST-Seqs method, which detects aneuploidy throughout the genome by selective amplification of long interspaced nuclear element sequences (LINE-1 elements). In a control group consisting of 15 patients with a hematologic malignancy with suspicion of LM, 2 cases had 1 CTC in their CSF, therefore the cutoff for a positive CTC test was set at 2 CTCs. Results: In total 80 patients with breast cancer were included from January 2016 till January 2022. In 16 out of 80 patients CSF cytology was positive of whom 14 (87.5%) had a positive CTC test. From the 2 patients in which the CTC test was negative, one patient had 1 CTC detected in CSF and for both patients a lower volume of CSF was available for the CTC test compared to the volume used for cytology. In 2 of the 16 cytology positive patients, who underwent a second LP, CTCs were positive in the CSF from the first LP, while cytology was only positive in the CSF of the second LP. Of the 64 patients with a negative cytology, 7 (10.9%) patients had a positive CTC test. Two of these 7 patients had typical symptoms of LM, a suspicious MRI and a course of disease matching with LM according to the neuro-oncologist. Overall survival (OS) was shorter in patients with a positive CTC test compared to patients with a negative test (median OS: 19.2 months vs. 3.4 months, log-rank test, $p=0.007$). When only patients with a negative cytology were included in this analysis, OS remains significantly shorter in the group with a positive CTC test ($n=7$) compared to the group with the negative CTCs ($n=57$) (median OS 19.3 months vs. 3.5 months, long-rank test, $p=0.003$). Additionally, ctDNA detection in CSF was compared to CSF cytology in 51 patients, of which 11 had a positive CSF cytology result. For 8 of these 11 patients ctDNA was detected (72.2%) while 1 of the 40 patients with a negative cytology had ctDNA. Discussion: Both CTC enumeration and ctDNA detection can be used to detect LM in CSF. CTC detection could even improve timely diagnosis of LM in patients with breast cancer. However, the added value of ctDNA seems less evident.

Disclosure(s):

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P1-05-24

DELAYS in DIAGNOSIS of Adolescent and Young Adult BREAST CANCER and LACK OF BREAST HEALTH EDUCATION, Community Based Research

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INTRO) The average AYA breast cancer patient is diagnosed at a higher stage and has a higher mortality rate compared to their 40+ counterparts [1,2,3]. Ruddy et al. (2014) establish a higher prevalence of delayed diagnosis in AYA patients [4]. Delays in treatment of just 6 weeks have been linked to poorer 5-year survival rates [5]. In this study, we attempt to confirm the findings of Ruddy et al. and further define factors affecting delays in diagnosis. METHODS) We distributed an online survey via social media outlets to women diagnosed < 40 years old in the USA. We interpreted 455 responses. RESULTS) Our findings determined that 70% of respondents (n=320) made extra efforts after detecting an abnormality and taking steps to obtain a diagnosis. This includes those with prompt and delayed diagnosis. 36% of survivors faced delays in diagnosis (defined by 8+ weeks duration from detection to diagnosis). 62% of survivors say that a physician never educated them on breast health prior to diagnosis. 54% have not heard of breast self-awareness (BSA) and 54% incorrectly defined breast self-exams (BSE), suggesting confusion in this distinction. DISCUSSION) These data confirm earlier findings that 1) women under 40 face a significant rate of delayed diagnosis; and 2) patient perceptions and medical provider perceptions contribute to these delays. We propose that earlier diagnosis of breast cancer in young women will initiate quicker treatment interventions which have been shown to increase 5-year survival rates and lower long-term mortality rates in the AYA breast cancer population [5,6]. CONCLUSION) Greater efforts should be made to educate young women on breast health, and the medical community should be made aware of these challenges so they can properly evaluate and assist young women to receive a prompt diagnosis.

Young Breast Cancer Project

YOUNG BREAST CANCER PROJECT

Missy Peters + Steph Tubman || Survivors + Patient Advocates

AAACR Selected Survivor Program 2022
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These women received diagnoses for an early breast cancer diagnosis due to lack of breast health education and/or lack of cancer care information/awareness presented with symptoms.

These women had delayed diagnosis of early stage breast cancer. We found 47% waited to see a doctor, 17% were assessed by a physician their symptom was OK and no diagnosis was ordered, 27% were a medical professional being told incorrect, and 9% waited to schedule a biopsy because they were reassured it was "nothing".

Mission + Background

The Young Breast Cancer Project advocates for early detection of disease through breast health education. We elevate young survivors' stories and forge alliances with the medical community to reduce delayed diagnoses and help save lives.

After a delayed diagnosis, Missy Peters started photographing fellow women diagnosed +40 to raise awareness that Young Women Get Breast Cancer Too. In doing so, she learned that too many young women face delays and difficulties seeking accurate diagnoses and access to prompt treatment.

Programmatic Areas



BREAST CANCER PORTRAIT PROJECT:
 Target Audience: Survivors. Those diagnosed with adolescent and young adult (AYA) breast cancer are invited to share their story at a portrait session with Missy. They're encouraged to use the great images to raise awareness in their social circles. With almost 100 stories collected, our qualitative dataset reveals the difficulties young women face leading up to a diagnosis of breast cancer.

COMMUNITY-BASED RESEARCH:
 Target Audience: Physicians. We believe in data-backed decision making. Our original survey validates the Portrait Project findings. It quantifies the delay and access difficulties young women face leading up to their breast cancer diagnosis. Missy has been accepted into CBOA's Quickstart program and will partner with an Academic Co-PI in 2022-2023 to seek peer review and publish these findings.

BREAST FRIEND NIGHTS
 Target Audience: Lay Public. An engaging event for "our friends" to learn about breast health - especially the signs and symptoms of breast cancer. Here we utilize live storytelling, the Portrait Project gallery and our signature "Boobie Booth" to educate attendees. We're planning events for 2022 in Los Angeles (Spring), NYC (Summer), San Diego (Fall) and hoping to add cities.

Community-Based Research: Understanding Prevalence + Causes of Delayed / Difficult AYA Diagnoses

INTRODUCTION:
 The average AYA breast cancer patient is diagnosed at a higher stage and has a higher mortality rate compared to their 40+ counterparts [1,2,3]. Hudis et al. (2014) establish a higher prevalence of delayed diagnosis in AYA patients [4]. Delays in treatment of just 6 weeks have been linked to poorer 5-year survival rates [5]. In this study, we attempt to confirm the findings of Hudis et al. and further define factors affecting delays in diagnosis. We distributed an online survey via social media outlets to women diagnosed +40 years old in the USA. We interviewed 407 responses.

RESEARCH QUESTIONS:

- What is the prevalence of delayed and/or difficult diagnosis in patients <40?
- Which factors most contribute to delayed and/or difficult diagnosis?
- To what extent do young breast cancer survivors understand BSE (breast self-exam) + BSA (breast self-awareness) as defined by the medical community?
- To what extent were young breast cancer survivors educated on breast health?

RESULTS + DISCUSSION:

Delayed Diagnosis
 We defined a delay as greater than 8 weeks from decision to diagnosis based on our interviews with survivors. Our findings indicate 36% of survivors that we surveyed faced delays in diagnosis.

Difficulties with Diagnosis
 79% of respondents (n=320) made extra efforts after learning an abnormality and taking steps to obtain a diagnosis. This includes: those with 10% just one of the listed, 27% physician had to press additional diagnoses, 27% sought a second or multiple opinions after learning an abnormality and taking steps to obtain a diagnosis. This includes: those with 10% just one of the listed, 27% physician had to press additional diagnoses, 27% sought a second or multiple opinions after learning an abnormality and taking steps to obtain a diagnosis.

Level of Risk

- 43% Unknown
- 19% Not known
- 38% Not known

Family History of Breast Cancer
 Our results suggest family history of disease alone is not a reliable predictor of breast cancer or average risk scores.

Genetic Link to Breast Cancer
 23% of survivors had a genetic link. Only 4% knew this prior to diagnosis which suggests previous surgery in successful and genetic testing should be more prevalent.

Factors Contributing to Delay
 We found that 88% of women detected their own breast or lymph abnormality, which is higher than previously reported [6]. 63% of those with a delay detected their own abnormality compared to 66% of those without a delay. Survivors with delay were allowed to select multiple reasons:

- 47% wanted to seek medical attention.
- 27% saw a physician and no diagnostic imaging was ordered.
- 22% had diagnostic imaging that did not lead to biopsy.
- 15% wanted to schedule a diagnosis because they were reassured by their provider they had "nothing to worry about".
- 6% had issues with insurance coverage.

Breast Health Knowledge

- 62% say that a physician never educated them on breast health prior to diagnosis.
- 54% have not heard of breast self-awareness (BSA) and 54% incorrectly defined breast self-exams (BSE), suggesting confusion in the distinction.

CONCLUSIONS + IMPLICATIONS FOR ADVOCACY:
 These data confirm earlier findings that 1) women under 40 face a significant rate of delayed diagnosis, and 2) patient perceptions and medical provider perceptions contribute to these delays. We propose that earlier diagnosis of breast cancer in young women will initiate quicker treatment interventions which have been shown to increase 5-year survival rates and lower long-term mortality rates in the AYA breast cancer population [2,6]. Greater efforts should be made to educate young women on breast health, and the medical community should be made aware of these challenges so they can properly evaluate and assist young women to receive a prompt diagnosis.

Sources + Acknowledgements
 These data confirm earlier findings that 1) women under 40 face a significant rate of delayed diagnosis, and 2) patient perceptions and medical provider perceptions contribute to these delays. We propose that earlier diagnosis of breast cancer in young women will initiate quicker treatment interventions which have been shown to increase 5-year survival rates and lower long-term mortality rates in the AYA breast cancer population [2,6]. Greater efforts should be made to educate young women on breast health, and the medical community should be made aware of these challenges so they can properly evaluate and assist young women to receive a prompt diagnosis.

Summary of poster presented at AACR summarizing our community based research and advocacy efforts for AYA breast cancer in the US.

Disclosure(s):
Missy Peters, AYA Survivor: No financial relationships to disclose
Steph Tubman, AYA Survivor: No financial relationships to disclose

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5:00 PM - 6:15 PM

P1-05-25

Clinical and biological features of 158 consecutive and unselected oligometastatic breast cancers

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Background: In order to determine the optimal treatment strategy for oligometastatic breast cancer (OMBC), effective and safe treatments for metastatic sites and sensitive and specific imaging techniques are needed. But it is also essential to know the incidence of oligometastatic

breast cancer and its clinical and biological characteristics [1]. Efficient imaging techniques and therapeutic tools exist, but knowledge of incidence, clinical and biological characteristics of OMBC is scarce. This is partly due to the lack of publications describing these data on recent, consecutive, and unselected series of OMBC. Methods: we retrospectively collected data from 998 patients diagnosed with synchronous or metachronous metastatic breast cancer (MBC) between January 2014 and December 2018 at our institution. The only criterion used to define OMBC was the presence of one to five metastases at diagnosis. Hormone receptor (HR) and HER2 receptor status, histology, SBR grade, number of metastases and organs affected were collected. Results: Of 998 MBC, 15.8% were OMBC (158/998). Among the series, 88% (139/158) of OMBC had 1 to 3 metastases and 86.7% (137/158) had only one organ involved. Among 158 patients, 52.5% (n=83) had bone metastases, 20.9% (n=33) had lymph node metastases, 14.6% (n=23) had liver metastases, 13.3% (n=21) had brain metastases, 8.2% (n=13) had lung metastases, and 3.8% (n=6) had others (skin, pancreas, adrenal). Among these 158 patients, 83.4% (n=131) had ductal breast carcinoma, 55.7% (n=88) had HR+/HER2- OMBC, 25.3% (n=40) had HER2+ OMBC and 19% (n=30) had HR-/HER2- OMBC. HR+/HER2- subtype was statistically associated with bone and bone only metastases (p=0.001), HER2+ subtype with brain metastases (p=0.001) and HR-/HER2- subtype with lymph node metastases (p=0.008). Visceral metastases (lung or liver) are not statistically associated with any biological subtypes. The proportion of OMBC with SBR grade III was statistically higher than in a series of 22,109 patients with MBC [2] (49.4% vs 35.2%; p< 0.001). Conclusion: OMBC is a heterogeneous entity. OMBC incidence is certainly much higher than the commonly used values. OMBC is not an indolent disease, and each subgroup, according to its biological and anatomical characteristics, may deserve a specific management. [1] Hellman S, Weichselbaum RR. Oligometastases. *J Clin Oncol Off J Am Soc Clin Oncol* 1995;13:8–10. <https://doi.org/10.1200/JCO.1995.13.1.8>. [2] Deluche E, Antoine A, Bachelot T, Lardy-Cleaud A, Dieras V, Brain E, et al. Contemporary outcomes of metastatic breast cancer among 22,000 women from the multicentre ESME cohort 2008–2016. *Eur J Cancer* 2020;129:60–70. <https://doi.org/10.1016/j.ejca.2020.01.016>. .

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5:00 PM - 6:15 PM

P1-05-26

A blood-based lipid panel for personalized risk assessment of breast cancer

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Background: The metabolic syndrome characterized in part by obesity, hyperinsulinemia, and insulin resistance is associated with increased risk of breast cancer. However there remains a need to establish a circulating biomarker metabolic profile indicative of increased risk of breast cancer. In the current study, we performed a comprehensive metabolomics screen to identify biomarkers indicative of increased risk of breast cancer. Methods: Unbiased metabolomics profiling was conducted on an initial Development Set of plasmas collected from 353 newly-diagnosed breast cancer cases and 141 controls. A deep learning neural network with 3 layers each containing 32 nodes based on 11 individual lipids corresponding to discrete lipid subclasses was built for risk prediction of breast cancer. The model was validated in an independent Test Set consisting of 79 breast cancer cases and 163 controls. Using a nested case:control matched design, we evaluated the performance of the model among body mass index (BMI) strata (≥ 30 or $< 30\text{kg/m}^2$). Results: An 11-marker lipid biomarker panel encompassing lipid subclasses with known pro-inflammatory and tumor promoting roles yielded an AUC of 0.75 (95% CI: 0.70-0.79) for distinguishing breast cancer cases from controls in the Development Set. Predictive performance of the lipid panel was comparable when stratifying cases into hormone-receptor (HR) positive, HER2-positive/HR negative, and triple-negative breast cancer subtypes. The biomarker panel had an AUC of 0.74 (95% CI: 0.68-0.81) in the independent Test Set. The predictive performance of the panel was most pronounced among obese subjects (BMI ≥ 30) with an AUC of 0.81 (95% CI: 0.71-0.91) in the Test Set.

Conclusions: The lipid-based biomarker panel has utility for identifying women with 'metabolic obesity' who are at increased risk of breast cancer and would benefit from tailored screening.

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P1-05-27

Liquid Biopsy for HER2 Status Assessment in Breast Cancer Using Surrogate DNA Methylation Markers

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Background: Emerging HER2-targeted drugs especially antibody–drug conjugates (ADCs) are promising and provide more options for breast cancer management. Current assessment of HER2 status and treatment decisions are mainly dependent on immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) on the primary tumor tissues. With the disease progression, the molecular status of the tumor may evolve and become discordant with the primary site. However, longitudinal monitoring of HER2 status is limited by infeasible repeated sampling of the tumor tissues. A non-invasive and accurate approach to obtaining real-time samples for measuring HER2 alterations is thus an unmet need for surveillance and guiding treatment selection in breast cancer. Detecting HER2 aberration in cell-free DNA (cfDNA) can

allow repeated sampling and avoid effects from tumor heterogeneity of tissue biopsy. Previous approaches for HER2 status determination using liquid biopsy were mostly dependent on the detection of copy number changes in cfDNA, but the limited signal-to-noise ratio poses a great challenge to the accuracy and robustness of the tests. In this study, we identified a group of DNA methylation markers for determining HER2 status in cfDNA for breast cancer. Methods: Genome-wide DNA methylation sequencing was conducted in tissue (25 HER2-positive and 35 HER2-negative) and plasma (32 HER2-positive and 107 HER2-negative) samples to identify specific methylation markers for HER2 status. HER2-positive samples were defined by IHC 3+ and 2+ with FISH positive, while HER2-negative ones were IHC 0/1+ and 2+ with FISH negative. Candidate markers were verified in another two sets of plasma samples (1. 30 HER2-positive and 40 HER2-negative; 2. 33 HER2-positive and 53 HER2-negative) by using quantitative methylation-specific PCR (qMSP). The performance of the markers was estimated by the Wilcoxon test, receiver operating characteristic curve, and logistic regression modelling. Results: 36 HER2 status-specific markers were discovered from genome-wide DNA methylation sequencing. Based on the qMSP results, 11 markers were verified by the performance analyses. The individual area under the curve (AUC) of these markers was from 0.58 to 0.68. From logistic regression modelling and 2-fold cross-validation, a 7-marker diagnostic model was built and validated on plasma samples, with the highest AUC of 0.812. Conclusion: cfDNA methylation detection inferring HER2 overexpression is a novel and non-invasive option for monitoring HER2 status in breast cancer patients, with a potential application in response prediction of HER2-targeted treatments. Further validation of the test is undergoing in large multi-centre cohorts in China.

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5:00 PM - 6:15 PM

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Decreases in Circulating Tumor Associated Cells Predicts PFS and OS In A Pooled Analysis Of Phase I Clinical Trials Using SV-BR-1-GM Therapy With Or Without Immune Check-Point Inhibitors In Metastatic Breast Cancer Patients

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Background: In metastatic Breast Cancer (mBC), Circulating Tumor Cells (CTCs) are clinical indicators of worse prognosis and indicate patients (pts) not responding to current therapy. However CTCs are rare, found in < 20% of mBC pts, and many pts without CTCs may also progress. Recently an inflammatory pro-tumorigenic PD-L1 expressing macrophage (Cancer associated macrophage-like cell [CAML]) was identified in the blood, which was found in >90% of mBC pts and may indicate tumor response to new therapies (JCO 40[16_Suppl] 2022). SV-BR-1-GM is a mBC cell line derived with antigen presenting characteristics was developed for treatment of mBC as a monotherapy (monoTx), or in combination with checkpoint inhibitors (comboTx). We report preliminary post-hoc results of a pooled analysis of n=18 monoTx mBCs pts and interim results of n=15 comboTx to analyze the predictive value of CTCs & CAMLs, as well as CAML PD-L1 expression, isolated from pt peripheral blood pre & post treatment to predict drug response, with end point outcomes of Progression Free Survival (PFS) and Overall Survival (OS) at 24 months. Methods: The SV-BR-1-GM regimen includes low pre-dose cyclophosphamide, intradermal inoculation of ~20 million irradiated SV-BR-1-GM cells and post-dose local interferon- α with cycles every 2 weeks x 3, then monthly. ComboTx adds an anti-PD-1 antibody with cycles every 3 weeks. Blinded blood samples were taken at baseline (BL), prior to starting SV-BR-1-GM therapy (n=33), and a 2nd sample (T1) taken after therapy initiation (~52 days) obtained as part of the exploratory portion of 2 prospective phase I clinical

drug studies, NCT03066947 & NCT03328026, to evaluate the predictive value of CTCs/CAMLS and CAML PD-L1 measured by LifeTracDx liquid biopsy. The quantities of CTCs & CAMLS were analyzed based on PFS using RECIST v1.1 and OS hazard ratios (HRs) by censored univariate analysis at 24 months. Results: A total of 33 mBC pts were pooled from monoTx (n=18), or comboTx (n =15), all with available blood samples at BL. CTCs were found in 30% (n=10/33) of pts at BL, and CAMLS were found in 94% (n=31/33) at BL. Presence of CTCs at BL did not correlate with worse PFS (HR=1.0, p=0.8550), but did trend for pts with worse survival (HR=5.1, p=0.0641). T1 samples were available from 61% (n=20/33) pts. A drop in CAMLS or CTCs after treatment at T1 was observed in 50% of pts, which correlated with a significantly improved PFS HR=11.8, p=0.0019 and OS HR=226.3, p=0.0397. Overall, pts with a decrease in CTCs/CAMLS after induction of SV-BR-1-GM therapy had a ~350% improvement in median PFS (1.9 mo. vs 6.6 mo.) and a ~200% improvement in median OS (6.3 mo. vs 12.4 mo). When stratified between monoTx and comboTx, pts with a decrease in CTCs/CAMLS had an improved PFS (HR 11.9, p=0.0136) in the monoTx group and an improved PFS (HR 17.5, p=0.0017) in the comboTx group. Further, while expression of CAML PDL1 at BL was not correlated with improved PFS (HR=1.0, p=0.9078), CAML PD-L1 expression at BL was correlated with significantly better OS HR=9.5, p=0.0116, consistent with long term benefit of SV-BR-1-GM therapy in this group of pts. Conclusions: We observed that treatment with the SV-BR-1-GM regimen was associated with decreases in the presence of CTCs and CAMLS in 50% of patients, which also significantly correlated with ~350% better median PFS and ~200% better median OS within 2 years. SV-BR-1-GM therapy alone, or as a combination treatment with anti-PD-1, appears to have improved long term clinical outcomes in a large portion of heavily pre-treated mBC patients compared to other typical standard of care published results.

Disclosure(s):

Daniel Adams, n/a: Creatv MicroTech, Inc.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Salary (Ongoing)

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5:00 PM - 6:15 PM

P1-05-29

Breast cancer laterality: Is age a factor?

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BACKGROUND: Studies have consistently demonstrated that breast cancers arise in the left breast more often than the right breast, but no factors have been able to account for this. Some studies have shown age younger than 45 years and late age at menarche to be associated with somewhat higher incidence of cancer in the right breast. However, most of these studies were conducted in the 1990s. We sought to determine if demographic factors, pathologic findings, or treatment impact laterality. **METHODS:** We performed a single-institution IRB-approved retrospective chart review of US female breast cancer patients diagnosed with DCIS (stage 0) or stages I-III breast cancer from 1997 to April 2020. Clinicopathologic characteristics, demographic, and treatment information were collected. Statistical analyses evaluated differences in laterality. Association between laterality and continuous variables was determined using Kruskal-Wallis test. Association of laterality and categorical variables was determined using Chi-square test or Fisher exact test if applicable. **RESULTS:** 5328 female patients with 5474 breast cancers were evaluated with a median age of 60 years old. Majority of tumors were stage T1(2542, 54.4%) and 75% were IDC. Overall left-sided cancer showed a predominance (2797, 51.1%). Breast cancer laterality was not significantly associated with grade, receptor status, tumor size, pathologic type, or recurrent tumors. Laterality was evaluated regarding age, based on age less than 61 years old versus greater than or equal to age 61. Laterality was significantly associated with age overall with an increase in left-sided breast cancers (2797 vs 2677, $p=0.029$). Left-sided breast cancer was significantly increased in women greater than or equal to age 61, 1456 (53%) vs right-sided 1290 (47%). Whereas, right-sided breast cancer was significantly associated with age less than 61, (1387, 50.8% vs left 1341, 49.2%, $p=0.004$). **CONCLUSION:** Our analysis confirms prior studies that overall left-

sided breast cancer is more common in women. However, there are age differences with left-sided breast cancers more prevalent in older age women greater than or equal to age 61. On the other hand, right-sided breast cancer was seen more often in women under the age of 61. Further studies are needed to better ascertain why the overall laterality of breast cancer occurs more frequently in the left breast, but also to determine an explanation for the laterality age differences. Anatomical factors such as blood supply, breast size, inherited genetic mutations, tumor genomics, lactation history and others are possible factors that need to be further explored. Studies are ongoing. This information will be potentially helpful in allocating diagnostic and therapeutic resources for breast cancer patients.

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P1-05-30

Concordance of preoperative breast MRI finding with definitive postoperative pathology report, after neoadjuvant systemic treatment in patients with breast cancer

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Neoadjuvant, i.e. preoperative, systemic antineoplastic treatment (NAT), in patients with breast cancer enables in vivo monitoring of tumor response to applied therapy, tailoring treatment in real-time accordingly, sparing surgical procedures, better quality of life for patients and implies better patient survival for particular patient, if a pathological complete response (pCR) to treatment is achieved. Use of MRI in monitoring response to NAT has shown in various studies sensitivity and specificity of at least 70% in the detection of residual disease, with a high positive and negative predictive value. Studies have shown higher accuracy in predicting pCR in HER2 positive tumors, and a higher rate of false negative results in HER2 negative tumors. Here we report findings of our pilot project where we tested the accuracy of the MRI, and the concordance of preoperative MRI findings after NAT, with the definitive pathology report after the surgery was performed, in breast cancer patients with different disease biology, in the real clinical practice. The focused pathological substrate was the primary tumor in the breast. For the simplicity of this pilot analysis, we did not include here the status of the axilla, which will be included in our larger analysis pending. We performed our analysis on a cohort of 200 breast cancer patients who underwent NAT, in our institution, University Hospital for Tumors, in Zagreb, Croatia. Median age of the analyzed patient cohort was 62 years. The representation of individual breast cancer intrinsic subtype surrogates was as follows: HER2 nonluminal tumor 23.5% (47/200), triple negative breast cancer 21.5% (43/200), luminal HER2 positive 22.5% (45/200) and luminal HER2 negative 32.5% (65/200). According to MRI of the primary tumor in the breast, radiological complete response (rCR) to NAT was achieved in 46.5% (93/200) of patients, and the finding of residual tumor was described in 53.5% (107/200) of patients. Postoperatively, pathology report of the primary breast tumor showed pCR in 29% (58/200) of patients, and residual disease in 71% (142/200) of cases. The overall concordance of MR and pathology reports was 62.4% in the assessment of complete response, and 75.35% in the assessment of residual disease. Analyzed according to subgroups, results are as follows: in the cohort of patients with HER2 nonluminal tumors, concordance of MRI and pathology report in the assessment of complete response was 88%, while for residual disease concordance was 70%; in the cohort with triple-negative breast cancer patients, concordance of MRI and pathology report in the assessment of complete response was 83%, and residual disease 87.8%; in the group with luminal HER2-positive breast cancer concordance of MRI and pathology report in assessing complete response, as well as residual disease, was 97%; while in the group with luminal HER2-negative breast cancer, concordance of MRI and pathology report findings in assessing complete response was only 50.5%, and residual disease 77%. Results of our analysis showed relatively high overall concordance between MRI and pathology findings, which is in line with results of large studies worldwide and confirms MRI as a good method in monitoring response to NAT in breast cancer patients. By subgroup analysis, patients with luminal HER2-negative tumors are distinguished. This group has the lowest prevalence of complete response overall, as well as the lowest concordance of MRI and pathology report findings in the detection of these cases. This confirms the weaker response of this type of tumor to neoadjuvant treatment, but also indicates the need for additional caution when analyzing MRI findings in these patients, as well as for considering additional diagnostic arsenal, complementing the standardly – utilised MRI.

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5:00 PM - 6:15 PM

P1-05-31

A single center retrospective analysis of 259 cases of metaplastic breast cancer

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Introduction: Metaplastic breast cancer (MBC) is a rare breast tumor. WHO histological classification of breast tumors in 2019 divided MBC into the following seven types: low-grade adenosquamous carcinoma, fibromatoid metaplastic carcinoma, squamous cell carcinoma, spindle cell carcinoma, metaplastic carcinoma with mesenchymal differentiation, mixed metaplastic carcinoma and myoepithelial carcinoma. Based on single center data, this study intends to conduct a detailed analysis of the clinicopathological features, treatment and prognostic factors of MBC. Methods: We collected 259 MBCs treated in our center from 2006 to 2022. The patient's age, histological type, image feature, tumor size, lymph node metastasis,

tumor stage, immunohistochemical information, surgical plan and systemic adjuvant therapy were summarized and considered to explore the factors affecting the overall survival rate (OS) and disease-free survival rate (DFS). T-test and chi-square test were performed on the data. $P < 0.05$ showed that the difference was statistically significant. Kaplan-Meier survival was used to analyze the long-term efficacy. Results: The incidence rate of MBC in breast cancer patients in our center is about 0.5%. They included 105 cases of squamous cell carcinoma (40.5%), 49 cases of mixed metaplastic carcinoma (18.9%), 41 cases of spindle cell carcinoma (15.8%), 27 cases of metaplasia carcinoma secreting matrix (10.4%), 6 cases of metaplastic carcinoma with mesenchymal differentiation (2.3%), 6 cases of myoepithelial carcinoma (2.3%), 3 cases of low-grade adenosquamous carcinoma (1.2%), 1 case of fibromatoid metaplasia carcinoma (0.4%) and 21 cases of unknown (8.1%). MBC were mainly three negative subtypes, which were 204 cases (78.8%), 41 cases (15.8%) luminal subtypes and 14 cases (5.4%) HER2 positive subtypes. There was no significant difference in the distribution of breast cancer subtypes among different histological types of MBC. There were 63 cases (24.3%) in clinical stage I, 171 cases (66.0%) in stage II, 23 cases (8.9%) in stage III and 2 cases (0.8%) in stage IV. 58 patients underwent core needle biopsy, of which only 7 (12.1%) reported histological types consistent with MBC. Among 154 patients with molybdenum target reports, 59 of them (38.3%) had malignant calcifications. The diagnostic coincidence rates of MRI, ultrasound and molybdenum target were 90.0%, 85.1% and 74.7% respectively. 258 cases of MBC received surgical treatment, including 183 cases of total mastectomy (70.9%), 53 cases of breast conserving surgery (20.5%) and 22 cases of quadrant resection (8.5%); 132 patients (51.2%) underwent axillary lymph node dissection and 93 patients (36.0%) underwent sentinel lymph node biopsy. 24 patients (9.3%) received neoadjuvant chemotherapy, of which only 2 (8.3%) achieved pathological complete remission. 56 patients (21.6%) received adjuvant radiotherapy, with a median of 25 times. 167 patients (64.5%) received adjuvant chemotherapy, and anthracycline sequential paclitaxel was the most commonly used regimen. The median follow-up was 31 months. The five-year DFS was 82.0%, and the five-year OS was 89.4%. Through Cox regression analysis, it was found that patients' N stage ($P=0.036$) and receiving anthracycline sequential paclitaxel adjuvant chemotherapy ($P=0.004$) were independent prognostic factors. Conclusion: The histological types of MBC are complex. MRI is of high value in diagnosis. Conventional CNB is difficult to meet the needs of pathological tissue classification. Patients without lymph node metastasis and receiving anthracycline sequential paclitaxel adjuvant chemotherapy are associated with better prognosis. Through multidisciplinary standardized diagnosis and treatment, there is no significant difference between the prognosis of MBC and the common types of breast cancer. Keyword: metaplastic breast cancer; pathological characteristics; imaging; treatment; prognosis.

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5:00 PM - 6:15 PM

P1-05-32

Outcomes of diagnostic breast imaging in young women (less than 50 years old)

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INTRODUCTION The incidence of breast cancer is on the rise in the younger population, with 23 percent of all breast cancer diagnoses occurring in those under the age of 50. In Canada, screening mammography in women at average risk of breast cancer is recommended after the age of 50. Breast cancer in younger women is biologically more aggressive with greater rates of recurrence and metastatic disease. The sensitivity of mammograms to detect clinical breast abnormalities may be reduced due to increased breast density in this age group, leading to potential delayed diagnosis and poor outcomes. The frequency of false-negative diagnostic mammograms in young women is unknown. The purpose of this study is to describe the outcomes of diagnostic breast imaging in young women undergoing investigations for abnormal clinical breast findings and the frequency of delayed breast cancer diagnosis (more than 6 months after initial diagnostic mammography). **METHODS** We conducted a retrospective electronic chart review in women at average risk of breast cancer, aged between 30 and 50, who underwent diagnostic mammograms and/or breast ultrasounds (US) at our institution between 2018 to 2019 for symptomatic clinical presentations (breast pain, palpable mass, nipple discharge or breast skin changes). Patients undergoing routine screening mammograms were excluded. We collected demographics, findings of initial and follow-up breast imaging (using the Breast Imaging Reporting and Data System (BI-RADS) & breast density), and breast cancer diagnosis timelines where applicable. The primary outcome measure was the frequency of delayed breast cancer diagnosis defined as > 6 months from initial diagnostic imaging. Secondary outcomes included completion of recommended follow-up investigations and their

outcomes, total number of breast cancer diagnoses and stage. The study was approved by the local research ethics board and the results were summarized using descriptive analysis.

RESULTS We reviewed 400 electronic charts and identified 171 eligible patients. Mean age was 38 years; initial breast imaging included both diagnostic mammogram and US in 168 (87%), US alone in 20 (12%) and mammogram alone in 3 (2%) patients. Breast density was not routinely reported during this time frame. Ninety patients (53%) had benign findings (BIRADS 1 and 2), 41 (24%) had probable benign findings requiring short-term follow-up (BIRADS 3) while 30 (18%) patients had findings suspicious of malignancy (BIRADS 4&5) with biopsy recommended for diagnosis. In the BIRADS 3 group, 93% had recommended follow-up at a median of 7.6 months. Breast US alone was the most common subsequent investigation of which 15 % were benign lesions (BIRADS 1 & 2) and 68% remained in the BIRADS 3 category, while none were scored BIRADS 4 or 5. Among patients with BIRADS 4 & 5 scores, 83% underwent recommended biopsy at a median time of 3 weeks. Ten (6%) out of all 171 patients were diagnosed with breast cancer, all of which had BIRADS 4 or 5 on initial diagnostic imaging. Stage distribution was as follows: stage 0 - 2 patients, stage 1- 7 patients and stage 2 - 1 patients with no locally advanced or metastatic disease. The mean time from initial imaging to breast cancer diagnosis was 1.5 weeks (range 1 to 22 weeks). None of the patients had delayed breast cancer diagnosis in our cohort.

CONCLUSION More than half of patients with clinical breast findings in our cohort had benign findings on diagnostic mammogram and/or US (BIRADS 1&2) with no subsequent breast diagnosis. Majority of patients requiring further investigations (BIRADS 0, 3, 4 and 5) underwent recommended follow-up (imaging or biopsy). Ultimately, a total of 10 patients were diagnosed with breast cancer at a median time of 1.5 weeks from original diagnostic imaging with no delayed breast cancer diagnosis. We, therefore, conclude that diagnostic mammograms and US are appropriate diagnostic investigations for clinical breast concerns in women between 30-50 years.

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RNA in Extracellular vesicles used for the prediction of distant metastasis of breast cancer and the function of TGM2 in promoting breast cancer development

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Background: Extracellular vesicles (EVs) can be released by living cells during the process of tumor metastasis. Since EVs could contain various of molecular with high stability, a growing number of evidences indicated that those molecular can be utilized as biomarkers of liquid biopsy for metastatic prediction. Therefore, we aimed to identify genes and build a model that can predict the risk of metastasis in breast cancer patients with acceptable sensitivity and accuracy. Methods: Pretreatment plasma EV-RNAs of patients diagnosed at Fudan University Shanghai Cancer Center from 2017 to 2018 were extracted and analyzed by next generation sequencing (NGS) and bioinformatics, including breast cancer patients (n=114) and benign cases (n=18). Weighted correlation network analysis (WGCNA) was utilized to determine the relationship between clinical features and genes. The Kaplan-Meier was used for survival analysis in public database. By 100 times of 5 folds cross-validation, we used logistic regression analysis to set up the model. The receiver operating characteristic curve (ROC) and area under curve (AUC) were used to assess the predicted capacity of the model. QRT-PCR was conducted to further confirm the expression of genes selected by the predicting model in 175 breast cancer patients with and without metastasis, along with 5 EV-RNAs of tumor samples and paired normal adjacent breast tissues. The functions of candidate genes on cell proliferation, metastasis, and invasion were determined by a series of in vitro experiments in cancer lines. RNA sequencing and bioinformatic analysis were performed to explore the mechanism of the candidate genes. Moreover, co-immunoprecipitation (Co-IP) was used to reveal interacting proteins. Results: WGCNA screened 40 hub genes which were significantly associated with the distant metastasis in patients with breast cancer. A total of 207 upregulated genes were identified in patients with distant metastasis. After intersection, 6 genes were selected. Survival analysis suggested that high expression of IGFBP5, BCL6B, TGM2, and SH3PXD2A were correlated with poor distant metastasis-free survival (DMFS). The metastasis predicting model built based on those genes showed an AUC value of 0.923 with diagnostic accuracy of 91.2%. In the validation cohort, data showed the AUC value of each single gene were 0.835, 0.818, 0.845, 0.834, for TGM2, IGFBP5, BCL6B, and SH3PXD2A respectively. Among those four genes, TGM2 was significantly upregulated with clinical stages and correlated with poor prognosis. Moreover, TGM2 showed the highest abundance in tumor tissue EVs. Functional experiments revealed that TGM2 promoted breast cancer proliferation, metastasis, and invasion in vitro. The initially upregulated expression of TGM2 in EVs of cell lines was significantly decreased by adding the exosome release inhibitor GW4869. In addition, EVs from TGM2 overexpressed cells promoted cell migration and invasion of wild-type cells. Mechanistically, TGM2 was positively correlated with EMT, Hedgehog and IL6-JAK-STAT3

pathways. Co-IP assay found that TGM2 interacted with TMF1, which was an effector for degradation of STAT3 through the ubiquitin-proteasome pathway. Interfering the expression of TMF1 remarkably promoted the migration ability of cells and reversed by TGM2 overexpression. Conclusion: Based on the plasma EV-RNAs, we constructed a model with promising predicted capacity of distant metastasis in patients with breast cancer. TGM2, as the most effective predictor, can promote the progression and metastasis of breast cancer by targeting TMF1/STAT3. Key words Breast Cancer; Extracellular vesicles; Metastasis; Prediction model; TGM2

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MicroRNAs as Prognostic Markers in Breast Cancer

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Background: Breast cancer (BC) is the most common cancer and the second leading cause of cancer death in American women. BC disproportionately affects women of ethnic minorities, especially Black and Hispanic. While this disparity has been acknowledged and social determinations of health remains an important contributor, BC pathophysiology is yet to be elucidated in minorities. MicroRNAs (miRNA), including but not limited to let-7, 125-3p, 192-5p, 451a, play regulatory roles in cancer pathobiology and progression in many cancer types, including but not limited to BC. In our lab, in vitro and in vivo studies on mouse models demonstrated that miR-23b and miR-27b had crucial roles in cancer progression in BC via mechanisms that involves nischarin, an integrin-binding protein, and were associated with worse outcome. Moreover, miRNAs can be detected and are stable in blood samples, and thus the detection has a profound clinical impact on diagnosis. Study Design: Between April 2021 and May 2022, 30 newly diagnosed patients with BC and 30 patients without any cancer diagnosis at University Medical Center- New Orleans were enrolled on the study (IRB# 936). 86% of patients are African American or Hispanics. Plasma samples were collected before any medical intervention for BC. Plasma miRNAs were isolated and miRNA expression were performed utilizing RT-PCR. Results: Expressions of let-7 and 125a miRNAs are two times higher in plasma of patients with BC compared to patients without a diagnosis of cancer. There was no difference in miRNA expression in circulatory 23b, 27b, 192-5p, and 451a. Among breast cancer types, there are two-fold decreased expression of 192-5p and 451a in triple negative compared to hormone positive BC. Conclusion: This project will add to the body of knowledge on roles of miRNAs as prognostic markers in patients with BC, more importantly,

triple negative BC, and elucidate pathophysiologic mechanism contributing to racial disparity in breast cancer treatment and recurrence. In the near future, we aim to examine effects of chemotherapy and surgery on the expression of circulatory microRNAs.

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Identification of Circulating Tumor Cells captured by the FDA Cleared Parsortix® PC1 System from the Peripheral Blood of Metastatic Breast Cancer Patients using Immunofluorescence and Cytopathological Evaluations.

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Background: Circulating tumor cells (CTCs) captured from the blood of cancer patients may serve as a non-invasive surrogate source of tumor material to investigate tumor characteristics in real-time. The Parsortix® PC1 System, the first FDA-cleared medical device for the capture and harvest of CTCs from peripheral blood of metastatic breast cancer (MBC) patients for use in subsequent user-validated downstream analyses, enables the epitope independent capture of CTCs with diverse phenotypes based on cell size and deformability. In this study, CTCs isolated from the blood of MBC patients by the Parsortix® PC1 System were identified using an immunofluorescence (IF) based assay for detection of epithelial CTCs followed by Wright-Giemsa staining and cytomorphological review. The aim of this study was to determine the proportion of MBC patients and self-declared female healthy volunteers (HVs) that had one or more CTCs identified in the population of cells harvested from their peripheral blood by the Parsortix® PC1 System. Methods: Peripheral blood from 75 HVs and 77 patients with MBC was prospectively collected into K2EDTA tubes at the University of Rochester Medical Center. The blood collected from each subject (8.6±1.2mL) was processed on a Parsortix® PC1 System within 8 hours of collection. The cells harvested by the system were cytospun onto a charged slide and IF stained using an optimised antibody panel. The IF panel consisted of a nuclear dye (DAPI), positive selection markers targeting epithelial CTCs (Cytokeratins (CK) and EpCAM), and negative selection markers targeting white blood cells, such as lymphocytes, macrophages, granulocytes, monocytes, fibroblasts, and cells of megakaryoblastic potential. The stained slides were imaged using fluorescence microscopy and CTCs were defined as nucleated cells (DAPI+) that were positive for CK and/or EpCAM and negative for the blood lineage markers. The IF slides were subsequently stained with Wright-Giemsa and analysed by a qualified pathologist using light microscopy. Morphological features of malignant cells were used to define and identify CTCs. All laboratory testing and analysis was performed by

operators blinded to the clinical status of each subject. Results: On the evaluable IF-stained slides, cells classified as CTCs based on their IF staining pattern were identified in 45.3% (34/75) of the MBC patients (range = 0 – 125 CTCs, mean = 7) and in 5.6% (4/71) of the HVs (range = 0 – 8 CTCs, mean = 0). No EpCAM+, CK- CTCs were identified in either MBC patients or HVs. In the 34 MBC patients with one or more CTCs observed, 70.6% had only CK+, EpCAM- cells, while the remaining 29.4% had at least one CK+, EpCAM+ cell. In the HVs, one out of the four CTC-positive donors had only CK+, EpCAM+ cells while the other three had only CK+, EpCAM- cells. On the evaluable Wright-Giemsa stained slides, cells classified as CTCs by the pathologist were identified in 57.1% (40/70) of the MBC patients (range = 0 – 41 CTCs, mean = 4) and in 4.4% (3/68) of the HVs (range = 0 – 14, mean = 0). Conclusions: This study demonstrated the ability of ANGLE's Parsortix® PC1 System to capture and harvest CTCs from a significantly larger proportion of MBC patients compared to HV subjects. The presence of epithelial cells in subjects without diagnosed disease has been previously described in the literature, with their significance being unclear. This study also demonstrated that the cells harvested by the Parsortix® PC1 System can be successfully evaluated using both IF staining and Wright-Giemsa cytomorphological assessment for the identification of CTCs. Interestingly, a high proportion of the identified CTCs did not express EpCAM, further highlighting the limitations of using EpCAM-based approaches to capture CTCs.

Disclosure(s):

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AI-Based Smartphone App Using a Single-Lead ECG for Automated QTc Diagnostics in Oncology

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Introduction: Long QT syndrome is a common cardiotoxic side effect of various anti-tumor drugs. Previous cardiological monitoring of oncological patients is primarily complex and requires for non-internal oncologists a consultation. Therefore, the QTc-Tracker smartphone APP was developed, which enabled a tele-cardiological diagnosis of the QTc time with standard single-lead ECG devices. As a result, diagnosis times could already be reduced by 99%. The further development examined an automatic determination of the QT time using the smartphone APP. However, since single-lead ECG devices are significantly more susceptible to interference, the determination of the QT time is more complex than with 12-lead ECGs.

Methods: The QTc-Tracker smartphone APP was developed to determine the QT time. Self-tracker single-lead ECG devices were used to record the lead I signal. The ECG recordings were analyzed in the APP and passed on to an external cardiologist as reference. The APP used artificial intelligence and was trained in the first phase and validated in the second phase. The first phase aimed to improve QT time detection. The results of the APP were compared with the findings of the external cardiologist. In both phases, ECGs from breast cancer patients receiving ribociclib were used. Results: A total of 1889 single-lead ECGs were carried out. 248 of these could not be evaluated (13%). QTc prolongation, according to CTCAE, was diagnosed

in 41 cases (2.5%). 878 of the evaluable ECGs were used for the training phase and 763 for the evaluation phase. In the first group (before the improvement), the sensitivity to automatically detect a prolongation of the QT time was 36%, and the specificity was 96%. In the evaluation collective (after the training), the sensitivity went up to 85%, and the specificity was unchanged at 96%. Conclusions: The trained method of the QTc tracker is able to reliably detect a QT time lengthening even without a cardiological diagnosis only by using single-lead self-tracker ECG's. In the rare cases in which an elongation was not detected, the cardiac diagnosis was only a few milliseconds above the threshold value. This artificial intelligence-based smartphone APP is not intended to replace the cardiological diagnosis, but it can simplify routine processes and help to decide which patients need a cardiological examination more urgently.

Disclosure(s):

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5:00 PM - 6:15 PM

P1-06-01

Associations of historic and contemporary “redlining” with breast cancer stage at diagnosis.

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Breast cancer is the most commonly diagnosed cancer among US women across all racial/ethnic groups. Stage at diagnosis is one of the major factors determining breast cancer prognosis. The 5-year relative survival for breast cancer ranges from 99% for localized stage at diagnosis, to 84% for regional stage, and to 27% for distant (metastatic) stage breast cancer. The proportion of women diagnosed with breast cancer at later stages (regional and distant) in the US are higher among women with lower socio-economic status and among non-Hispanic Black women. Historic mortgage security redlining, implemented by the Home Owners' Loan Corporation (HOLC) in the 1930s across numerous US cities, continues to have a negative influence on breast cancer stage at diagnosis, largely due to continued social and economic isolation and poor living environments resulting in many adverse consequences, including lower education, limited job opportunities, no/limited health insurance coverage, and suboptimal access to care, including cancer screening services. Additionally, studies have reported that living in areas with greater contemporary mortgage lending bias towards the non-Hispanic Black population (measured as higher odds of mortgage denial) is associated with late-stage breast cancer diagnosis in several US metropolitan areas.

In this study, we aim to examine the association between the historic HOLC-based “redlining” and contemporary mortgage lending bias and stage of breast cancer at diagnosis among women aged 18 years and older in New Jersey diagnosed with first primary invasive breast cancer in 2010-2015 (N= 32,939). The study population was derived from the New Jersey State Cancer Registry. Historic “redlining” data based on 1930s neighborhood boundaries and transformed to corresponding 2010 census tracts borders were obtained from Inter-university Consortium for Political and Social Research. Mortgage lending bias score for the study period was calculated at the census tract level following methodology developed by Beyers and colleagues. Associations between census tract-level historic “redlining”, contemporary mortgage lending bias and breast cancer stage at diagnosis were evaluated using multinomial logistic regression models after adjusting for age alone, and then for age, race/ethnicity, marital status, and health insurance status.

The study included 21,038 local, 9,765 regional, and 2,136 distant stage breast cancer cases. After adjusting for age, race/ethnicity, marital status, and health insurance, women living in historically redlined census tracts were more likely to be diagnosed with regional (OR=1.23;

95% CI 1.03-1.48) and distant (OR=1.55; 95% CI 1.09-2.22) stage breast cancer compared to women living in other census tracts. Odds for regional (OR=1.14; 95% CI 1.06-1.23) and distant (OR=1.33; 95% CI 1.16-1.53) stage breast cancer were also significantly higher for women living in areas with highest mortgage lending bias score. Stratifying by age (< 65 and >=65 years) showed similar patterns (data not shown).

Both historic “redlining” and contemporary mortgage lending bias were associated with being diagnosed with breast cancer at later stages, notably distant stage. Targeting the legacy of systematic racism and addressing any contemporary discriminatory policies may help reduce breast cancer disparities in the diagnosis stage and thus mortality.

Association between the historic redlining and contemporary mortgage lending bias and stage of breast cancer at diagnosis among women aged ≥18 years in New Jersey, 2010-2015

Measure of bias	Local	Regional			Distant		
	Number (%) n=21038	Number (%) N=9768	Age-adjusted odds ratio (95% confidence interval)	Fully-adjusted odds ratio* (95% confidence interval)	Number (%) N=2137	Age-adjusted odds ratio (95% confidence interval)	Fully-adjusted odds ratio* (95% confidence interval)
Historic “Redlining”[^]							
A. Best	552 (2.6%)	238 (2.4%)	Reference	Reference	42 (2.0%)	Reference	Reference
B. Still Desirable	1880 (8.9%)	869 (8.9%)	1.12 (0.94-1.33)	1.08 (0.90-1.28)	179 (8.4%)	1.22 (0.86-1.73)	1.14 (0.80-1.61)
C. Definitely Declining	2582 (12.3%)	1368 (14.0%)	1.26 (1.07-1.49)	1.16 (0.98-1.37)	232 (15.1%)	1.22 (1.16-2.26)	1.44 (1.03-2.02)
D. Hazardous	1152 (5.5%)	715 (7.3%)	1.26 (1.21-1.74)	1.23 (1.03-1.48)	175 (8.2%)	1.98 (1.39-2.82)	1.55 (1.09-2.22)
Not Classified	14872 (70.7%)	6575 (67.3%)	1.07 (0.91-1.25)	1.09 (0.93-1.27)	1417 (66.3%)	1.23 (0.89-1.69)	1.23 (0.89-1.69)
Contemporary mortgage lending bias							
Q1-Lowest Score	6381 (30.3%)	2762 (28.3%)	Reference	Reference	539 (25.2%)	Reference	Reference
Q2	6031 (28.7%)	2594 (26.6%)	1.0 (0.94-1.07)	1.01 (0.94-1.07)	582 (27.2%)	1.14 (1.01-1.29)	1.12 (0.99-1.27)
Q3	5090 (24.2%)	2377 (24.3%)	1.08 (1.01-1.16)	1.06 (0.99-1.14)	540 (25.3%)	1.26 (1.11-1.42)	1.21 (1.07-1.37)
Q4-Highest Score	3514 (16.7%)	2005 (20.5%)	1.3 (1.21-1.39)	1.14 (1.06-1.23)	471 (22.0%)	1.6 (1.40-1.82)	1.33 (1.16-1.53)
Not Classified	22 (0.1%)	27 (0.3%)	2.67 (1.54-4.63)	2.23 (1.28-3.88)	4 (0.2%)	1.98 (0.69-5.74)	1.59 (0.54-4.64)

Note: For contemporary mortgage lending bias, highest score is indicative of highest bias (highest proportion of mortgage denial) towards Black people.

* Fully adjusted model includes covariates: age, race/ethnicity, marital status, health insurance status

[^]Areas designated “Best” were individual housing markets with sufficient levels of financing and were preserved exclusively for White and wealthy population. Areas defined as “Hazardous” were those lacking financial resources and were designated for Black and poor population.

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P1-06-02

The effect of race on pathologic complete response rates and overall survival in patients with triple negative breast cancer

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Introduction: Despite the recent overall improvement in survival for patients with breast cancer, racial disparities in outcomes persist. While studies have demonstrated that socioeconomic factors and access to treatment play a role, differences in tumor biology may also contribute. Black women are significantly more likely to develop triple negative breast cancer (TNBC), the deadliest of the breast cancer subtypes, with more TNBC patients progressing to incurable, metastatic disease than patients with any other breast cancer subtype. Studies have demonstrated that TNBC patients who achieve a pathologic complete response (pCR), defined as no residual invasive cancer in the breast or lymph nodes after neoadjuvant chemotherapy (NAC), have improved survival. We hypothesize that rates of pCR and overall survival (OS) in patients with TNBC may differ by race/ethnicity, which may account in part for the disparities in outcomes observed. **Methods:** Adult female patients with stage I-III TNBC diagnosed in 2010-2019 who received NAC followed by surgery were identified from the National Cancer Database (NCDB). Race/ethnicity was defined as Hispanic (H), Non-Hispanic White (NHW), Non-Hispanic Black (NHB), Non-Hispanic Asian (NHA), and Non-Hispanic Other (NHO). pCR was defined as no invasive cancer in either the breast or axilla (ypT0/is,N0) at surgery. Logistic regression was used to estimate the association of race/ethnicity with achievement of pCR after adjustment for covariates. Unadjusted OS was estimated using the Kaplan-Meier method, and the log-rank test was used to compare groups. Cox Proportional Hazards models were used to estimate the association of race/ethnicity and achievement of pCR with OS after adjustment for covariates. Additional interaction and subgroup analyses were also conducted. **Results:** Of the 40,890 patients identified, 29.8% (n=12,173) demonstrated pCR after NAC. The unadjusted 5-year OS rates for those who achieved pCR were significantly higher compared to patients with no pCR (0.917, 95% CI 0.911-0.923 vs 0.667, 95% CI 0.661-0.673, log-rank $p < 0.001$). Hispanic patients were more likely to achieve pCR (OR 1.19, 95% CI 1.08-1.31, $p=0.001$), and NHB patients were less likely to achieve pCR (OR 0.89, 95% CI 0.83-0.95, $p=0.001$) compared to NHW, even after adjustment. Unadjusted OS was also notably lower for NHB patients compared to every other race group (5-year OS rate: NHB 0.709 vs NHW 0.746 vs NHO 0.771 vs H 0.772 vs NHA 0.816, log-rank $p < 0.001$); however, this difference did not persist after adjustment for patient and disease factors, including achievement of pCR. Interval from diagnosis to start of chemotherapy (OR 0.95, 95% CI 0.94-0.96, $p < 0.001$) and duration after chemotherapy start to surgery (OR 1.02, 95% CI 1.02-1.03, $p < 0.001$) were associated with the odds of achieving pCR. Overall, the effect of achieving pCR on OS did not differ by race/ethnicity (interaction $p=0.10$). **Discussion:** Achieving pCR after NAC in patients with TNBC is associated with a significant improvement in OS. Yet, rates of pCR appear to differ based on race/ethnicity, with NHB patients demonstrating significantly lower rates of pCR than NHW patients, which may contribute to the disparities in survival outcomes observed. In addition to addressing socioeconomic factors and access to treatment, further research examining whether biological differences exist based on race that influence response of TNBC to current standard therapies is essential for improving survival outcomes for this disproportionately affected patient population.

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P1-06-03

Differences in Breast Cancers among American-Indians and Whites in the United States

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Differences in Breast Cancers among American-Indians and Whites in the United States
Background - The United States has made substantial progress in improving breast cancer (BC) outcomes over the years, but unfortunately, this improvement has not impacted all races equally. BC death rates have not improved significantly for American Indian (AI) women, whereas, it significantly decreased for White women. In addition, AI women were more likely to be diagnosed at a younger age with a late-stage disease. We sought to determine the reasons for these disparities. Methods - This is a retrospective cohort study using a hospital registry database (the National Cancer Data Base) (NCDB). We identified female AIs and non-Hispanic Whites in the US diagnosed with BC between the years 2004 and 2016. We compared patient and tumor characteristics between the 2 groups and its effect on age and stage at diagnosis.

We also determined hazard ratios (HRs) for overall survival using Cox regression models, both before and after adjustment for covariates. Results – Data on 6,866 AIs and 1,987,324 White women diagnosed with BC were analyzed. The mean (SD) age at diagnosis was significantly younger for AI than for White women (57.72 ± 12.23 vs. 61.87 ± 13.21). AI women traveled double the distance to their treatment facilities, lived in lower median income zip codes, reported a higher percentage of no insurance, and higher comorbidities than Whites. Furthermore, AIs were less likely to be diagnosed with Stage 0 and I BCs, had a larger tumor size, greater number of positive lymph nodes at diagnosis, and higher proportion of triple negative and HER2-positive BCs than Whites. Whites were more likely to have other cancers diagnosed prior to or after their BC diagnosis. All the above tests for comparisons were significant (p -value < 0.001). Correlation between patient/tumor characteristics with age and stage at diagnosis was not significantly different between AIs and Whites. Unadjusted overall survival (OS) was significantly worse for AIs as compared to Whites (HR=1.07; 95% CI: 1.01-1.14, p -value = 0.025). After adjustment of all covariates including age, travel distance, median income of residential zip code, insurance status, cancer sequence, comorbidities, stage, tumor size, number of positive lymph nodes, grade, histology, and hormonal/HER2 status, OS was not significantly different between AIs and Whites (HR=1.04; 95% CI: 0.90-1.20, p -value = 0.601). Conclusion - Our study showed significant differences in patient and tumor characteristics among AI and White BC patients which adversely impacted BC outcomes in AIs. Survival was lower in AIs, but when adjusted for various covariates, the survival difference disappeared. Improvement in BC outcomes in AIs will involve not only improved and early access to screening to identify patients at younger ages and earlier stages at diagnosis, but also long term plans to provide affordable and the full spectrum of cancer care closer to home.

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P1-06-04

IMPACTS OF TREATMENT DELAY ON BREAST CANCER MORTALITY AND BENEFIT OF TIMELY CARE IN BLACK AND NON-BLACK WOMEN

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BACKGROUND: The impact of treatment delays on cancer outcomes has been well documented, but few published studies explicitly attempt to identify subgroups which would benefit the most from potential interventions improving timeliness of care. Using the state of North Carolina and breast cancer as an example, we sought to quantify race-specific associations between frontline treatment delay and breast cancer mortality, and estimate the potential impact of improvements in timeliness by racial sub-group. **METHODS:** We conducted a retrospective cohort study, utilizing multipayer insurance claims linked to cancer registry data from the Cancer Information and Population Health Resource, of females diagnosed with stage I-III breast cancer from 2004 to 2014. Our exposure of interest was treatment delay, defined as initial cancer directed therapy received ≥ 60 days after diagnosis. Our outcome was death certificate identified breast cancer mortality within 5-years of follow-up. To quantify the association between treatment delay and mortality we estimated hazard ratios (HR) and 95% confidence limits (CL) where non-breast cancer deaths were treated as competing events. We then simulated the effect of treating all patients within 60 days using inverse probability of treatment weighting (IPTW), and estimated the potential impact by comparing the simulated data with observed data. Models were adjusted for age and stage at diagnosis, tumor grade, hormone receptor status, and modality of first treatment. Models were stratified by race, dichotomized as Black or non-Black, and geographic subregion for evaluation. **RESULTS:** Our analytic cohort comprised 21,200 patients, of whom 19% were Black. Treatment delays >60

days were twice as frequent among Black compared with non-Black patients (13.5% vs. 6.5%). We found a positive association between treatment delay and breast cancer mortality in the overall cohort (HR=1.3; CL: 1.1, 1.6). The association differed between Black (HR=1.4; CL: 1.1, 1.8) and Non-Black (HR=1.2; CL: 0.9, 1.6) patient subgroups. For both racial groups, the strength of the relationship between treatment delay and mortality varied across geographic subregions. The estimated potential improvement in 5-year cumulative breast cancer mortality from delivering timely care to all patients differed in magnitude across sub-populations. The magnitude of potential improvement in breast cancer mortality at 5 years in the overall analytic cohort was 0.3% (5-year risk of breast cancer mortality in observed cohort: 7.2% vs 6.9% with simulated universal timely treatment). In the Black subcohort, the potential decrease in mortality for timely treatment was 1.0% (observed: 12.3% vs simulated: 11.4%), while in the non-Black population the potential decrease was 0.1% (observed: 6.1% vs simulated: 5.9%).

CONCLUSIONS: The magnitude of association between delayed treatment of stage I-III breast cancer and breast cancer mortality differed between Black and non-Black patients, highlighting that interventions to avert treatment delays may have a meaningful impact for this group.

Further research is needed to identify factors underlying this difference, which may include a direct effect of differences in timeliness, or downstream differences in the intensity and quality of cancer care beyond the 60-day landmark for delayed patients. Our findings suggest that comprehensive intervention at the state level to improve the timeliness of breast cancer treatment could potentially reduce breast cancer mortality, and that targeting such intervention to patient groups with larger projected benefit, such as Black patients, may be a more efficient use of resources. We have illustrated how a counterfactual approach may be useful in identifying subgroups where focused intervention efforts may yield greater improvements in outcomes.

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Access to medical coverage in newly diagnosed Breast cancer patients a minority population during the COVID 19 pandemic

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Background:

Hispanics are among the most significant minorities in the United States, and assessing their health needs is vital in formulating health policies. The social, environmental, and biological background affect their morbidity and mortality, with cancer being the leading cause of mortality in Hispanics. Although implementing the Affordable Care Act improved access to health care, disparities and challenges in Hispanics' access to health care remain.(1)

In our study, we are trying to assess the COVID-19 pandemic implications on the socioeconomic status of Hispanics with newly diagnosed breast cancer and how that is affecting their outcome.

Methods:

This is a retrospective study demonstrating the nature of breast cancer screening, diagnosis, and management during COVID-19 lockdown and post-vaccine compared to the pre-COVID-19 era. The retrospective review was conducted at Mays Cancer Center in San Antonio, IRB approved by UT Health San Antonio. The data were abstracted from the medical record system (EPIC). Pearson's Chi-squared and logistic regression tests were used to determine the relationship between time and stage at diagnosis and association with funding status

Result:

696 subjects with newly diagnosed breast cancer were identified and divided into three cohorts: Cohort A: 264 pts in a pre-covid era: From 2018-February 2020, Cohort B: 171 patients during the covid-19 lockdown, and Cohort C: from April 2020-Dec-2020 with 261 patients in the post-vaccine era.

A higher percentage of patients had Tis identified in Cohort A (26%) compared to Cohort B (19%) and Cohort C(12%) (p0.003). These numbers have changed to an increasing percentage of patients with T1 or T2. N0 or N1 in Cohort B (62%) and Cohort C (68%), p0.003).

Presentation of locally advanced (T3/T4 with any N) and metastatic disease remained relatively similar in all cohorts, with more metastatic cases at presentation in Cohort A (p0.003). Many patients of Hispanic ethnicity (OR 1.47, p0.1) were not funded by commercial insurance or Medicare. (OR 2.33, 95% CI 1.43, 3.77, p< 0.001). A high proportion of Hispanic ethnicity in post covid era (cohort B and C) OR 1.78, 95% CI (1.16,2.79) (p0.009) required neoadjuvant chemotherapy suggesting more advanced and possibly aggressive cancer histology. We observed that unfunded patients are less likely to have hormonal receptor-positive breast cancer (p0.001).

Conclusion:

Population health is likely affected by socioeconomic status, which eventually affects their health care. In a minority Hispanic population, low average income and educational attainment are likely the obstacles to getting timely appropriate health.(2)

A higher proportion of Hispanic patients were not insured when compared to non-Hispanics leading possibly to more advanced and aggressive histologies at presentation.

References:

1-Velasco-Mondragon et al. Hispanic health in the USA: a scoping review of the literature. Public Health Rev 37, 31 (2016).

2- Escarce JJ, Kapur K. Access to and Quality of Health Care. In: National Research Council (US) Panel on Hispanics in the United States; Tienda M, Mitchell F, editors. Hispanics and the Future of America. Washington (DC): National Academies Press (US); 2006. 10.

Neoadjuvant chemotherapy use in Hispanic population

Characteristic	OR [†]	95% CI [†]	p-value
TimePeriod			
Lockdown	0.89	0.50, 1.56	0.7
PostVaccine	1.08	0.66, 1.75	0.8
Ethnicity			
Hispanic	1.78	1.16, 2.79	0.009

[†] OR = Odds Ratio, CI = Confidence Interval

Relationship between neoadjuvant chemotherapy use in hispanic population with funding status

Characteristic	OR [†]	95% CI [†]	p-value
TimePeriod			
Lockdown	0.91	0.51, 1.61	0.8
PostVaccine	1.06	0.65, 1.73	0.8
Ethnicity			
Hispanic	1.47	0.93, 2.34	0.10
Funding			
Unfunded: carelink and medicaid	2.33	1.43, 3.77	<0.001

[†] OR = Odds Ratio, CI = Confidence Interval

Disclosure(s):

Tamarah Aldawoodi, MD: No financial relationships to disclose

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Marcela Mazo-Canola, MD: No financial relationships to disclose

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5:00 PM - 6:15 PM

P1-06-07

Interrogating the Molecular Profile of Breast Cancer Tumors in Hispanics Living in Puerto Rico (PRH)

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Breast cancer (BC) has the highest incidence and mortality rates among Puerto Rican women. However, the representation of Hispanics living in Puerto Rico (PRH) in breast cancer clinical trials may be limited due to the lack of a defined genetic profile from BC tumors in Puerto Rican patients. Mutations in genes associated with tumor suppressors, tumor progression, and genome stability are shared among all BCs. Nonetheless, differences in the frequency of these mutations have been observed among racial/ethnic groups. This study aims to characterize the genomic landscape of BC tumors in PRH and identify the most common genetic mutations. We conducted secondary data analysis to evaluate the mutational profile of 189 BC tumors from PRH who underwent NGS testing from 2015 to 2020 and compared the prevalence of breast tumor somatic mutations and gene amplifications with profiles reported for other races/ethnicities available through The Cancer Genome Atlas (TCGA) and the AACR Genomics Evidence Neoplasia Information Exchange (GENIE). The most mutated genes among PRH breast tumors were TP53, PIK3CA, ARID1A, NF1, and RB1, while the most frequent gene amplifications were FGF19, H3F3B, ZN703, MCL1, and ADGRA2. H1047R and E545K were the most frequent specific mutations in PRH for PIK3CA; R248Q and R273C for TP53 and Q1212*, S634* and Q557fs for ARID1A. Statistically significant differences were found between populations. This study reports a unique mutational profile of BC tumors in PRH and makes comparisons with non-Hispanic and USH populations, providing novel knowledge to increase Hispanic representation in future BC studies and treatments.

Disclosure(s):

Norianne Martinez-Viota, n/a: No financial relationships to disclose

Xavier Bittman-Soto, n/a: No financial relationships to disclose

Ingrid M. Montes-Rodriguez, PhD: No financial relationships to disclose

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P1-07-01

Ki-67 index after neoadjuvant endocrine therapy as a prognostic biomarker in patients with HR+/HER2- early breast cancer: a systematic review and meta-analysis

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Background: Neoadjuvant treatment allows to better distinguish responders from non-responders, and to tailor post-neoadjuvant treatment according to tumor response in patients with HER2+ and triple-negative early breast cancer. For HR+/HER2- tumors, the pathologic complete response is less likely to occur, and residual disease is predictive of inferior recurrence-free or overall survival. Therefore, Ki-67 index, a prognostic biomarker in early breast cancer, is often used in clinical trials as an endpoint for evaluating response to neoadjuvant endocrine therapy (NET). In this systematic review and meta-analysis, we aim to assess if Ki-67 level after NET is associated with disease recurrence and/or survival. Methods: We conducted a systematic literature search of PubMed, Embase, CENTRAL, and conference proceedings (ASCO and ESMO annual meetings, ESMO Breast, and SABCS) up to June 28, 2022, to identify clinical trials or observational studies reporting Ki-67 index after NET in patients with HR+/HER2- early breast cancer treated with NET (PROSPERO number CRD42021282338). We excluded studies in which all patients received neoadjuvant chemotherapy, or from which separate data from patients receiving only NET was not retrieved.

Here we report data from studies screened for the availability of the primary endpoint - recurrence-free survival (RFS), and the secondary endpoint - overall survival (OS), comparing patients with low Ki-67 versus high Ki-67 index after NET, as defined per each study. We performed a sensitivity analysis of the studies measuring the post-NET Ki-67 index in a pre-planned core biopsy. We used the Higgins I2 index to evaluate the heterogeneity between included studies, which did not reach statistical significance. Therefore, we used a fixed effects model to combine RFS and OS hazard ratios (HR) with 95% confidence intervals (CI). Results: We included 11 studies reporting data from 4,231 patients: nine clinical trials (n=3,926), one pooled analysis of two clinical trials (n=217), and one retrospective cohort study (n=88). Nine studies included only post-menopausal women (n=4,069), one included both post- and premenopausal women (n=88), and one included only premenopausal women (n=74). NET was aromatase inhibitor (AI) in four studies (n=3,359), tamoxifen or AI in four (n=465), tamoxifen in two (n=190), and one study with AI or fulvestrant (n=217). There were no studies with targeted agents combined with NET. No study restricted the use of adjuvant chemotherapy in high-risk patients. Three studies evaluated post-NET Ki-67 in a pre-planned core biopsy after a window of treatment of two to four weeks (n=3,348), while the other eight evaluated KI67 in the surgery specimen (n=883). The timing of post-NET evaluation ranged from 2 to 24 weeks. The median follow-up for RFS ranged between 37 and 95 months, and between 62 to 84 months for OS. We found a statistically significant association of adverse RFS (HR 2.43, 95% CI 1.99-2.98) and OS (2.66, 95% CI 1.65-4.28) with higher Ki-67 after NET. The sensitivity analysis of the three studies evaluating post-NET Ki-67 in a pre-planned core biopsy showed the same association with RFS (HR 2.41, 95% CI 1.77-3.30). These three studies did not report OS data. Conclusion: Our data reinforce the role of Ki-67 index after NET as a valuable biomarker of response or resistance to endocrine therapy in women with HR+/HER2- early breast cancer. Despite the use of adjuvant chemotherapy in most of the high-risk patients included in this analysis, the reduction of Ki-67 after NET is strongly associated with survival outcomes (RFS/OS), even after a short course of two to four weeks NET. Ki-67 index post-NET might be a useful tool to help tailoring the use of adjuvant chemotherapy in HR+/HER2-negative breast cancer patients, particularly in low-resource settings where the access to genomic assays is limited.

Disclosure(s):

Diogo Martins-Branco, MD, MSc: Daiichi Sankyo Portugal Lda.: Consulting Fees (e.g., advisory boards) (Terminated, February 3, 2022); F. Hoffmann-La Roche Ltd: Institutional grant (Ongoing); Merck Sharp & Dohme, Lda.: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, March 23, 2021); Novartis Farma - Produtos Farmacêuticos SA: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, December 10, 2021), Travel/meeting grant (Terminated, December 10, 2021)

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Roberto Salgado, MD, PhD: BMS: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing); Merck: Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Research support and lectures (Ongoing); Puma Biotechnology: research support (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing)

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Evandro de Azambuja, MD, PhD: Astra-Zeneca: Contracted Research (Ongoing); Libbs: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), travel support (Ongoing); Pierre Fabre: Consulting Fees (e.g., advisory boards) (Ongoing); Roche/GNE: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), travel support (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing); Servier: Contracted Research (Ongoing); Zodiac: Consulting Fees (e.g., advisory boards) (Ongoing)

12/6/2022

5:00 PM - 6:15 PM

P1-07-02

Using clinical characteristics and molecular markers to predict the risk of subsequent ipsilateral breast events after excision of DCIS

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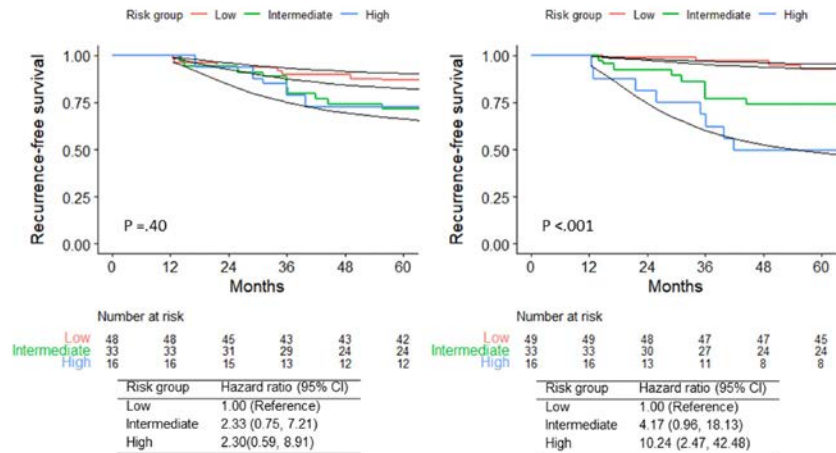
PURPOSE To examine incremental values of estrogen receptor (ER) status, body mass index (BMI), menopausal status, and a previously reported multi-gene classifier over commonly used clinical factors (i.e. age, tumor grade, comedonecrosis, surgical margins, and treatment) in predicting risk of any ipsilateral recurrence (IR) event within five years after DCIS diagnosis.

METHODS A derivation cohort consisted of participants in the Translational Breast Cancer Research Consortium (TBCRC) 038, a retrospective multicenter cohort study in women undergoing surgical resection for DCIS between 01/01/1998 and 02/29/2016 (n=216). The validation cohort, the Repository of Archival Human Breast Tissue (RAHBT) at Washington University School of Medicine, provided cases meeting the same eligibility criteria as TBCRC038 (n=97). Participants in both cohorts had RNA-seq data and either developed IR 1-5y after initial DCIS diagnosis or were free from subsequent breast events for at least five years. The previously reported 812-gene classifier had been developed from a subset of the TBCRC038 samples using a negative-binomial regression model to identify differentially expressed genes in the primary tumor associated with subsequent recurrence events. This classifier has been shown to be highly correlated with 5-year invasive, DCIS, and all breast cancer events, and validated in the RAHBT cohort. Cox proportional hazards regression was used to estimate hazard ratios (HRs) of IR in the TBCRC038 cohort (76 with IR). The clinical score was developed using clinical predictors (aforementioned clinical factors and ER) and their regression coefficients from the model with the maximum predictive accuracy (e.g. c-index) and the minimum number of predictors; the summary score integrated the clinical score and multi-gene classifier. Predictive performance of both clinical and summary scores was validated in the RAHBT cohort (20 with IR).

RESULTS In the TBCRC cohort derivation set, we used a multivariable model based on clinical factors alone (clinical score) and found that ER status, but not BMI or menopausal status, was independently associated with a higher IR risk (HR=2.06, 95% CI 1.18-3.58). Adding the multi-gene classifier to the clinical factors-based model (summary score) in the TBCRC038 test set increased predictive accuracy (c-index 0.68 to 0.70), with the genomic classifier-adjusted HR of 14.96 (95% CI 8.64-25.91). The summary score had higher predictive performance for IR risk than clinical score alone (c-index 0.82 vs. 0.70). In the RAHBT validation samples, model performance was similarly improved using summary scores clinical factors-based model plus multigene classifier as compared to clinical scores alone (c-index 0.74 vs. 0.58).

CONCLUSION Combining clinical factors and a multigene classifier provided more accurate risk estimates of IR within five years after excision of DCIS than clinical factors alone.

Figure 1. Observed and predicted recurrence-free survival in the first five years after initial DCIS diagnosis in the RAHBT validation cohort, by risk groups defined by clinical scores (left) and clinical score plus multigene classifier (right).



Disclosure(s):

- Ying Liu, PhD:** No financial relationships to disclose
- Siri H. Strand, PhD:** No financial relationships to disclose
- Lorraine King, PhD:** NCI Precancer Atlas: Contracted Research (Ongoing)
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5:00 PM - 6:15 PM

P1-07-03

Unmet needs and future applications of breast cancer multigene signatures in routine clinical practice: results from the European PROCURE Project

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Background: Several Breast Cancer Multigene Signatures (BCMS) are available to profile early breast cancer (eBC) that according to current evidence, can provide reliable information on the risk of recurrence. However, knowledge regarding their perceived value and use in clinical practice is scarce. The first results regarding the panelists' opinions on the clinical utility of BCMS were presented at SABCS Symposium 2021 (Poster P4-06-08). Here we discuss present and future recommendations for improving the use of BCMS resulting from the PROCURE Project. Methods: The Delphi survey developed by the 8 members of the Scientific Committee was administered twice to oncologists, pathologists, and surgeons across Europe. The questionnaire included 5 sections: 1) Participants' profile and experience with BCMS, 2) Current clinical practice in eBC and use of BCMS, 3) Participants' opinion on the utility of the BCMS in eBC according to patient profiles, 4) Agreement with a set of recommendations on the use of BCMS in clinical practice and 5) Identification of unmet needs and future applications of

BCMS. 70% agreement was used to determine consensus on a topic. Results: 133 panelists from 11 European countries completed both rounds of the survey. Experts were mostly medical oncologists (72.2%) with extensive experience (more than 5 years) in the management of BC patients (97.0%) and in the use of BCMS (73.4%). Most of them worked in university hospitals (86.5%). Regarding recommendations for improving BCMS utility, according to panelists' opinion, these genomic tests should provide prognostic as well as predictive information (82.0%), especially to help physicians when deciding on the most appropriate adjuvant chemotherapy (81.2%). Also, their evidence should be based mostly on prospective randomized clinical trials (85.0%) and they should evaluate the clinical and pathological features of the disease (91.0%). Another aspect agreed by panelists is that patients should have the right to access their BCMS results to take part in treatment decisions (85.7%). Finally, when thinking about future applications of BCMS, consensus was only reached after the second Delphi round, and according to panelists, there is a need for validating BCMS in order to know if they can predict treatment benefits in patients with ER-positive advanced/metastatic BC (78.2%) and in triple-negative eBC patients (72.2%). Likewise, panelists also agreed on the need of developing newly validated tests to evaluate the risk of distant recurrence and predict treatment benefits in the neoadjuvant setting (71.4% and 81.2%, respectively). However, no consensus was reached on the need for BCMS to give an accurate prognosis for patients with ER+ advanced and/or metastatic BC (50.4%), HER2+ advanced BC (21.8%), or triple-negative advanced BC (36.8%). Conclusions: The panelists who participated in the PROCURE Project had an extensive experience in the management of eBC patients as well as using BCMS; however, the high degree of importance that they attributed to both prognostic and predictive information reflects a misconception on the correct interpretation of BCMS results because, even if those test can be used to predict the benefit of adjuvant chemotherapy, they are primarily prognostic tools but not predictive about the effect of a specific cytotoxic intervention. These results in conjunction with the agreements regarding treatment benefit prediction reached in the neoadjuvant, the triple-negative eBC, and the metastatic settings reinforce the idea that more training is needed to highlight that BCMS should be used in the context of risk assessment in intermediate-risk eBC as well as the possibility of running those tests in core biopsies.

Disclosure(s):

Michael Gnant, MD, FACS, FEBShon: Amgen: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); DaiichiSankyo: Consulting Fees (e.g., advisory boards) (Terminated, July 1, 2022); EliLilly: Consulting Fees (e.g., advisory boards) (Ongoing); LifeBrain: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Terminated, July 1, 2022); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); PierreFabre: Consulting Fees (e.g., advisory boards) (Terminated, July 1, 2022); Sandoz: Salary (Ongoing); Veracyte: Consulting Fees (e.g., advisory boards) (Terminated, July 1, 2022)

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P1-07-04

Claims-derived comorbidities associations with real-world overall survival (rwOS) among patients with metastatic breast cancer in an electronic health record-claims linked dataset

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Introduction: Comorbid conditions can significantly impact various aspects of cancer care and therefore are often utilized as covariates to control for selection bias in observational studies. Oncology based electronic health record (EHR) data is often used as a source for comorbidity information but may be subject to missingness due to differences in clinician documentation. Utilizing additional data sources, such as health care claims data, may allow for greater capture of comorbidities. This study used a claims data linked to oncology EHR to identify comorbidities and related patient characteristics, as well as the association between a claims-derived comorbidity index and real-world overall survival (rwOS) among outpatient metastatic breast cancer (mBC) patients, to characterize the comorbidities data from this data source. Methods: We selected patients diagnosed with mBC between 2013 and 2021 from a linkage of mBC de-identified EHR-derived Flatiron Health Research Database (FHRD) and Komodo Health claims data. Charlson Comorbidity Index (CCI) were identified based on the presence of a pre-specified International Classification of Diseases (ICD) codes within 12 months preceding cancer diagnosis. To understand comorbidity data within this linkage, patient characteristics were assessed after the study cohort was stratified by the presence of any comorbidity assessed as part of CCI. We calculated the CCI for the study cohort as well as the prevalence of comorbid conditions that are used as part of the CCI. Kaplan-Meier estimates and Cox proportional hazards model were used to estimate median survival time and hazard ratios (HRs) of rwOS among patients with a CCI score of 1 and 2+. Results: The study cohort had 3,213 patients with a median age of 63 [IQR(52, 76)] and 98.7% were female. White patients accounted for 60.1% of the study population while Black and Hispanic/Latino patients accounted for 12.5% and 7.4% of the study cohort, respectively. Patients with comorbidities were older (mean age of 65 vs 61), had a higher (2+) ECOG performance status (PS) score (14.0% vs 9.7%), and were more likely to be Black (16.0% vs 11.0%) or Hispanic/Latino 10.8% vs 6.3%). Twenty percent of the patients had diabetes, 8.2% had peripheral vascular disease, 7.5% had mild liver disease, and 6.3% had congestive heart failure. According to index values,

21.0% of the study cohort had a CCI score of 1, and 18.0% had a score of 2 and above. The median survival times in years for patients with a CCI score of 1 and 2+ were 2.51 [95% CI 2.29,2.81] and 2.05 [95% CI 1.83,2.42], respectively. Based on univariate analysis, patients with a CCI score greater than zero had a higher risk of mortality (CCI 1: HR = 1.25 [95%CI 1.10, 1.41, p< 0.01], CCI 2+: HR = 1.54 [95%CI 1.35, 1.76, p< 0.01]). In the multivariate analysis, adjusted for age, ethnicity/race, and baseline ECOG PS score, the HR for the CCI 1 group was not statistically significant (HR=1.12 [95%CI 0.99, 1.27, p=0.08]). However, the risk of mortality was statistically significant for the CCI 2+ group (HR=1.31 [95%CI 1.14, 1.50], p < 0.01) in the adjusted analysis. Conclusion: Claims data linked to EHR can be used to identify comorbidities and describe patient characteristics. As anticipated, generally, the presence of more comorbid conditions was associated with worse rWOS for patients with mBC. This finding supports use of this linked dataset for similar future studies.

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P1-07-05

Clinical utility of twenty-five gene-expression profiling using LAMP method in early stage breast cancer

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Background The 21-gene Recurrence Score (RS) (Oncotype DX®) is one of the most frequently used multigene assays to predict prognosis and response to treatment for estrogen receptor-positive breast cancer. Although the result of two prospective randomized trials, TAILORx and RxPONDER trial have increasingly established the clinical utility of Oncotype DX®, the cost and testing period are disadvantages especially in Asian countries. To overcome these disadvantages, we developed a new multi-gene assay using Loop-Mediated Isothermal Amplification (LAMP) . We have previously selected a twenty-five genes set through comprehensive gene expression analysis of breast cancer samples from more than 500 cases (patent pending). Although these twenty-five genes are different from those used in conventional assays, their physiological functions are similar to those of Oncotype DX®, and it

is expected that the results will be equivalent to Oncotype DX® as a predictor of prognosis and chemotherapeutic efficacy. This new assay can be performed in own institution, and the result can be obtained less than one hour. It can lead to significantly reduce costs and testing time compared to conventional assays. Based on these backgrounds, we constructed the prediction algorithm based on the new gene expression profiles using LAMP and evaluated its performance in this study. Methods Total RNA was extracted using Maxwell® RSC RNA FFPE Kit (Promega) from FFPE tumor samples of postoperative breast cancer tissue which Oncotype DX® have already tested in our institution between January 2009 to January 2021 and was quantified by Reverse-transcription LAMP enabling one-step reaction from reverse transcription to amplification under isothermal condition (63°C). Samples were divided into three groups, low-RS (RS 0-10), RS-intermediate (RS 11-25) and RS-high (RS ≥26) based on Oncotype DX®-RS. Using the obtained mRNA amplification detection time as an explanatory variable and Oncotype DX®-RS as an objective variable, a prediction algorithm based on expression profiles based on LAMP method was constructed and evaluated its performance with 4-fold cross-validation. The prediction algorithm was trained using extreme gradient boosting (XGBoost) algorithm that parameters used default of R package "xgboost". We also performed the quality analysis of mRNA excluded from this analysis due to poor mRNA quality. The percentage of mRNA above 200nt (DV200) was calculated by electrophoresis, and the correlation between the degree of mRNA degradation and the number of years of storage was calculated. Results Of the 221 cases which have tested Oncotype DX® during the study period, 90 samples were used in the analysis, and the remaining samples were excluded from this study due to poor mRNA quality. Of the 90 samples, 19 cases were RS-low, 42 cases were RS-intermediate, and 30 cases were RS-high, respectively. The correlation coefficient between Oncotype DX®-RS and our LAMP method-based predicted RS was $r=0.911$ (95%CI 0.900–0.921, p -value < 0.001). The overall concordance rate with the predicted risk of recurrence (high/intermediated/low-RS) was 0.9343 (95%CI: 0.9174-0.9486, p -value < 0.001). Regarding the quality analysis of mRNA excluded from this analysis, we found the inverse correlation between the degree of mRNA degradation and the storage periods, namely higher DV200 with shorter periods. In particular, there was less mRNA degradation in specimens that had been stored for less than one year. Conclusion Our new gene expression profiling by the LAMP method suggested to have same discriminately ability with Oncotype DX® to predict the risk of recurrence in early breast cancer patients. The duration of mRNA storage and the fixation time in the FFPE preparation process are suggested to be important for maintaining the quality of mRNA. We are planning to further studies with increase sample size and analyze the correlation with prognosis.

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5:00 PM - 6:15 PM

P1-07-07

Cross-talk of Four Types of RNA Modification Proteins with Adenosine Reveals the Landscape of Multivariate Prognostic Patterns in Breast Cancer

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Background: BRCA is the most common malignant tumour, and its heterogeneity is one of its major characteristics. m6A, m1A, APA, and A-to-I RNA editing constitute the four most common adenosine-associated RNA modifications and represent the most typical and critical forms of epigenetic regulation contributing to the immunoinflammatory response, tumorigenesis and tumour heterogeneity. However, the cross-talk and potential combined profiles of these RMPs in multivariate prognostic patterns of BRCA remain unknown. Methods: A total of 48 published RMPs were analysed and found to display significant expression alterations and genomic mutation rates between tumour and normal tissues in the TCGA-BRCA cohort. Data from 4188 BRCA patients with clinical outcomes were downloaded from the GEO, METABRIC and TCGA databases, normalized and merged into one cohort. The prognostic value and interconnections of these RMPs were also studied. The four PRGs with the greatest prognostic value were then selected to construct diverse RMP-associated prognostic models through uniCox, differential expression analysis, LASSO regression and multiCox. Alterations in biological functional pathways, genomic mutations, immune infiltrations, RNAss scores and drug sensitivities among different models, as well as their prognostic value, were then explored. Results: Utilizing a large number of samples and a comprehensive set of genes contributing to adenosine-associated RNA modification, our study revealed the joint potential bio-functions and underlying features of these diverse RMPs and provided effective models (PRG clusters, gene clusters and the risk model) for predicting the clinical outcomes of BRCA. The individuals with higher risk scores showed poor prognoses, cell cycle function enrichment, upregulation of stemness scores, higher TMBs, immune activation and specific drug resistance. This work highlights the significance of comprehensively examining post-transcriptional RNA modification genes.

Conclusions: Here, we designed and verified an advanced forecasting model to reveal the underlying links between BRCA and RMPs and precisely predict the clinical outcomes of multivariate prognostic patterns for individuals.

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P1-07-08

Prediction of breast cancer late recurrence according to Clinical Treatment Score post-five years (CTS5) and progesterone receptor in a wider patient population

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Background The duration of adjuvant endocrine therapy remains a continuous challenge in hormone-receptor positive (HR+) early breast cancer. The Clinical Treatment Score post-five years (CTS5) is an online model used to predict late distant metastasis for women with HR+ breast cancer who are recurrence-free 5 years after endocrine therapy (ET). It incorporates patients age, tumor size, grade, and number of positive lymph nodes, and is an important tool to help in this treatment decision. There is a paucity of data in premenopausal women and whether other variables could add additional information. **Methods** A single-center retrospective analysis of patients that have received adjuvant ET for 5 years, between January 2007 and December 2008 at the Instituto Nacional de Cancer (INCA), Brazil. Disease-Free Survival (DFS) was compared between the low, intermediate, and high-risk subgroups. Data analysis was descriptive and exploratory. Kaplan-Meier estimates and Cox regression models were used. **Results** A total of 183 patients were enrolled, 26.5% being premenopausal. Median age at diagnosis was 66 years. Tumor stage: I (44%) and II (56%). ET consisted of tamoxifen (88%), anastrozol (6%), and a switch (6%). There were 39.5%, 39.5% and 21% of patients in the low, intermediate, and high-risk (L/I/H) subgroups, respectively. Progesterone-receptor was $\geq 20\%$ in 71% of tumors and in 55%, 49% and 34% in the L/I/H subgroups, respectively. Median follow up was 88.9 months. After 5 years, the median DFS was 100%, 96.3% and 68.2% in L/I/H subgroups ($p < 0,001$). Progesterone-receptor was also an independent prognostic factor for late recurrence ($p < 0,05$). **Conclusion** CTS5 performed well in a wider patient population including premenopausal women. Progesterone-receptor was an independent prognostic factor for DFS and should be further considered into the model.

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P1-07-09

Clinical and pathologic characteristics in early breast cancer Her2-low and high risk Oncotype DX RS

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Background: Recent data suggest that HER2-low breast cancer (BC) may represent a distinct entity. Approximately 55-60% of BC are considered as Her2-low, of which 80% are Luminal-like tumors. Recent studies support potential clinic-pathological and molecular features differences between Estrogen Receptor (ER) positive HER2-low and ER positive Her2-0 disease. Among patients (pts) with high genomic risk (Oncotype DX RS) HER2-low expression was associated with a significant improvement in overall survival compared to Her2-0. The objective of our study is to compare disease characteristics and outcomes between HER2-low and Her2-0 in estrogen receptor (ER) positive, early (e) BC. (Murtai R et al. *The Breast*. 60(2021)62-69.

Methods: A single center retrospective study of all pts. with ER positive, Her2 negative eBC, for whom Oncotype DX test was performed between 1/Nov/2012 and 14/Febr/2019. The pts were separated into HER2-low (immunohistochemistry (IHC) +1 or + 2 and in situ hybridization not

amplified) or HER2-0. Clinic-pathological features included were: demographics, tumour size, nodal status, histologic grade, Her2 expression, ER and progesterone receptor (PR), Ki-67, presence of lymph-vascular (LV1) tumor cell invasion and Oncotype recurrence score (RS) result.

Results: A total of 344 pts were screened, of whom 297 pts were included (Exclusion for: Her2 “negative” expression (45 pts); HER2 positive disease by IHC (1 pts); metastatic disease (1 pts)). The distribution of HER2-0 and HER2-low subgroups was 121 pts (41%) and 176 pts (59%). The pathological characteristics according to Her2 expression status are summarized in Table 1.

Median age was 57 year (38-79), similar between both groups: Her2-0 58 yr (41-78) and 56 yr (38-79) in Her2 low.

The postmenopausal status was 76 pts (62,8%) Her2-0 Vs 113 pts (64,2%) in Her2 low. 1 pts was male.

Proliferation Index: Ki67% < 20 was: 65 pts (53,7%) Her2-0 Vs 86 pts (48,5%) in Her2 low; 65 pts (13,5%) had Lympho-vascular invasion in Her2 low; 115 pts (95%) were ER positive in Her2-0 Vs 157 pts (89,2%) in Her2 low; PR positive > 20 was 106 pts (87,6%) in Her2-0 Vs 137 (78,7%) in Her2 Low. The median follow-up was 72 month (SD+- 22,52).

5 pts had a recurrence: 4 pts were Her2 low (1 local and 3 distant metastasis) and 1 Her2-0 with distant metastasis. Most of the pts received adjuvant hormone therapy.

There were no statistically significant differences between both groups owing to neither the clinic-pathologic features nor the recurrence score. It was not reached the minimum number of events for a survival analysis.

Conclusions: Our results show that HER2-low eBC pts have similar characteristics and survival rates compared to HER2-0 BC pts without significant differences.

Table 1. Baseline pathological characteristics.

Characteristics	HER2-0 (n= 121)	HER2-Low (n=176)
Tumor Size n (%)		
pT1ab	14 (11,6)	22 (12,5)
pT1c	84 (69,48)	123 (69,9)
pT2	23 (19,9)	31 (27,6)
Node Status n (%)		
pN0	90 (74,4)	133 (75,6)
pN1mic	29 (24)	42 (23,9)
pN1	2 (1,7)	1 (0,6)
Grade n (%)		
Low	23 (19,3)	24 (13,7)
Intermediate	84 (70,6)	130 (74,3)
High	12 (10,1)	20 (11,4)
UnKnow		1 (0,6)
Histologic Types n (%)		
IDC	100 (82,6)	150 (85)
ILC	15 (12,4)	20 (11,4)
Other	6 (5)	6 (3,4)

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5:00 PM - 6:15 PM

P1-08-01

Virtual molecular and precision medicine (vMAP) clinic to improve access to clinical trials for patients with metastatic breast cancer: an academic-community collaboration

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Background: Despite improved outcomes for patients with metastatic breast cancer (MBC), attributed in part to advancements in precision therapeutics, clinical trial enrollment and genomic testing are relatively underutilized in the community oncology setting. To address this need, we launched a virtual molecular and precision medicine (vMAP) clinic to improve access for patients in our community network. Here we describe the initial results from the virtual clinic initiative. **Methods:** In 2020, the vMAP clinic was launched to provide real-time access to precision medicine expertise through virtual, email-based consultation directed to a multidisciplinary team. As part of the service, providers contacted vMAP regarding patients with MBC at the time of initial presentation or disease progression. Upon receipt, the vMAP team (including breast medical oncologists, a breast oncology research nurse, a research assistant, and ad hoc consultation from cancer genetics and molecular pathology representatives) engaged in discussion to identify potential clinical trials with slot availability or standard of care (SOC) options and provided recommendations to the referring provider within 72 hours. Relevant patient data and vMAP referral outcomes were recorded. Providers across the community network were surveyed at project onset and after seventeen months. **Results:** In its first 14-month period (June 2020-July 2021), 47 cases from 16 providers across seven community oncology sites and one academic site were referred to vMAP. A majority (88.6%) of patients had undergone somatic genomic testing (tissue-based, plasma-based, or both) to inform treatment guidance. All cases were screened for available clinical trials as well as SOC options at the time of referral. The average response time to the referring provider with a finalized recommendation was 1.77 days (range 0-5). Forty cases (85.1%) had clinical trial options identified on vMAP pre-screen. Subsequently, 22 patients (46.8%) screened for vMAP recommended clinical trials with 18 (38.3%) initiating enrollment. Of the remaining patients that did not pursue clinical trial screening, 17 (36.2%) started vMAP-recommended SOC treatment, five (10.6%) pursued a different treatment, one (2.1%) was not a candidate for further treatment, and two (4.3%) opted to receive care at a non-affiliated institution, and subsequent treatment information was not available. Reasons that patients did not enroll on trials included trial ineligibility, formal clinical trial screening failure, and patient/provider preference. At project onset, network provider survey results confirmed a previously suggested demand for improvements in processes surrounding genomic testing interpretation and clinical trial enrollment. Post-referral survey results indicated vMAP recommendations and pre-screenings improved the processes surrounding interpretation of genomic testing and clinical trial screening and enrollment, with high rates of referring provider satisfaction. **Conclusion:** A precision medicine virtual clinic demonstrated an efficient and flexible means to offer real-time interpretation of genomic and molecular test results and identification of appropriate treatment options, including clinical trials when applicable, for patients with MBC. The service highlights an example of an academic-community collaboration model to expand precision medicine and clinical trial access for patients with metastatic breast cancer.

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P1-08-02

Implementation of Integrative Medicine Program for Breast Medical Oncology Professionals in an Academic Cancer Center

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BACKGROUND: Integrative medicine such as acupuncture, meditation, yoga and massage are highly desired by breast cancer survivors. Breast medical oncology professionals including physicians, advanced nurse practitioners and physician assistants are often the first clinicians that patients would expect to discuss the use of integrative medicine. Many distressing symptoms, such as hot flashes, insomnia, anxiety, and pain, are common and remain challenging to manage with limited pharmacological intervention available and potential toxicities. Evidence-based integrative medicine approaches, including acupuncture, meditation, yoga, and massage, may help reduce this symptom burden and improve quality of life. However, many breast medical oncology professions are not familiar with current evidence and knowledge in integrative medicine. Therefore, there is an urgent need to educate them on the fundamentals of evidence-based integrative medicine interventions that could improve quality of life for breast cancer survivors. **METHODS:** We designed the Integrative Oncology training Program for breast medicine professionals at our institution. The program faculty are composed of five breast medical oncologists, five integrative medicine faculty, and one education coordinator. **RESULTS:** We developed an online, interdisciplinary five-hour course on evidence-based integrative oncology with essential knowledge on integrative medicine approaches for breast cancer survivors. We determined the topic of interest based on feedback from the program faculty. The integrative medicine approaches in management of hot flashes, arthralgia, insomnia, and cannabis uses are some examples that were highly in-demand. The program summarizes high-quality evidence in herbal supplements, acupuncture, meditation, and yoga, pertinent to the audience, as well as the referral flow to our Integrative Medicine Service. **CONCLUSIONS:** Integrative medicine education programs for oncological professionals are needed to disseminate integrative medicine knowledge and to prepare them to guide our patients on integrative and complementary approaches during and after anticancer treatments.

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P1-08-03

EXPLORATORY ANALYSIS OF A MOBILE APP THAT ADDRESSES RADIOTHERAPY INFORMATIONAL NEEDS FOR BREAST CANCER PATIENTS

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INTRODUCTION Radiotherapy is an area of medicine that is little known by patients and that requires a long time for the doctor to be able to explain and resolve the doubts that arise in the first consultation, which may cause anxiety and low adherence to treatment recommendations. A mobile app called Canswer was developed to address this problem in a novel way to help patients learn about radiation oncology in their free time. **OBJECTIVE** Developed a mobile app that provides oncology radiotherapy information to patients. **MATERIAL AND METHODS** The patients who attended the consultation for the first time were provided with information and obtained verbal consent, later they were provided with the Canswer application on their mobile device, and at the end, a Likert-type perception survey was applied and the Cancer Treatment Survey (CATS), which analyzed the information needs of patients. Anxiety and depression were analyzed through the Hospital Anxiety and Depression Scale (HADS). **RESULTS** Of the total number of patients recruited, 17 patients from northeast Mexico with breast cancer agreed that the use of the application would be useful to them and were interested in receiving additional information after their first-time radiotherapy consultation from March to June 2022. Average age of respondents was 45 years. A total of 7 patients (41%) had doubts about radiotherapy after consultation. When analyzing their knowledge, only 1 patient identified that radiotherapy works by DNA damage, the rest had wrong information, 14 patients thought that this treatment works by heating the cells; 2 thought that radiation therapy causes cells to burst. 8 patients (47%) understood how teletherapy works and 5 how brachytherapy works (19%). A question was included about the best skin care during breast radiotherapy in which 76% correctly answered that the skin should be washed daily with water and neutral soap, but 24% answered that hydrating creams should be applied just before stepping into the machine. Regarding the duration of the consultation, a total of 10 patients (60%) thought it was too short. 47% felt the limited time of the consultation did not allow an adequate evaluation. 100% of the respondents were satisfied with the information provided about the type of treatment, its benefits, and adverse effects, however, 47% persisted with doubts at the end of the consultation. 47% of patients (n=8) had some level of anxiety with 29% mild, 11% moderate and 6% severe. Incidence of depression was 24% with 18% having mild form and 6% severe. Regarding the information provided by the doctor during the consultation, 8 patients (47%) would like their doctor to have told them more about anxiety and depression, 7 about sexuality concerns (41%), and 6 (35%) about alternative medicine. 79% of patients wanted to know more about the side effects the treatment might cause after their visit, and 71% reported wanting to know more about how to prevent side effects. 66% also reported that they would like more information about how the treatment feels when it begins. **DISCUSSION AND CONCLUSION** This analysis revealed that most patients have doubts about radiotherapy, even after the information provided in their first consultation. This may be multifactorial but a key factor may be work overload at radiotherapy centers and a consultation of short duration. This application seems to be an effective, easily accessible, free tool that provides the necessary information, even on topics that are difficult to explain in a standard consultation. Important aspects that the app needs to focus on in future updates include side effects and their management, sexuality, nutrition, depression, and alternative medicine. This application also revealed misconceptions that should be routinely addressed, such as skin care during treatment. Link to app: https://www.canswer.info/?page_id=393

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P1-08-04

Therapeutic Advances in Metastatic Triple-Negative Breast Cancer: Identifying and Reducing Clinician Knowledge Gaps

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Background: Characterization of the aggressive biology of triple-negative breast cancer (TNBC), defined by its lack of estrogen receptor, progesterone receptor, and human epidermal growth factor 2 (HER2) expression, has led to the development of more effective treatments for patients, but research indicates that clinicians face challenges in maintaining a working knowledge of evolving data. This study was conducted to determine what learning gaps exist in the area of therapeutic advances in TNBC and to investigate whether an online, case-based continuing medical education (CME)/nursing continuing professional development (NCPD)-approved activity could address gaps in clinicians' knowledge regarding the personalized care of patients with metastatic TNBC.

Methods: The CME/NCPD-approved live webinar series titled Metastatic Triple-Negative Breast Cancer: Applying Treatment Advances to Personalized Care was presented by Sara A. Hurvitz, MD, FACP, on July 13 and July 15, 2021, and was made accessible as a CME/NCPD-approved enduring webinar archive starting on July 23, 2021. Learners participated in a 1-hour activity that highlighted emerging therapeutic targets in TNBC, with an emphasis on current challenges and new opportunities in the management of metastatic disease. Learners completed a repeated-pairs pre- and post-activity assessment consisting of case-based questions that gauged their ability to apply emerging data to clinical decision making. Baseline knowledge gaps and subsequent learning gains were calculated based on percentages of learners obtaining correct responses on the pre- and post-activity assessments. Significance was assessed using a chi-squared test. In addition, learners reported self-perceived gains in confidence and competence using 5-point Likert scale questions.

Results: As of June 28, 2022, 811 clinicians had completed the activity for credit; 62 learners participated in the live webinar, while 749 participated in the online enduring activity. Baseline assessment data revealed gaps in knowledge regarding emerging actionable targets and management of treatment-related adverse events (Table 1). Learners participating in the enduring activity scored an average of 43% on pretest topics; after completing the activity, the posttest average rose to 92%. The activity resulted in significant gains in knowledge and competence related to these topics, with $P < 0.0001$ for all learning gains. Upon completion of the activity, 86% of learners self-reported that knowledge acquired from this activity would be

utilized to improve the outcomes of their patients, and 86% of learners self-reported that based on the information learned during the activity, they felt more confident in treating patients with metastatic TNBC.

Conclusions: These data indicate that a substantial knowledge gap exists regarding the latest developments in the treatment of metastatic TNBC. They also demonstrate that online, case-based CME/NCPD-approved activities can result in statistically significant improvements in clinicians' knowledge of therapeutic advances and management of treatment-related adverse events for patients with metastatic TNBC.

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Table 1: Baseline Knowledge Gaps and Post-Activity Learning Gains

Case-based question topic	n	Pretest correct responses (%)	Posttest correct responses (%)	Knowledge gap at baseline (%)	Learning gain (%)
Testing for activating mutations in TNBC	787	14.99	92.38	85.01	77.38
Safety of treatment with olaparib	779	27.98	91.14	72.03	63.16
Management of immune-related adverse events	783	52.49	94.13	47.51	41.63
Selection of systemic therapy for recurrent PD-L1–positive TNBC	792	55.43	83.08	44.57	27.65
Selection of first-line systemic therapy for PD-L1–positive TNBC	772	64.90	97.80	35.10	32.90

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P1-08-05

Educating pathologists in quantitating stromal tumor-infiltrating lymphocytes in breast cancer for artificial intelligence applications

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Background Immune cells in the tumor microenvironment play an important role in cancer development [1]. In triple negative breast cancer (TNBC), stromal tumor-infiltrating lymphocytes (sTILs) have been identified as a biomarker with both predictive and prognostic clinical values [2]. The High Throughput Truthing project collected sTILs density estimates in hematoxylin and eosin stained invasive breast cancer biopsy specimens. The goal of the project is to produce a dataset to validate artificial intelligence and machine learning models [3]. After collecting annotations from pathologists for a pilot study, we observed a high level of interobserver variability in sTILs density estimates. To improve pathologist accuracy in breast cancer sTILs assessment, we created educational materials using an expert panel and pilot study data. Method The pilot study data consisted of 640 unique regions of interest (ROIs) derived from 64 digital whole slide images. We categorized ROIs based on their mean sTILs density as “10% or less”, “11% to 40%”, or “greater than 40%”, and selected 72 unique ROIs from those with the highest and lowest pathologist variability in each density bin. In a series of eight one-hour sessions, each ROI was reviewed in a group setting by at least three members of our expert panel, which consisted of one clinical scientist and seven board-certified pathologists trained in breast cancer sTILs assessment. Experts provided estimates of the percent of tumor-associated stroma and sTILs density, and commentary on features that confound sTILs assessment for each ROI. Results We created a set of educational materials to teach the sTILs assessment methodology in breast cancer. These materials include an introduction to the clinical relevance of tumor infiltrating lymphocytes in the breast cancer microenvironment, a tutorial for assessing sTILs according to published guidelines [4], and a discussion of specific pitfalls that may be encountered. Expert panel annotations, comments, and pitfalls were used to generate a reference document and interactive tests: one with expert feedback on each ROI and one to determine proficiency. Conclusions Educational materials designed by an expert panel will serve as reference materials for learning sTILs assessment in breast cancer. Our work provides valuable education for pathologists, and directly supports their ability to provide up-to-date diagnostic information used in caring for breast cancer patients. References: 1.

Zitvogel, L., Tesniere, A. & Kroemer, G. Cancer despite immunosurveillance: immunoselection and immunosubversion | Nature Reviews Immunology. <https://www.nature.com/articles/nri1936>.
2. Loi, S. et al. Tumor-Infiltrating Lymphocytes and Prognosis: A Pooled Individual Patient Analysis of Early-Stage Triple-Negative Breast Cancers. *J Clin Oncol* 37, 559–569 (2019).
3. Dudgeon, S. N. et al. A pathologist-annotated dataset for validating artificial intelligence: A project description and pilot study. *Journal of Pathology Informatics* 12, 45 (2021).
4. Salgado, R. et al. The evaluation of tumor-infiltrating lymphocytes (TILs) in breast cancer: recommendations by an International TILs Working Group 2014. *Annals of Oncology* 26, 259–271 (2015).

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Oncology nursing in India: are we up to speed?

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Background: Cancer management is a critical component of healthcare worldwide. Improvement in cancer care has improved the longevity of patients, and they require continued care from healthcare workers, including nurses. Although nurses in India are trained to care for patients in general, courses dedicated to cancer care are few. The present study evaluated the knowledge of nurses involved in cancer management via an online survey. **Materials and methods:** A survey pertaining to nursing practices in cancer management was distributed electronically to nurses in India from January to April 2022. The survey was designed to evaluate treatment-specific knowledge and confidence of the nurses in managing patients with cancer. The data received was analyzed using Microsoft Excel 2016. The responses were divided into two groups: responses marked 4 and 5 on the scale were grouped as confident responses, whereas those marked 1, 2, and 3 were grouped as unconfident responses. Chi-squared analyses were performed using the OpenEpi online tool. **Results:** A total of 422 nurses replied to the questionnaire; of these, 399 (94.55%) said that they have experience in caring for patients with cancer. Of the 399, 198 (49.62%) worked in specialized cancer care centers and the remaining 201 (50.38%) worked in general hospitals. Nearly two-third of the nurses (n = 262; 65.7%) replied that they studied cancer care as a part of their nursing curriculum, whereas the remaining learnt through personal experience. A total of 335 (84%) nurses had undergone a specialized course in chemotherapy management, and most were confident about their knowledge on chemotherapy administration, central line management, and side effect and precaution management. Only 41 (10.3%) had undergone a specialized course in oncology-directed surgical management; yet based on their primary nursing training more than half of the nurses were confident of performing pre- and postoperative management. With respect to a more specialized surgical care, only 144 (36.1%) were confident in providing stoma care and 181 (45.4%) were confident in teaching preventive lymphedema care after surgery. Although a majority had completed a specialized course in post-radiation management (n = 255; 93.2%), only half were confident in identifying skin-induced changes and providing care for patients receiving radiotherapy. Furthermore, only half of the nurses were aware of the role of nursing staff in brachytherapy (n = 200; 50.1%). Most nurses did not undergo any specialized course (n = 360; 90.2%) in palliative management; 124 (31.1%) nurses said that they were not very confident in adequately counselling patient relatives with regard to symptomatic treatment. Nurses working in specialized cancer centers (n = 198) were significantly more confident in administering and managing central lines for chemotherapy; performing adequate chemotherapy drug disposal; and assessing the needs of cancer patients and their family members than their counterparts working in general hospitals (n = 201) (all p < 0.05). Only 54.4% of the respondents were aware of oncology-directed nursing programs available in the country, and only half were able to access them (n = 160; 55.2%) owing to the lack of guidance (n = 130; 32.58%), time (n = 93; 23.31%), and funds (n = 46; 11.53%). Hence, when asked whether they would be inclined to attend a hybrid course, majority (n = 349; 87.47%) indicated in the affirmative. Also, 338 (84.7%) nurses replied that they would be inclined to participate in cancer screening programs after pursuing such a specialized course. **Conclusions:** The results of this study highlight the lacunae in nurses' oncology training. Thus, there is an obvious need to redesign the existing oncology-directed nursing programs to include palliative care and organ-site specific care. Designing these courses in the hybrid format may improve its accessibility and the willingness of nurses to attend.

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5:00 PM - 6:15 PM

P1-08-07

Educational Opportunities to Improve HER2 Testing and Use of Newer Therapies for HER2-Positive MBC Among Community Healthcare Professionals

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Background: The management of HER2-positive (HER2+) metastatic breast cancer (MBC) has continued to evolve, with multiple FDA approvals of novel HER2-targeted agents since late 2019. Considering the growing HER2+ MBC treatment armamentarium and the emerging HER2-low MBC subtype, we undertook an analysis of the current implementation of guideline and expert recommendations for HER2 testing and treatment of HER2+ MBC with recently approved agents among oncology healthcare professionals (HCPs) participating in educational programs on these topics.

Methods: Between January 2020 and April 2022, we conducted several expert-designed educational activities for HCPs focusing on recommended HER2 testing and treatment of HER2+ MBC. Polling questions on HCP knowledge, practice patterns, and confidence in the evaluation of HER2 status and the use of newer targeted therapies in the setting of HER2+ MBC were assessed across the activities and compared with expert recommendations.

Results: Among 129 HCPs participating in 2 educational activities held from July 2020 to March 2021, 53% reported confidence to appropriately apply current HER2 testing guidelines to patient care. Similarly, among 407 HCPs who participated in 4 educational programs from May 2020 to January 2021, 24% reported confidence to incorporate recently approved drugs (including trastuzumab deruxtecan [T-DXd], neratinib, and tucatinib) into the care of patients with HER2+ MBC. The percentage of HCPs reporting confidence in the use of these new drugs remained low over this time period.

Comparison of treatment recommendations for various HER2+ MBC case scenarios across 7 educational activities from January 2020 through April 2022 showed considerable discordance between experts and HCPs regarding the implementation of newly approved HER2-targeted regimens (Table). For patients with disease progression after 2 lines of therapy and no central nervous system (CNS) metastases, 27% to 57% of HCPs (n = 571) chose T-DXd in agreement with experts. For patients with disease progression after 2 lines of therapy with CNS metastases, 27% to 42% of HCPs (n = 597) chose a tucatinib-based regimen in agreement with experts. Treatment choice concurrence between HCPs and experts did not increase over the course of this study for either of these patient scenarios.

Conclusions: These data suggest that some HCPs are challenged to optimally incorporate

recommendations for HER2 testing and the implementation of novel HER2-targeted therapies in the care of patients with HER2+ MBC. Educational activities designed to improve the knowledge and confidence of HCPs would benefit patients with HER2+ MBC. A detailed analysis of trends over time and by role on the care team will be presented.

Table. Expert and HCP Treatment Selections for Case Scenarios in HER2+ MBC

HER2+ MBC Case	Activity Date, Mo/Yr	Responses, n	Expert Recommendation*	HCP With Treatment Choice Concordant With Expert Choice by Activity Timing, %			
				1/20 - 6/20 Approvals: T-DXd [†] , Tucatinib [‡]	7/20 - 12/20	7/21 - 12/21	1/22 - 4/22 Approvals: T-DXd [†]
Prior adjuvant AC-THP and THP for MBC with PD, no CNS mets	4/22	64	T-DXd	-	-	-	52
Prior THP for MBC with PD, no CNS mets	3/22	20	T-DXd/T-DM1	-	-	-	35/15
Prior THP and T-DM1 with PD, no CNS mets	1/20 - 5/20	223	T-DXd	47	-	-	-
	5/20	48	T-DXd	27	-	-	-
	6/20	44	T-DXd/tucatinib [‡] *	57/20	-	-	-
	9/20 - 12/20	203	T-DXd/tucatinib [‡] *	-	32/24	-	-
	7/21 - 2/22	29	T-DXd	-	-	45	-
Prior THP and T-DM1 with PD, CNS mets	3/22	24	T-DXd	-	-	-	46
	1/20 - 5/20	242	Tucatinib [‡] /neratinib [§] *	27/13	-	-	-
	6/20	37	Tucatinib [‡]	41	-	-	-
	9/20 - 12/20	206	Tucatinib [‡]	-	36	-	-
	12/20	112	Tucatinib [‡] ± SRS	-	42	-	-

*Per expert HCP educators. †For HER2+ unresectable/MBC after ≥2 prior anti-HER2 regimens for MBC. ‡For HER2+ unresectable/MBC (including brain mets) after ≥1 prior anti-HER2 regimens for MBC. §For HER2+ unresectable/MBC after prior anti-HER2 regimen for MBC or in neoadjuvant or adjuvant setting with disease recurrence ≤6 mo after therapy. †With capecitabine and trastuzumab. ‡With capecitabine. §Both treatments considered optimal for case.
AC-THP, docetaxel/cyclophosphamide followed by paclitaxel/trastuzumab/pertuzumab; mets, metastases; PD, progressive disease; SRS, stereotactic radiosurgery; T-DM1, trastuzumab emtansine; THP, docetaxel/trastuzumab/pertuzumab.

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Ryan P. Topping, PhD: No financial relationships to disclose
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P1-08-08

Approach to Prevention and Management of Chemotherapy Toxicities in a Interprofessional Education Program

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Background: Interprofessional collaboration and team-based care in oncology has become increasingly important given the complexity of new therapies and their associated side effect profiles. It has been demonstrated that clear and thorough communication improves patient satisfaction and patient adherence. Previously, students described a deficit of adequate oncology education in their curriculum. Incorporating learners from different educational disciplines to care for oncology patients in a breast clinic is an innovative idea that has not been previously published. Objectives: This study will evaluate patient satisfaction and learners' competencies and confidence after an interprofessional education collaboration aimed at enhancing chemotherapy education and toxicity management. Methods: A single center study was conducted at the University of Maryland Greenebaum Comprehensive Cancer Center (UMGCCC) from August 2020 through April 2021. Patient population was adults receiving chemotherapy for breast cancer. Learner population was medical and pharmacy students and residents. Learners received a brief educational orientation and then completed education and assessment sessions with patients. Sessions were prior to first chemotherapy, 2-4 days after chemotherapy, and then 1-3 days prior to next cycle of chemotherapy. Surveys of satisfaction and competencies were prospective but chart review for symptoms and interventions were retrospective. Results: 20 learners and 9 patients participated in the experience. Median of 4 encounters per patient were completed. 79 chemotherapy issues/toxicities were identified with 11 (14%) interfering in daily activities. 47 interventions were made and improvement was seen in 44 (56%) problems. Patient survey revealed that all 9 patients (100%) reported they were completely satisfied with education aimed at understanding side effects. One patient reported they were somewhat satisfied with understanding how to use their medication correctly and safely while the other 8 reported very satisfied (89%). Learners self-assessment tool revealed improvement in confidence in teach back ($p=0.002$) and interprofessional education competencies ($p=0.01$). Discussion: Incorporating medical and pharmacy learners in interprofessional care can help patients understand their treatment and help in management of toxicity. Limitations of the experience included faculty's involvement in the discussions and interventions may overestimate the contribution of learners. In addition, the retrospective nature

of the chart review may underestimate the symptoms for patients and overestimate the proportion of problems that were improved.

Disclosure(s):

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Paula Rosenblatt, MD: General Electric: Consulting Fees (e.g., advisory boards) (Terminated, June 2, 2022)

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P1-08-09

DIVAS - DC Pink Divas Intervening Virtually to Advance Saving Lives: Assessing the impact of digital behavioral health breast cancer education program for Black women

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Breast cancer is now the most common cancer. Thirty years of increased awareness, early diagnosis, and treatment access contributed to a 40% decline in breast cancer deaths. Yet, in 2021, more than 281,550 new cases of invasive and 49,290 new cases of non-invasive breast cancer will be diagnosed in U.S. women. Black women are 40% more likely to die of breast cancer - the highest breast cancer death rate across racial and ethnic groups. Today, the Black-white breast cancer mortality gap persists, and Black metastatic breast cancer (MBC) patients have a poorer prognosis. The pandemic exacerbated breast cancer disparities. In 2020, delays and avoidance contributed to an 85% breast cancer screening drop while MBC patients' risk of severe illness and death from COVID-19 elevated. Therapy interruptions and abandonment increased, and conversely, clinical trial enrollment decreased. COVID-19 has accelerated the digital platform shift to telemedicine, online psychosocial support programs, virtual patient navigation, and digital engagement across the oncology care continuum. DC Pink Divas Intervening Virtually to Advance Saving Lives (DIVAS) is an award-winning evidence-based training, outreach, and patient navigation program developed to address the educational needs of Black early-stage, MBC breast cancer patients, survivors, and caretakers and provide strategies to educate, empower and impact women by increasing breast health knowledge, decreasing gaps in screenings and access, increasing awareness of MBC to ensure that where a woman lives, will not determine if she lives through a 1-year commitment of attendance in 8 cohort-based education modules where Black breast cancer mortality is highest.

The DIVAS Health Behavioral Change Model adapts the Precaution Adoption Process Model, Health Behavior Model, and Social-Ecological Model. DIVAS implements innovative virtual outreach programs, training, and intervention strategies to empower Advocates to educate peers, providers, and policymakers. 3 Cohorts of Black women impacted by breast cancer trained as Lay Breast Health Advocates from 2011, 2020, and 2021 (N = 57; 77.5 % 45 years or younger; 36.7% early-stage 0-II, 50% late stage III-IV, 10.3% caretakers) self-reported their lifestyle behaviors, breast cancer diagnosis, breast health education, social media use, and interest in a digital-based lifestyle intervention. Participants completed pre-and post-surveys, interviews, and journaling over 10.5+ hours of education modules to understand their breast health, provider-related challenges, and community-related resources.

Findings provide evidence that cohort-tailored education is a successful method of supporting

Black women in a behavioral-health intervention. The provision of printed culturally attuned information along with the digital-based instruction from a Black woman health care provider or public health expert is effective in helping Black breast cancer survivors transition into patient empowerment, improve QOL and contribute to better patient outcomes. After the intervention and completion of breast health modules, participants reported increased: self-efficacy in communicating with providers (70%) and self-efficacy in making treatment decisions (70%) self-confidence (85%), and a decrease in lifestyle risk factors (87%). Patient-centric behavioral health interventions in breast cancer education must be advanced digitally to address the pandemic's compounded crisis.

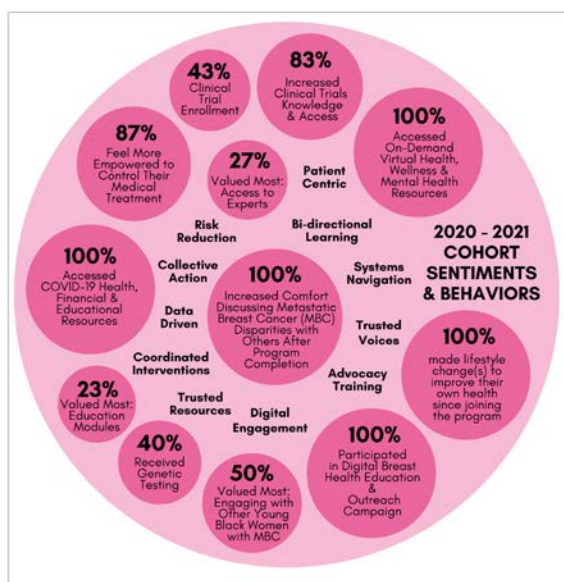
DC Pink Divas provides insights to combat rising disparities by educating, empowering, and mobilizing Black lay breast health advocates to improve outcomes. Collaborative digital interventions across the care continuum to improve awareness, access, adherence, infrastructure, culturally attuned training, and support are evidence-based methods for navigating the cancer care transformation accelerated by COVID-19 to advance breast health equity.

DIVAS Logic Model 2011- 2022



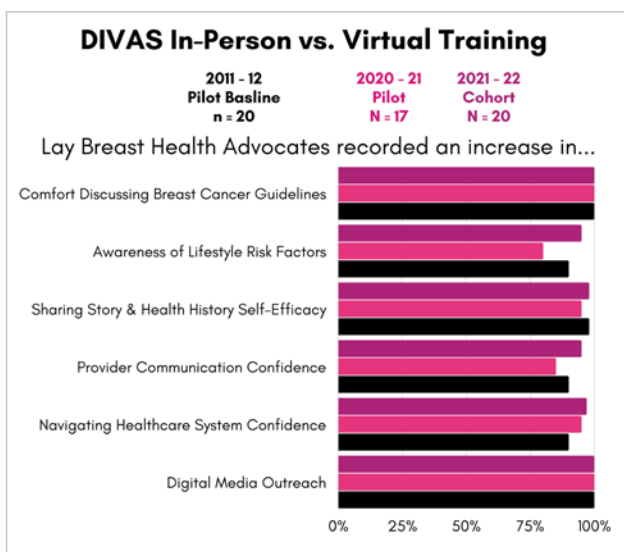
Logic model demonstrating inputs, activities, outputs and short and long term outcomes

2020- 2021 Cohort Sentiments and Behaviors



Cohort outcomes from DC Pink Divas

DIVAS In-Person vs Virtual Training



Lay Breast Health Advocates recorded outcomes from cohorts 2011, 2020, and 2021

Disclosure(s):

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P1-08-10

A web-based Patient Decision Aid Toolkit for unaffected BRCA mutation carriers.

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Women with a pathogenic mutation in the BRCA1 or BRCA2 genes have an elevated lifetime risk of developing breast and ovarian cancer. To address this risk, women are managed with a combination of surveillance and/or risk-reduction strategies. Decisions about risk management strategies can be complex, personal and multifactorial. Women often struggle with the decision-

making process. In addition, within the clinical environment, there may be variations in recommendations between clinicians that can leave women uncertain and less able to choose a risk management pathway. The overall aim of this project is the development of a web-based patient decision aid toolkit for BRCA mutation carriers that will improve the decision-making process by providing the user with information about their cancer risk, options for risk management and potential benefits and side effects. Development of the patient decision aid was guided by the International Patient Decision Aid Standards (IPDAS). With appropriate ethical approval, a mixed methods approach was used to identify suitable content for the decision aid. A decision-making needs assessment was conducted to identify the information needs of women with a BRCA mutation. Semi-structured interviews were held with cancer unaffected BRCA mutation carriers (n = 16) and key stakeholders including healthcare professionals, policy makers and patient group representatives (n= 10). Data were analysed by thematic analysis. Systematic scoping reviews were conducted to synthesise relevant evidence on risk-management options, benefits, harms and the development and testing of patient decision aids in general. Content for the decision aid was refined using a Delphi process to build consensus on items for inclusion in the decision aid amongst a diverse panel of experts (n=13). A prototype patient decision aid was developed which included written information as well as visual depictions of risk, videos and photographs to enhance the patient's information experience. A 'values clarification' activity was included to enable women to work through their own values and preferences relating to risk management interventions and their associated benefits and side-effects. Initial 'sandpit' testing of the decision aid prototype was performed by the research team and advisory group. Usability testing was conducted with BRCA mutation carriers (n = 8) and healthcare professionals (n = 8) using both qualitative interviews and quantitative surveys. The research team made final revisions to the decision aid based on participant feedback and committee consensus. This evidence-based patient decision aid can be used by BRCA mutation carriers unaccompanied or during a clinical consultation. We envisage that this decision aid will improve the decision-making process by assisting women and clinicians during shared decision-making regarding cancer risk management.

Disclosure(s):

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P1-08-11

Using co-design to develop culturally and linguistically appropriate breast cancer education materials

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Background: Engaging diverse community members in research is vital to communicate and disseminate information to their communities. Co-design is a participatory approach to design solutions to problems and can be used to develop materials by bringing together individuals from diverse backgrounds. There is currently a gap in research of health education materials (i.e., Infographics) being created that employ a community co-design approach. We describe use of the co-design process to develop an infographic on breast cancer risk factors for broad community dissemination. Methods: The Community Leadership Committee (CLC) that represents the demographics of the Greater Los Angeles area was formed in 2015 and members were drawn from community and advocacy organizations, representing the four largest racial/ethnic groups (African American, Chinese, Latina, and Non-Hispanic White). The primary role of the CLC was to help create teachable, culturally-responsive materials on breast cancer and the environment. To address their communities' informational needs about breast cancer and the environment, the CLC determined elected to develop infographics. Focus groups were held in summer of 2017 to evaluate the initial drafts of the infographics for clarity, utility, cultural and linguistic appropriateness and effectiveness. Focus group participants were recruited by the CLC members to and were conducted in English, Spanish, or Mandarin Chinese. Results: CLC members (N=18) informed the design and development of the infographic. Members of the CLC member ages ranged from 49 to 79. All members were female, 42%% were foreign-born, 34%% spoke Spanish, 20% spoke Chinese, and 75% were breast cancer survivors. A total of 6 focus groups were conducted with 53 women. The groups consisted of 4 groups in the English language [African American (N=12), non-Hispanic White (N=7), Chinese (N=9), and Hispanic/Latina (6)], one in Spanish (N=7), and Mandarin Chinese (N=12). The infographic went through 6 versions before being finalized, translated into Spanish and Chinese, and printed. Focus groups occurred between initial draft and draft #3. Some of the common themes included the importance of representation, readability, and visualization. CLC members preferred materials that included less text and more graphics to make it faster and easier to read. Collaboration with the CLC and findings from the focus groups led to the development and refinement of the final infographics Discussion: We have described the development of health education materials through a co-design process to increase the awareness of breast cancer risk. These findings emphasize the importance of involving people with lived experience and end users. Co-design is vital to ensuring the health education materials were appropriate, engaging, culturally and linguistically competent. Health education materials that resonate with their intended audience have the potential to influence health behaviors resulting in risk reduction.

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Michele Rakoff, n/a: No financial relationships to disclose

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Susan Neuhausen, PhD: No financial relationships to disclose

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P1-08-12

Improving Cancer-related Symptom Burden and Quality of Life with CancerLife™, a Digital Self-Care Therapeutic for Cancer Patients

Presenting Author(s) and Co-Author(s):

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Charles Coltman, Ignatius Beard, and Scott A. Irwin Background Collecting patient-reported outcomes have been shown to improve outcomes in patients with cancer; however, implementing methods to collect and utilize these data, such as remote patient monitoring, has been limited due to staffing resources, workflow disruption, EMR integration, and cost barriers. A self-care patient engagement consumer app is one solution to help alleviate these barriers. The purpose of this study was to demonstrate that the self-reporting of symptoms by patients using a novel patient engagement mobile application, at any time, from anywhere, would have a meaningful impact on symptom burden while improving Quality of Life (QoL) without the aforementioned barriers, most importantly workflow disruption. **Design** A blinded, two-arm, randomized, controlled trial of CancerLife™ was conducted. Participants with breast cancer were recruited nationwide via Facebook ads and asked to complete an online qualification survey. If qualified, they received a text message with a link to complete the consent and enrollment process, then randomly assigned via 1:3 ratio to control or the CancerLife™ intervention. Overall health state (EQ-5D) and QoL (EQ-VAS) were compared with usual care every three weeks from 9 weeks to 24 weeks post-baseline. Virtual monitoring of common cancer-related symptoms (symptom count) was also done for the CancerLife™ group. **Results** A total of 1006 participants were recruited online, and 499 completed the registration, consenting process, and download app procedure and were enrolled. A total of 189 participants in both groups completed the 24-week study. Participants that enrolled represented a wide national geographic area inclusive of 117 different area codes, which suggests the solution can address the challenges of care disparities. A significant main improvement effect of intervention favoring CancerLife™ was found for both the EQ-VAS ($F(1, 5) = 22.1, p < 0.01$) of 14.2% and 9.9% on the EQ5-D ($F(1, 5) = 14.3, p < 0.01$). Post-hoc paired t-test comparisons indicated significantly higher mean differences at 18 and 21 weeks ($p < 0.05$) on the EQ-VAS and at 21 weeks ($p < 0.05$) on the EQ5-D, with similar trends at 9, 15, and 24 weeks on the EQ-VAS and 15, 18, and 24 weeks on the EQ5-D. Further, the CancerLife™ group demonstrated a significant decrease in symptom count (mean $\Delta = -9.11, -78.1\%, t = -2.62, p < 0.001$) at 24 weeks. **Conclusions** This study demonstrates that a patient engagement app with a novel data collection platform could lower symptom burden and improve overall QoL with minimal barriers to implementation. Since remote patient monitoring systems are hard to implement inside cancer care settings due to costs, IT system integration, and workflow disruption, a direct-to-consumer-based app, which can be used in any care setting by any patient, and accessed through any connected device, shows significant promise to ameliorate symptom burden, raise overall QoL, and address disparities of access to care and care outcomes for cancer patients. Providers may consider this as a tool to improve their population quality metrics, care and care utilization outcomes, disparities, and patient satisfaction scores without significant startup, maintenance, resource, and workflow costs.

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P1-09-02

Oncological, Cosmetic and Quality of life outcomes following breast conservation surgery in patients presenting after non-oncological excision of breast primary: A prospective follow up study

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Background For early-stage breast cancer BCS followed by radiation therapy has been validated as safe alternative to Radical Mastectomy. One peculiar problem faced in developing countries is patients in whom primary tumor has been excised elsewhere. There is a lack of clear treatment history and pre-operative examination and imaging in such patients, which makes accurate staging and planning for definitive surgery much more challenging. We did this retrospective analysis to assess clinical, cosmetic and QOL outcomes in the above-mentioned group of patients. Methods Patients between 18 and 80 years diagnosed with biopsy proven carcinoma breast that had the primary tumor excised outside and underwent BCS at our institute were included. They were subjected to routine history and physical examination as per the institute standard of care. Overall survival was estimated using Kaplan Meier curve. Expected 4 years survival was calculated using percentage of people who were alive out of those patients whose follow up was known at the end of 4 years. Cosmetic outcome was assessed using patient reported BCTOS 12 scores whereas quality of life outcome was assessed using patient reported EORTC and SF 36 questionnaire scores. Results Twenty-two patients were enrolled. Overall survival at 4 years was 72% comparable in NACT and No NACT

($p < 0.29$). 5.45% patients had local recurrence. Cosmetic outcome was excellent to good in 90% patients, similar between NACT and No NACT ($p 0.69$). Quality of life was excellent-good in 65% patients (EORTC) which was significantly higher in No NACT group ($p 0.05$) Conclusion BCS after scar excision following non oncological resection of breast primary may be an acceptable modality of treatment with good cosmetic and Quality of life outcomes.

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5:00 PM - 6:15 PM

P1-09-03

Impact of BRCA1/2 pathogenic variants on ipsilateral breast tumor recurrence and prognosis following breast-conserving surgery

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Background The risk of ipsilateral breast tumor recurrence (IBTR) and the prognostic outcome of breast-conserving surgery (BCS) for germline BRCA1/2 pathogenic variant (BRCA1/2+) carriers remain controversial. We examined differences in IBTR and prognosis between

BRCA1/2+ carriers and non-carriers following BCS for breast cancer. Methods Clinical and pathological data were collected by retrospectively reviewing charts of consecutive patients with stage 0-III breast cancer who underwent genetic testing for germline BRCA1/2 and BCS between 1996 and 2020. Patients with variants of breast cancer-associated genes other than BRCA1/2 were excluded. We compared the incidence of IBTR and prognosis, including overall survival (OS), breast cancer-specific survival (BCSS), and distant recurrence-free survival (DRFS), between BRCA1/2+ carriers and non-carriers. Results We analyzed 551 patients (587 breasts with cancer), including 30 BRCA1+ carriers (32 breasts) and 31 BRCA2+ carriers (32 breasts). The median follow-up was 5.8 years (7.2 and 5.3 years for carriers and non-carriers, respectively). The median age at breast cancer diagnosis was 43 and 46 years for carriers and non-carriers, respectively, indicating younger onset of cancer in carriers (age \leq 40 years; 46.9% for carriers vs. 27.5% for non-carriers, $p = 0.001$). In carriers, breast cancer more frequently expressed estrogen receptor-negative (56.2% for BRCA1+ carriers and 15.6% for BRCA2+ carriers vs. 22.0% for non-carriers, $p = 0.013$), progesterone receptor-negative (62.5% for BRCA1+ carriers and 31.3% for BRCA2+ carriers vs. 29.5%, $p = 0.005$), nuclear grade III (45.3% for carriers vs. 29.5% for non-carriers, $p = 0.010$), or a higher Ki-67 index (Ki-67 index $>$ 20) (89.5% vs. 61.8%, $p = 0.001$) than non-carriers. Moreover, carriers underwent chemotherapy more frequently than non-carriers (62.5% vs. 42.4%, $p = 0.002$). Cancer stage, tumor size, HER2 status, presence of lymphovascular invasion, and the rate of positive or close surgical margins did not statistically differ between the examined groups. No statistical differences were detected in the number of patients who underwent whole-breast radiotherapy following BCS: 59 breasts in carriers and 503 in non-carriers (92.2% vs. 96.4%). During follow-up, we noted that 9 breasts of BRCA1/2+ carriers (5 [15.6%] for BRCA1+ and 4 [12.5%] for BRCA2+) and 35 breasts (6.7%) of non-carriers developed IBTR ($p = 0.035$). In an analysis excluding patients who did not undergo radiotherapy, the rate of IBTR remained significantly higher in BRCA1/2+ carriers ($p = 0.034$) than that in non-carriers. The median time to IBTR was 10.2 years in carriers (10.2 years for BRCA1+ and 8.5 years for BRCA2+) and 3.5 years in non-carriers. Carriers were more likely than non-carriers to exhibit distinct subtypes of recurrent tumors in the ipsilateral breast (66.7% for carriers vs. 19.4% for non-carriers, $p = 0.006$), occurring in a different quadrant from the primary tumor (50.0% vs. 27.3%, $p = 0.215$). No significant differences in OS ($p = 0.068$), BCSS ($p = 0.109$), or DRFS ($p = 0.359$) were noted between carriers and non-carriers. Conclusion BRCA1/2+ carriers exhibited a higher risk of IBTR after BCS and a longer time to IBTR than non-carriers. One limitation of the present study is a longer follow-up period for carriers than for non-carriers, as carriers typically underwent long-term observation at our institution; hence, further data accumulation is warranted for validating these findings. Subtypes and quadrants of IBTR were frequently distinct in carriers, indicating the increased incidence of new primary breast cancer. Although the prognosis did not differ between carriers and non-carriers, our results suggest the necessity for long-term intensive breast surveillance of BRCA1/2+ carriers after BCS.

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5:00 PM - 6:15 PM

P1-09-04

Comparison of length and quality of life (QoL) and the side effects of therapy between breast conserving surgery with intraoperative radiotherapy (TARGIT-IORT) versus mastectomy for in-breast-recurrence of breast cancer

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Background: Mastectomy is the treatment recommended by most national and international guidelines for in-breast-recurrence of breast cancer after breast conserving surgery (BCS) and external beam radiation therapy (EBRT). In selected cases it is possible to preserve the breast if TARGIT-IORT can be given during the second lumpectomy. We present a comparative analysis of overall survival, QoL and side effects. Methods: We identified patients who had local recurrence of breast cancer after BCS and EBRT in our prospectively maintained database. Patients were included if they had undergone either a mastectomy or BCS along with TARGIT-IORT. Patients with distant disease were excluded. Identified patients were contacted and offered participation in a prospective QoL-analysis using the BREAST-Q questionnaire. The cohorts were compared for confounding parameters, overall survival, side effects, physical, sexual and psychosocial wellbeing and satisfaction with the surgical result. Results: 36 patients treated for local recurrence were included in this analysis, 21 had received a mastectomy and 16 patients had chosen to preserve their breast and after interdisciplinary tumor board decision received BCS and TARGIT-IORT. Mean follow-up was 12.8 years since primary diagnosis and 4.2 years since recurrence. There were no significant differences between both groups regarding age, ER, PR, HER2neu, tumor size or nodal status at primary diagnosis or at recurrence and the distribution of invasive versus non-invasive recurrences. 1 patient in the BCT and TARGIT-IORT group (6.7%) and 3 patients in the mastectomy group (14.3%) died during follow up. Overall survival was numerically longer for BCS and TARGIT-IORT either calculated from primary diagnosis (median 18 years versus 8 years) or from recurrence

(median 5.1 years versus 3.2 years). The numbers were too small for formal statistical analysis. No patient had another local recurrence of breast cancer during follow-up. 12 patients in the mastectomy group and 10 patients in the BCS and IORT group returned the BREAST-Q questionnaire. Psychosocial wellbeing, sexual wellbeing and satisfaction with the surgeon did not differ between both groups. Physical wellbeing was significantly superior for those whose breast could be preserved (median score for BCS and TARGIT-IORT group was 91 (71-100) vs. 66 (14-100) for the mastectomy group, p-value = 0.021). Whereas most side effects were comparable and showed no significant differences, patient-reported incidence and severity of lymphedema of the arm on the side of surgery was significantly worse in the mastectomy group (p=0.007). Conclusion: Many patients who have local recurrence of breast cancer are reluctant to lose their breast. We found that preserving the breast by use of TARGIT-IORT was safe with no re-recurrence and no detriment to overall survival. This is necessarily a small series, because local recurrence is rare, yet, this novel approach led to a statistically significant improvement in physical wellbeing and incidence and severity of lymphedema. These data increase the confidence in offering breast preservation and TARGIT-IORT for surgery of in-breast-recurrence of breast cancer.

Disclosure(s):

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5:00 PM - 6:15 PM

P1-09-05

Effect of Wire vs Magnetic Seed Localization on Lumpectomy Cavity Size

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Purpose/Objectives To assess whether an association exists between surgical localization technique and size of lumpectomy cavity on radiation (RT) planning CT scan. Adjuvant RT with boost to lumpectomy cavity has been shown to improve local control compared to adjuvant whole breast radiation alone, but larger cavity sizes can lead to worse cosmetic outcomes following boost administration, which could lead providers to omit boost. Therefore, decreasing

cavity size could increase guideline-concordant boost administration and minimize adverse cosmetic outcomes. **Materials/Methods** A retrospective review was conducted of all patients undergoing breast conserving surgery with either wire- or magnetic seed -guided lumpectomy followed by adjuvant RT at a single institution from 2018 to 2021. Data were collected from pre-surgical work-up, surgical pathology, and radiation planning. Women undergoing bracketed wire localization and patients treated by a surgeon who only performed wire localized procedures were excluded. The primary outcome was lumpectomy cavity size as measured on planning CT. We first conducted an overlapping weights propensity score analysis to account for imbalance between groups in age, BMI, breast size as measured on planning CT scan, pre-operative imaging tumor volume, neoadjuvant therapies, lumpectomy histology (DCIS alone vs DCIS + invasive vs invasive alone vs invasive with lobular features vs no residual), and multifocality. Multivariable analysis (MVA) of CT cavity volume included the above weighted variables as well as surgeon and radiation oncologist. Secondary analyses included MVA of total pathologic volume, bivariable analysis of boost delivery, bivariable analysis of electron vs photon boost, stratification by surgeon, and fixed effect model for year of surgery. **Results** Of 617 women who received lumpectomy during the study period, 387 were included in final analysis. Patients who underwent seed localization were less likely to have multifocal disease, less likely to have calcifications on mammogram, more likely to have ultrasound measurements for pre-op imaging, and had smaller tumor size on pre-op imaging. Four surgeons performed all cases, with rates of seed use per surgeon ranging from 27.7% to 70.7% but generally increasing throughout the study period. There was no difference between wire and seed localization in the need for additional margins based on intra-operative margin analysis (58.4 vs 62.7%, $p = 0.5$). There was no difference in positive margins (6.4 vs 5.4%, $p = 0.81$) or second surgeries (9.4 vs 8.1%, $p = 0.79$). Rates of close margins were the same for DCIS (23.4 vs 17.3%, $p = 0.35$) and invasive carcinoma (7.6 vs 6.8%, $p = 0.97$) between techniques. Initial uncorrected bivariable analysis shows wire localization has a non-significant trend toward increased CT cavity volume (4.56cc, $p = 0.15$) and a significant association with total pathology volume (21.7cc, $p = 0.004$). For the primary outcome, breast size, time from surgery to simulation, and surgeon were all significantly associated with CT cavity volume but there was no significant difference by localization technique ($p=0.38$). For pathology volume, there was a non-significant trend toward increased specimen volume with wire localization ($p = 0.07$), and significant associations with BMI, histology, and pre-op imaging volume. When stratified by surgeon, there was no surgeon for whom one localization technique led to significantly different CT or pathology volume over the other. There were no significant changes of the treatment effect over time ($p = 0.79$). There was no significant difference between wire and seed localization in indicated boost delivery (85% vs 79%, $p = 0.14$) or electron boost (42% vs 56%, $p = 0.13$). **Conclusion** There was no significant difference in CT cavity size between wire localization and magnetic seed localization, suggesting that the choice between these surgical techniques does not impede RT boost delivery.

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5:00 PM - 6:15 PM

P1-09-06

Save the breast after neoadjuvant therapy – identifying radiological and tumor related factors of importance for breast conserving surgery after neoadjuvant chemotherapy

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Background

Neoadjuvant chemotherapy (NAC) is an established treatment option in early breast cancer. NAC potentially downstages the tumor and, combined with oncoplastic techniques, may increase the eligibility for breast conserving surgery (BCS). NAC can also result in less surgical morbidity of the axilla if axillary clearance can be avoided. In addition, preoperative medical treatment allows for a thorough evaluation of treatment response and lays the foundation for adjuvant treatment decisions. The aim of the study was to prospectively estimate the proportion of BCS post NAC and the relation to well-defined factors associated with BCS post NAC.

Materials and methods

This observational prospective cohort study included 226 patients in the SCAN-B neoadjuvant cohort (Clinical trials: NCT02306096) receiving NAC between 2014 and 2019. Eligibility for BCS was based on the assessment of the surgeon at time of diagnosis and again post NAC. All the covariables were defined at time of diagnosis from mammograms and core needle biopsies, except for pathological complete response (pCR). Treatment generally consisted of 6 to 7 three-weekly treatment cycles of anthracycline- and taxane-based chemotherapy, given in sequence. In HER2-positive disease, HER2-directed antibodies were added as appropriate. The primary aim was to estimate the proportion of BCS after NAC and the secondary aim was to evaluate factors as predictors of BCS, including gene expression and surrogate molecular subtypes (St. Gallen), breast density, and other putative modifying factors. Uni- and multivariable logistic regression analysis were performed including covariates of clinical relevance and/or associated with the outcome measures (BCS versus mastectomy).

Results

The BCS rate increased during the study years, from 37% to 52%. pCR was achieved in 69 patients (30%). Predictors with a negative association to BCS were larger tumor size on mammography (T3 vs T1) (odds ratio (OR)=0.20, 95% confidence interval (CI) [0.06,0.64]), lack of visibility on ultrasound (OR=0.08, 95% CI [0.001,0.63]), lobular histological subtype vs other subtypes (OR=0,20, 95% CI [0.06,0.61]). Factors positively associated with BCS were benign axillary lymph node status (OR=2.26, 95% CI [1.26,4.06]) and surrogate molecular subtypes; patients with triple negative and HER-2 positive tumors had the highest probability of receiving BCS, 65% and 54%, respectively. Gene expression subtypes had a similar trend of being associated with BCS; patients with basal like and HER-2 enriched tumors had higher odds ratio for BCT than patients with luminal subtypes (Table 1). In the multivariable logistic regression analysis, tumor size on mammography and axillary status had the strongest association to BCS (OR=0.95, 95% CI [0.92,0.98] and OR=2.08, 95% CI [0.99,4.35], respectively).

Conclusions

Our study shows that the rate of BCS after NAC increased over the study years, but mastectomy rate in the study was still close to 50%. With increasing number of patients achieving pCR after NAC, the BCS rate should be possible to increase further. Predictors of BCS after NAC were identified, and benign axillary lymph nodes and smaller tumor size defined at time of diagnosis were the strongest predictors of BCS, supporting that initial tumor stage was important for the choice of surgery after NAC.

Table 1. Baseline characteristics and univariable logistic regression

	All patients (n = 226)	Breast conserving surgery (n = 118)	Mastectomy (n = 108)	Odds Ratio (CI95%)	p-value
Age, years					
Age, risk per year				0.996 (0.975-1.018)	0.733
< 50	88 (39)	45 (51)	43 (49)	Ref	
50-59	61 (27)	35 (57)	26 (43)	1.286 (0.667-2.482)	0.453
60-69	57 (25)	31 (54)	26 (46)	1.139 (0.584-2.222)	0.702
≥70	20 (9)	7 (35)	13 (65)	0.515 (0.188-1.412)	0.197
Axillary status					
Malign lymphnode ¹	153 (68)	71 (46)	82 (54)	Ref	
Benign lymphnode	71 (32)	47 (66)	24 (34)	2.262 (1.259-4.062)	0.006
Nodal status unavailable	2				
Visibility on mammography					
Visible	196 (90)	104 (53)	92 (47)	Ref	
Not visible	22 (10)	11 (50)	11 (50)	0.785 (0.366-2.136)	0.785
Unknown	8				
Mammographic tumour size², mm					
Size, risk per mm				0.954 (0.933-0.976)	<0.001
≤20 (T1)	46 (23)	26 (57)	20 (43)	Ref	
21-50 (T2)	126 (65)	74 (58)	53 (42)	1.060 (0.536-2.095)	0.868
>50 (T3)	24 (12)	5 (21)	19 (79)	0.202 (0.064-0.636)	0.006
Visibility on ultrasound					
Visible	205 (95)	114 (56)	91 (44)	Ref	
Not visible	11 (5)	1 (9)	10 (91)	0.080 (0.0010-0.635)	0.017
Unknown	10				
Histological subtype					
Ductal	177 (79)	96 (54)	81 (46)	Ref	
Lobular	21 (9)	4 (19)	17 (81)	0.199 (0.064-0.614)	0.005
Other invasive	25 (11)	16 (64)	9 (36)	1.500 (0.629-3.575)	0.360
Subtype unknown	3				
Molecular subtype (St. Gallen)					
Triple negative	68 (30)	44 (65)	24 (35)	Ref	
Her-2 positive	68 (30)	37 (54)	31 (46)	1.212 (0.478-3.074)	0.685
Luminal A	11 (5)	5 (45)	6 (55)	0.421 (0.126-1.646)	0.230
Luminal B	77 (34)	31 (40)	46 (60)	0.368 (0.187-0.722)	0.004
Subtype unknown	2				
Molecular subtype (Genexpression)					
Basal-like	63 (32)	41 (65)	22 (35)	Ref	
Her-2 enriched	51 (26)	27 (53)	24 (47)	0.604 (0.284-1.285)	0.190
Luminal A	34 (17)	15 (44)	19 (56)	0.424 (0.181-0.994)	0.048
Luminal B	49 (25)	24 (49)	25 (51)	0.515 (0.240-1.105)	0.088
Subtype unknown	29				
Pathological complete respons³					
No	157 (70)	76 (48)	81 (52)	Ref	
Yes	69 (30)	42 (61)	27 (39)	1.658 (0.932-2.949)	0.085

1. Determined by biopsy or sentinel node. 2. Only tumors visible on mammography. 3. Defined as ypT0/ypTis/ypN0.

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P1-09-07

Omission of Axillary Surgery for Ipsilateral Breast Tumor Recurrence with Negative Nodes after Previous Breast-Conserving Surgery: Is It Oncologically Safe?

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Background

Salvage mastectomy is traditionally recommended for patients who developed ipsilateral breast tumor recurrence (IBTR) in light of the previous breast irradiation. However, it remains controversial whether surgical axillary staging (SAS) is necessary for IBTR patients with negative nodes. This study aimed to evaluate the oncologic safety of omitting SAS for IBTR.

Methods

We retrospectively identified patients who developed invasive IBTR with negative nodes after undergoing breast-conserving surgery (BCS). Patterns of care in nodal staging were analyzed based on prior axillary staging status. Clinicopathologic characteristics and adjuvant treatment of the initial tumor, as well as the IBTR, were compared between SAS and no SAS groups. Kaplan-Meier method and Cox regression model were utilized to compare the loco-regional recurrence-free survival (LRRFS), distant metastasis-free survival (DMFS), and overall survival (OS) rates after IBTR removal between the two groups.

Results

A total of 154 IBTR patients were eligible for final analysis. Compared to no SAS group, SAS group was less likely to undergo ALND (15.1% vs 73.3%, $p < 0.001$) at initial BCS, had a longer recurrence interval (2.8 vs 2.1 years, $p=0.03$), and were more likely to have discordant molecular subtype with primary tumor (35.8% vs 12.9%, $p=0.001$). However, the extent of axillary staging did not affect systemic or radiation recommendations. In the subgroup of patients without previous ALND, the clinicopathologic characteristics were roughly comparable. Pathologic analysis revealed pathologically uninvolved nodal status in approximately 85% of patients receiving SAS at time of IBTR in the overall population and the subgroup (Table 1). No significant differences were observed in LRRFS, DMFS and OS between the two groups (Table 2).

Conclusion

For node-negative IBTR patients, we observed selection bias on the basis of prior ALND, shorter recurrence interval, and concordant molecular subtype favoring no SAS, but comparable LRRFS, DMFS, and OS. These results support wider consideration of sparing SAS in the management of IBTR, especially in patients without previous ALND.

Pathologic axillary staging in patients receiving axillary surgery at time of IBTR

Table 1. Pathologic axillary staging in patients receiving axillary surgery at time of IBTR

Pathologic axillary staging	Surgical axillary staging	
	Total patients (N=53)	No prior ALND (N=45)
pN0	45 (84.9%)	39 (86.7%)
pN1	5 (9.4%)	4 (8.9%)
pN2-3	1 (1.9%)	1 (2.2%)
pNx	2 (3.8%)	1 (2.2%)

Cox regression analysis of LRRFS, DMFS, and OS after IBTR

Table 2. Cox regression analysis of LRRFS, DMFS, and OS after IBTR

Variables	Total patients with IBTR (N=154)			Patients without prior ALND (N=72)		
	No. of events	2-year survival probability (95%CI)	<i>p</i> value	No. of events	2-year survival probability (95%CI)	<i>p</i> value
LRRFS			0.5			0.77
Axilla surgery	2	93.5 (84.8-100.0)		2	91.6 (80.5-100.0)	
No axilla surgery	9	91.0 (84.1-98.4)		1	91.7 (77.3-100.0)	
DMFS			0.76			0.83
Axilla surgery	9	78.3 (65.4-93.9)		7	80.3 (66.6-96.9)	
No axilla surgery	19	79.2 (69.8-90.0)		4	83.6(67.1-100.0)	
OS			0.65			0.78
Axilla surgery	3	93.7 (85.1-100.0)		2	97.5 (92.8-100.0)	
No axilla surgery	7	94.6 (88.9-100.0)		1	95.7 (87.3-100.0)	

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Comparisons of aesthetic outcomes and prognosis of conventional breast conserving surgery, oncoplastic breast conserving surgery and breast conserving surgery plus immediate lipofilling in early breast cancer

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Background: Conventional breast conserving surgery (CBCS) considered as a confined alternative to mastectomy could lead to potentially breast deformities. Oncoplastic breast conserving surgery (OBCS) as well as breast conserving surgery (BCS) plus immediate lipofilling have been shown to be reliable techniques for maintaining the natural breast contours, however, few studies compared those three surgical options for oncological safety, complications and aesthetic outcomes in early breast cancer (EBC). Methods: We retrospectively reviewed the data of BC patients who underwent BCS between January 2017 and December 2021 from The First Affiliated Hospital of Chongqing Medical University. We included female patients who received BCS for unilateral stage 0-III BC. Those who had bilateral BC, incomplete surgical records, unfinished adjuvant therapy, multiple primary malignant tumors and lost to follow-up and were excluded. Patient-reported outcome measures (PROMs) were assessed using the BREAST-Q Version 2.0. We utilized a multivariable linear regression model to identify clinical factors correlated with the BREAST-Q score, and the log-rank test and Cox regression models were used to compare the survival difference between groups. Results: Of 268 patients, 90 (33.6%) underwent CBCS, 53 (19.8%) underwent OBCS and 125 (46.6%) underwent BCS plus immediate lipofilling. Patients in OBCS and BCS plus immediate lipofilling groups were younger than those in CBCS group (mean age: 43.9yrs vs 49.1yrs, $P=0.001$ and 45.7yrs vs 49.1yrs, $P=0.008$). The largest tumor size and heaviest BCS specimen were observed in the OBCS group compared with CBCS (mean tumor size: 23.4mm vs 17.3mm, $P<0.001$ and median excised weight: 122.0g vs 36.5g, $P<0.001$) and BCS plus immediate lipofilling group (mean tumor size: 23.4mm vs 17.4mm, $P<0.001$ and median excised weight: 122.0g vs 37.0g, $P<0.001$). It was balanced for pathological type, Ki-67, ER and PR expression between three groups. In the multivariable linear regression models, with the CBCS group as referent, either OBCS or BCS plus immediate lipofilling groups had a significantly higher score in satisfaction with breast (Estimate: 9.27, $P=0.001$ and Estimate: 13.08, $P<0.001$) and psychosocial well-being (Estimate: 6.06, $P=0.021$ and Estimate: 9.34, $P<0.001$). Additionally, sexual well-being was improved among patients receiving BCS plus immediate lipofilling (Estimate: 6.19, $P=0.029$). Nevertheless, patients in OBCS group harbored worse physical well-being compared with CBCS (Estimate: -15.89, $P<0.001$). There was no significant statistical difference among three groups on re-excision rate ($P=0.721$) and postoperative complications ($P=0.663$). After 37-month median follow-up, identical event-free survival (EFS) was revealed among three groups (HROBCS vs CBCS: 3.93; 95%CI, 0.78-19.81, $P=0.098$; HRBCS plus Lipofilling vs CBCS: 1.15, 95%CI, 0.28-4.67, $P=0.847$). Conclusion: This study demonstrated that OBCS as well as BCS plus immediate lipofilling shared equivalent oncological safety but better cosmetic outcomes and patient satisfaction

when compared with CBCS for EBC patients, suggesting that further prospective randomized clinical trials are warranted to confirm our findings.

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P1-09-09

Salvage mastectomy is not always necessary for aggressive subtypes of ipsilateral breast cancer recurrence: A single-institution retrospective study

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Introduction: Patients with triple-negative (TN) or HER2-enriched ipsilateral breast cancer recurrence (IBCR) seem to be excluded from a second breast-conserving surgery (BCS) under the assumption that salvage mastectomy would provide better oncological outcomes.

Objectives: The objective of this study was to describe the clinical features of these patients, to compare the two surgical alternatives (salvage mastectomy versus second BCS) in terms of oncological results, and to identify independent factors influencing prognosis and surgical treatment. Methods: We retrospectively reviewed all the consecutive patients with histologically confirmed TN or HER2-enriched IBCR. Disease-free survival (DFS), distant disease-free survival (DDFS), overall survival (OS), and breast cancer-specific survival (BCSS) were analyzed and compared between the two groups. Results: Eighty-five patients were affected by TN or HER2-enriched IBCR, with a median age of 60 years (range, 32-87 years). The majority of patients (72.9%) were treated with salvage mastectomy. There was no significant difference in terms of DFS between patients receiving a second BCS or mastectomy ($p=0.596$). However, patients undergoing a second BCS had significantly better DDFS, OS, and BCSS compared to

mastectomy ($p=0.009$; $p=0.002$; $p=0.001$, respectively). Tumor dimension < 16 mm (78.3% versus 38.7%, hazard ratio (HR)=3.602, 95% confidence interval (95% CI)=1.534-8.459, $p=0.003$) was found to significantly increase the probability of receiving a second BCS and positively affects recurrence and survival outcomes (DFS: HR=8.065, 95% CI=2.320-28.034, $p=0.001$; DDFS: HR=17.011, 95% CI=3.853-75.099, $p=0.001$; OS: HR: 13.881, 95% CI=2.730-70.579, $p=0.002$; BCSS: HR=36.773, 95% CI=4.579-295.322, $p=0.001$). Second BCS represents an independent protective factor for OS and BCSS (OS: HR=0.246, 95% CI=0.027-0.697, $p=0.002$; BCSS: HR=0.313, 95% CI=0.092-0.511, $p=0.002$). Conclusion: Salvage mastectomy is not always necessary and it does not seem to increase survival compared to a second BCS. This reinforces the concept that the prognosis of TN and HER2-enriched BC recurrence is mainly driven by the biology of the disease, rather than by the extent of surgery. In patients with small (< 16 mm) aggressive subtypes of IBCR, a second conservative approach can still be evaluated and offered, presenting acceptable loco-regional control and survival.

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P1-09-10

Factors associate with borderline or invaded margins in breast cancer surgery at the Val d'Aurelle Montpellier CRLC

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Factors associate with borderline or invaded margins in breast cancer surgery at the Val d'Aurelle Montpellier CRLC Véronique Mboua Batoum*, Esther Dina Bell, Christianne Nsahlai, Junie Annick Metogo Ntsama , Esther Juliette Meka, Marian Gutowski, Simon Thezenas, William Jacot *Corresponding autor : vbatoum@gmail.com Introduction: The inadequate status of the resection margins after breast cancer surgery is an important predictor of local tumor recurrence. The objective of our study was to determine the factors associated with positive or invaded resection margins. Methodology: Our retrospective study included a cohort of 652 patients with early invasive breast cancer who underwent breast cancer conserving surgery at the Val d'Aurelle Regional Cancer Center. We defined positive margins as those with a distance of less than or equal to 2 mm from the tumour. The data were analysed using STATA® 10.0 software. Results: In our study, The median distance from the tumour to the surgical resection site was 5mm [0.0 - 35.0mm]. Resection margins were positive in 208 patients (31.9%). The rate of positive resection margins was significantly higher in non-menopausal patients (P =0,0050) , , in those with tumours less than 2 cm in size (P = 0,0004), with ductal carcinoma in situ (DCIS) component and without lymph node involvement (P =0,0082) . Re-excision surgery was performed in 229 patients (35.1%). Conclusion: Consideration of each of these factors associated with positive resection margins shoud help the surgeons to perform a wider excision, in other to obtain clear resection margin during the initial breast cancer surgery. Key words: breast cancer, conservative surgery, resection margins, risk factors for positive margins

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P1-09-11

Impact of breast surgical procedure on survival in BRCA mutated patients with invasive breast cancer: mastectomy versus conservative treatment.

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Introduction: Patients with BRCA1/2 mutations have a higher risk of developing breast cancer compared to the wild-type population. For patients with a BRCA mutation, there are no specific recommendations for surgical management. The aim of this study was therefore to retrospectively investigate overall survival (OS) and recurrence-free survival (RFS) of BRCA mutated patients with localized invasive breast cancer, by comparing conservative surgery versus mastectomy. Methods: This study was based on data from the Côte d'Or breast and gynecological cancer registry. Data from patients with a constitutional BRCA1/2 mutation who presented with invasive breast cancer were collected retrospectively from 1998 to 2018. The Kaplan-Meier method was used to describe RFS and OS. Results: A total of 104 patients were included in the analysis, of whom 69 had conservative surgery and 35 underwent mastectomy. Regarding survival, there was no significant difference in OS (HR =1.49; 95% confidence interval (CI) [0.76-2.93], p=0.25). Similarly, there was no significant difference in RFS (HR =1.40; 95% CI [0.81-2.40], p=0.22), survival without homolateral recurrence (HR =0.88; 95% CI [0.30-2.61], p=0.89), without contralateral recurrence (HR =1.50; 95% CI [0.55-4.09], p=0.42), or without distant metastatic recurrence (HR =1.42, 95% CI [0.69-2.90], p=0.33). Conclusion: In invasive breast cancer in a patient with a germline BRCA1/2 mutation, conservative surgery, when possible, appears to be a feasible option over total mastectomy, with no difference in overall survival. However, the patient should be informed of the aggressive nature of recurrence in this population requiring chemotherapy in most cases.

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P1-10-01

Postmastectomy electron beams radiation therapy (PMERT) : long term results

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Background/Purpose

This study evaluates the toxicity after radiotherapy after mastectomy without reconstruction in patients irradiated to the chest wall using previously reported technique of PMERT.

Materials/Methods

We included all women irradiated after mastectomy for not metastatic breast cancer with PMERT between 2007 and 2011 in the Department of Radiation Oncology of the Institut Curie. Previously reported technique using mostly electrons was evaluated in terms of efficacy and toxicity.

Acute and late toxicities were assessed retrospectively using CTCAE v.4.0. A clinical exam was weekly performed during radiotherapy and one and three months following the completion of radiotherapy. Patients were then followed as recommended in Institut Curie guidelines (Senorif).

Quantitative and qualitative data were described respectively as means and proportions. Statistical comparisons were computed using X² or Fischer's exact test for categorical data. Recurrence free survival (RFS) was defined as the time between the end of treatment and the date of recurrence or death. Overall survival was the same but recurrences were not taken into account. Patients who did not experienced any event were censored at the date of last news.

Results

Among the 796 women included, 51.3% had multifocal lesions, 10.1% a triple negative (TN) status and 18.8% a HER2+ positive status; 196 (24.6%) received a neoadjuvant chemotherapy, and 208 (26.1 %) a systemic therapy during radiotherapy (chemotherapy and/or targeted therapy); 514 (64.6%) had at least one positive lymph node (LN). Internal mammary chain (IMC) was treated in 85.6% of cases, supraclavicular LN (L4) in 88.3% of cases, infraclavicular (L3-2-IP+/- L1) LN in 77.9% of cases and low axilla (L1) in 14.9% of cases. With a median follow up of 113 months [range : 2-164] locoregional recurrence-free survival and overall survival at 10 years were respectively 94.02 (IC95% : 92.13-98.94) and 79.84 (IC95% : 76.83-

82.97). The median survival was not reached.

In the long term, 29.6% of patients had telangiectasia (grade 1: 23.3%, grade 2: 5.2% Grade 3: 1.1%).

Totally 279 patients (35.1%) had breast reconstruction, on average 21 months after the end of radiotherapy.

Twenty-five patients (3%) had early esophageal toxicity, not exceeding the grade 1. Of these patients, 21 had had chemotherapy and all were irradiated on the lymph nodes (24 including the IMC).

Irradiation of the IMC was not associated with an increased chronic lung toxicity (OR=1.03 [0.98-1.09]).

There were 35 patients who developed heart disease after the end of the treatment. Of them, 30 patients had received anthracyclines ($p=1.05$) and 9 trastuzumab ($p=1.09$). Four patients developed ischemic heart disease, 3/4 irradiated on the left chest wall, all on the CMI and supra and infraclavicular LN, but all of them presented multiple cardiovascular risk factors (2 to 4).

Conclusions

Our series have shown that the PMERT using the Institut Curie technique is effective and well tolerated.

Table 1 : patients and tumor characteristics (n=796)

Patients		n	%
Cardiac history	Ischemic cardiopathy	9	1.1
	Other	45	5.7
	Both	1	0.1
Cardiovascular risk factors	1 factor	259	32.5
	2 factors	82	10.3
	3 factors or more		4.8
History of respiratory disease	Yes	95	11.9
Hormonal status	Pre-menopausal	406	51
Previous cancer history	Yes	73	9.2

Breast cancer characteristics		n	%
Side	Left	387	48.6
Histological type	Ductal	606	76.1
	Lobular	123	15.5
	Mixed (ductal and lobular) or Other	67	8.4
Multifocality	Yes	408	51.3
Location in breast	Central/intern	301	39.8
	Extern	317	41.9
	Both (multiple lesions)	138	18.3
	NA	40	
Histological SBR grade	Grade I	45	5.7
	Grade II	352	44.3
	Grade III	397	50
	NA	2	
+ Histological subtypes	HR+ HER2-	566	71.1
	HER2+	150	18.8
	Triple negative	80	10.1
Lymphovascular invasion	Yes	396	55.1
Number of positive lymph nodes	0	282	28.9
	1 to 3	225	36.3
	More than 3		28.3
Tumor stage after neo-adjuvant treatment (n=213)	ypT0	49	23.8
	ypT1	55	33
	ypT2	68	14.1
	ypT3	29	2.4
	ypT4	5	
	NA	7	
Tumor stage without neo adjuvant treatment (n=583)	pT1 pT2	210	36.3
		296	51.2
	pT3	63	11.2
	pT4	7	1.2
	NA	5	

HR+ : hormonal receptor positive HER2+ : HER-2 overexpressed
Cardiovascular risk factor : (smoking, hypertension, dyslipidemia, diabetes, obesity, family history of coronary heart disease or vascular events) as described by the French Health Authority (HAS, Haute Autorité de Santé).

Table 2 : Efficiency (n=796, median follow-up: 113 months ; range : [2-164])

	10-year LRFS	10-year LRRFS	10-year MFS	10-year OS
Overall population	96.96 [95.62-98.32]	94.02 [92.13-95.94]	75.77 [72.6-79.08]	79.84 [76.83-82.97]
Receptor status				
HR+	98.2 [96.94-99.47]	94.82 [92.69-97.01]	75.54 [71.75-79.54]	80.39 [76.82-84.13]
HER2+	96.45 [92.96-100]	95.7 [91.95-99.59]	82.3 [75.99-89.14]	87.23 [81.63-93.21]
TNBC	89.1 [82.19-96.58]	85.14 [77.36-93.7]	65.53 [55.79-76.96]	62.56 [52.6-74.42]

HR+ : hormonal receptor positive HER 2+ : Her-2 overexpressed TNBC : Triple negative or basal-like cancer
 OS : overall survival LRFS : local recurrence free survival LRRFS : locoregional recurrence free survival MFS : metastasis free survival

Multivariate analysis : long term toxicity

	Cutaneous toxicity		Lung toxicity		Cardiac toxicity		Oedema	
	OR	p	OR	p	OR	p	OR	p
Patient characteristics								
Cardiac history	0.98 [0.91-1.05]	0.53	0.96 [0.9-1.04]	0.32	1.03 [0.97-1.09]	0.28	1.01 [0.97-1.06]	0.56
Pulmonary history	1 [0.95-1.05]	0.91	1.1 [1.04-1.17]	<0.01	1.02 [0.98-1.07]	0.32	1.03 [1-1.07]	0.09
Menopausal status	1.05 [1.01-1.09]	0.01	1.01 [0.97-1.04]	0.79	1.04 [1.01-1.07]	0.01	1.03 [1-1.05]	0.03
Treatment								
Left sided irradiation	1 [0.97-1.04]	0.85	0.99 [0.95-1.02]	0.51	1.01 [0.98-1.04]	0.52	1.02 [1-1.05]	0.06
Anthracycline use	0.99 [0.94-1.03]	0.54	0.94 [0.9-0.99]	0.02	1.05 [1.01-1.09]	0.01	1.01 [0.98-1.04]	0.61
Anti-HER2 use	0.99 [0.93-1.06]	0.85	1.03 [0.96-1.11]	0.37	1.09 [1.04-1.16]	<0.01	1 [0.96-1.05]	0.93
Hormone therapy	1.01 [0.97-1.06]	0.54	1 [0.95-1.05]	0.89	1 [0.97-1.04]	0.92	0.99 [0.96-1.03]	0.68
IMC irradiation	1 [0.95-1.05]	1.00	1.09 [0.98-1.09]	0.22	0.95 [0.91-0.98]	0.01	1 [0.96-1.03]	0.82
Axillary irradiation	0.98 [0.93-1.03]	0.41	1.06 [1.01-1.12]	0.02	1.02 [0.98-1.06]	0.31	1.04 [1.01-1.08]	0.03
Concurrent chemotherapy	1.01 [0.95-1.07]	0.68	0.97 [0.91-1.03]	0.36	0.96 [0.91-1.01]	0.09	0.99 [0.95-1.04]	0.76

IMC irradiation : Irradiation of the internal mammary chain
 OR : Odd ratio

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P1-10-02

FLASH-RT, ultra-high dose rate radiotherapy, is as effective as conventional dose rate radiotherapy in eradicating tumor in a preclinical model of breast cancer

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Problem Statement: Radiation therapy (RT) for breast cancer (BC) can induce skin and soft tissue fibrosis, raises concerns over cardiac and pulmonary injury, is associated with higher rates of lymphedema and shoulder dysfunction with regional nodal irradiation, and significantly increases complication rates in women undergoing implant-based reconstruction due to radiation toxicity. Although these toxicities are not generally associated with higher mortality, in general, they can represent significant setbacks with respect to quality of life. These toxicities dissuade some patients from breast conservation leading to unnecessary mastectomy and can lead patients to omit reconstruction after mastectomy or choose more extensive autologous breast reconstruction. Women with implant-based reconstruction and radiotherapy have known higher rates of reconstruction failure. **Purpose:** Ultra-high dose rate radiation (FLASH) has been shown to induce less normal tissue toxicity, therefore if tumor control of FLASH-RT would be comparable to conventional radiotherapy (CONV) then it has the potential to lower morbidity associated with radiotherapy for breast cancer and allow overall improved outcomes. At first, we aimed to determine the effectiveness of FLASH-RT compared to CONV in eradicating small breast tumors in an orthotopic BC model using single-fraction 20 or 30Gy RT to compare effectiveness of FLASH-RT vs CONV. **Methods:** Radiation sensitive, syngeneic mammary tumor cell line Py117, that efficiently forms non-metastatic orthotopic tumors in C57BL/6 mice, were injected (106 cells) into the left 4th mammary fat pad. 30mm³ tumors or a range of greater volumes (200-800mm³) were irradiated with single-fraction 20 or 30Gy with a 2x2cm radiation field (~17MeV beams), exposing only 5mm of the surrounding tissue. FLASH RT was delivered with 2Gy per pulse at dose rate ~200Gy/s compared to CONV dose rate of 0.13Gy/s **Results:** Single-fraction 20Gy suppressed 30mm³ tumor growth until ~day 15 post-RT then regrew for both FLASH and CONV, while 30mm³ tumors were eradicated with both FLASH and CONV at 30Gy. Larger tumors irradiated with 30Gy regressed until ~day 12 post-RT then regrew for both FLASH and CONV. There was no significant difference in growth suppression or tumor eradication between FLASH and CONV in any cohort. **Conclusion:** In this murine model of breast cancer, FLASH is as effective as CONV in controlling tumor growth. Future studies will extend the evaluation of the tumor control using clinically relevant fractionated dose schedules to be followed by comparisons of tumor control in xenograft models. Additional studies will assess normal tissue toxicity of FLASH vs CONV in murine models of implant-based breast reconstruction. We have established collaborations to understand differences in molecular pathways activated by FLASH vs CONV in tumor and normal tissue to explain the observed experimental differences in normal tissue, tumor, and cancer stem cells.

Disclosure(s):

Frederick Dirbas, MD: Hologic, Inc: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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P1-10-03

Ultra-hypofractionated Radiotherapy for Breast Cancer: A Brazilian Single-Institutional Series

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INTRODUCTION Extreme hypofractionation in patients with early-stage breast cancer has been studied in randomized phase III non-inferiority trials. There is scarce data on this strategy in Latin American patients. **OBJECTIVES** To describe the profile of patients diagnosed with breast cancer treated with radiotherapy with an ultra-hypofractionated regimen (5 fractions of 5.2 Gy, in one week), as well as the dosimetric aspects and acute toxicity related to the treatment. **METHOD** Retrospective cohort through a Brazilian uni-institutional series, with analysis of pathological, dosimetric, and toxicity variables. **RESULTS** Between May 2020 and March 2022, 67 patients were included, with a median age at diagnosis of 71 years (41-93). Regarding staging, 25.8% had in situ tumors, 60.6% of patients were IA, and only 3% were stage IIA. Nineteen percent of patients had histological grade 3; 24.6%, had nuclear grade 3. Hormone receptors were positive in 92.1% of patients. The mean ki67 was 19%, and HER2 was negative at 84.5%. All patients underwent conservative surgery, and 5 underwent reconstruction with autologous flaps. Fifty-one patients underwent hormone therapy and only 2 underwent adjuvant chemotherapy. All but two patients were treated with the conformal technique (VMAT was used due to unfavorable anatomy). The mean volume of the irradiated breast was 926 cm³ (ranging from 920 to 932 cm³). Regarding the constraints of the organs at risk, the average V8Gy of the ipsilateral lung was 11.4%, ranging from 0 to 24%. In the heart, the average volumes receiving 1.5Gy and 7Gy were, respectively, 9.2% and 0.7%. No patient had acute toxicity greater than grade 2. The effects on the skin appeared on average 20 days after the end of treatment, with resolution in a maximum of 3 months. The median follow-up time was 10 months (3 - 26). We did not observe any case of local-recurrence, of breast-cancer-related death. **CONCLUSION** Although our follow-up time is premature, we have found that ultra-hypofractionated radiotherapy was feasible, tolerable, and safe, for patients with early breast cancer. Also, the constraints on the organs at risk were respected. There were no high-

grade acute toxicities. Besides convenience, ultra-hypofractionation can improve access to radiotherapy in resource-scarce settings.

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P1-10-05

Safety of stereotactic body radiation therapy, stereotactic radiosurgery, and other radiation therapy with use of CDK 4/6 inhibitors for hormone receptor positive (HR+), HER2- metastatic breast cancer: a retrospective cohort study

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Objective Patients with hormone receptor positive (HR+), HER2- metastatic breast cancer frequently require radiation therapy (RT) in addition to systemic therapy for disease control and symptom management. CDK 4/6 inhibitors are increasingly used in the care of hormone positive breast cancers. Stereotactic body radiotherapy (SBRT), a form of very focused high dose radiation, is also increasingly used in the care of metastatic breast cancer. Limited data have reported on the safety of palliative RT with CDK4/6 inhibitors, with some reports demonstrating synergistic effects with potential for increased toxicity. The objective of our study is to assess toxicity among patients who received SBRT, stereotactic radiosurgery (SRS), or other high dose RT along with CDK 4/6 inhibitors for treatment of metastatic breast cancer. Methods Women with metastatic breast cancer who received SBRT, SRS, or other higher dose RT with CDK 4/6 inhibitors at any point in their treatment between 2013 and 2021 were retrospectively identified. Timing of radiation therapy, either before, during, or after CDK 4/6 inhibitor use was assessed, as well as the interval between the two treatments. Treatment sites

for radiotherapy included lung/chest, spine, and brain metastases. Physician assessed adverse events were obtained through clinical follow up and graded using CTCAE v5. Local control and OS were reported. Results Twenty patients met study inclusion criteria. Patients received radiation therapy and CDK 4/6 inhibitors concurrently (within 7 days) [n=7, 35%], within 30 days (RT pre-CDK 4/6 inhibitor use) [n=3, 15%], and greater than 30 days (RT pre-CDK 4/6 inhibitor use [n=6, 30%] and RT post-CDK 4/6 inhibitor use [n=4, 20%]). Radiation treatment sites were spine [n=10, 55%], brain [n=6, 30%], and lung/chest wall [n=3, 15%]. Radiation doses were as follows: 60 Gy in 5 fractions [n=1, 5%], 50 Gy in 5 fractions [n=2, 10%], 55 Gy in 20 fractions (chest wall recurrence) [n=1, 5%], 35 Gy in 15 fractions [n=1, 5%], 30 Gy in 10 fractions [n=6, 30%], 30 Gy in 3 fractions [n= 4, 20%], 24 Gy in 1 fraction [n=3, 15%], 20 Gy in 5 fractions [n=2, 10%]. Palbociclib was used in 85% of patients [n=17] and abemaciclib in 15% [n=3]. Median follow up for surviving patients was 4.7 years [IQR: 2.5-6.8 years]. Local control was achieved in 85% of patients [n=17]. Median OS was 2.7 years [IQR: 0.1-6.8 years]. Grade 2 toxicity [n=9, 45%] and grade 3 toxicity [n=3, 15%] was reported across all three treatment areas, with grade 2 or 3 fatigue [n=7, 35%] being the most frequently reported toxicity. In the spine treatment group, 1 patient who had CDK 4/6 inhibitor use within 30 days of radiotherapy experienced a grade 3 vertebral compression fracture as well as grade 3 fatigue. In the lung/chest wall treatment group, the patient treated to 55 Gy in 20 fractions to the chest wall with concurrent use had grade 3 skin/wound toxicity requiring prolonged wound care before healing. In the intra-cranial SRS group, grade 3 fatigue was reported in 1 patient with concurrent use. Conclusion The use of CDK 4/6 inhibitors concurrently with or within 30 days of radiation therapy was generally well tolerated with limited grade 3 toxicity. Two of three reports of grade 3 toxicity occurred with concurrent treatment. Due to the potential radiosensitizing properties of CDK 4/6 inhibitors, it may be prudent to hold combined treatment when clinically feasible. Further study is needed to validate these results.

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P1-10-06

Carcinoma en Cuirasse Secondary to Locally Advanced Breast Carcinoma: a case report

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Introduction & Objective This report highlights an unusual presentation of skin metastasis of inflammatory breast cancer that resembles a rare condition called Carcinoma en Cuirasse (CeC). CeC was first described by anatomist Alfred Velpeau in 1838 when he observed how the coalescing nodules and diffuse sclerodermoid induration found on the chest and abdomen in CeC resembled the medieval steel breastplate or a cuirasse. **Case Presentation** A 62-year-old female presented to the emergency department for evaluation of a palpable left breast mass and concurrent skin lesions for the past 5 months. Based on the erosion of the nipple, chest CT, as well as core needle and skin biopsy, a diagnosis of stage IV (cT4d, cN3, cM1) ER+, PR-, HER2/neu- advanced/ inflammatory breast carcinoma was made. The patient underwent a 20-week course of neoadjuvant chemotherapy followed by 25 treatments of neoadjuvant external beam radiotherapy (EBRT) with a total dose of 5000cGy to the left breast and the regional lymph node due to disease progression after 4 cycles of neoadjuvant chemotherapy. She proceeded to bilateral modified radical mastectomy and bilateral lymph node involvement was found, and later disease progressed with skin involvement outside the EBRT treatment field. Additional 25 treatment of palliative radiotherapy was utilized with another 5000cGy, followed by 2 months of chemotherapy to provide better palliation and quality of life. Upon completion of therapy, a unique skin metastasis pattern was noticed. Shortly afterward the patient passed away from severe sepsis secondary to multiple wounds infected by drug-resistant *Pseudomonas aeruginosa* followed by *Clostridium difficile* colitis. **Conclusion** This case shows clinical characteristics of Carcinoma en Cuirasse and provides important considerations for more research to be done to highlight the unique pattern of skin metastasis following radiation and the potential use for radiation to treat chemotherapy-resistant skin metastasis from recurrent invasive breast carcinoma.

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Chung-Tang Liu, n/a: No financial relationships to disclose

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P1-10-07

Role of postmastectomy radiation therapy in breast cancer patients according to pathologic nodal status after neoadjuvant chemotherapy

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Purpose: The role of post-mastectomy radiation therapy (PMRT) in breast cancer patients after neoadjuvant chemotherapy (NAC) is highly controversial. This study aimed to evaluate the impact of PMRT according to pathologic nodal status. **Methods and Materials:** We retrospectively reviewed 682 patients with clinical stage II-III breast cancer who underwent NAC and mastectomy from 2013 to 2017. Of total, 596 (87.4%) received PMRT and 86 (12.6%) did not. We investigated the relationship amongst locoregional recurrence-free survival (LRRFS), disease-free survival (DFS), overall survival (OS), and various prognostic factors. Subgroup analyses to identify the patients who may benefit from PMRT were also performed. **Results:** The median follow-up duration was 67 months. In ypN+ patients (n = 368, 51.2%), PMRT showed significant benefit for LRRFS, DFS, and OS (all $p < 0.001$). Based on multivariate analysis, histologic grade (HG) III (hazard ratio [HR] = 3.67, $p = 0.002$), lymphovascular invasion (LVI) (HR = 2.38, $p = 0.045$), and ypN2-3 (HR = 2.37, $p = 0.02$) were identified as significant risk factors for poor LRRFS. In ypN1 patients with more than two factors among (i) luminal subtype (ii) HG I-II and (iii) absence of LVI, PMRT showed no significant difference in LRRFS ($p = 0.18$). In ypN0 patients (n = 351, 48.8%), PMRT was not significantly associated with LRRFS, DFS, and OS. However, PMRT showed better LRRFS in triple-negative breast cancer (TNBC) subtype ($p = 0.04$). **Conclusion:** PMRT had a high impact on treatment outcomes in patients with residual lymph nodes following NAC and mastectomy. Among the ypN0 patients, PMRT may be beneficial only in the TNBC subtype.

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P1-10-08

Incidence of rib fracture following treatment with proton therapy for breast cancer

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Purpose: To determine the rate of rib fracture in a cohort of patients with breast cancer treated with proton therapy and enrolled on a prospective registry. In series investigating photon therapy for breast cancer, the rib fracture rate ranges from 0.3-13% Methods: From a prospective database, we identified patients treated with proton therapy for breast cancer at our institution between January 1, 2012 and December 31, 2020. Clinical and dosimetric data was extracted from the electronic medical record. The cumulative incidence method assessed rib fracture rate; the Fine-Gray test statistic assessed prognostic significance select variables. Results: 225 patients were identified, 223 women and 2 men. Median age at the time of radiation was 57.8 years (range, 25 – 87). 26% of patients were black, 69% white and 5% were other races or race not disclosed. 5% were Hispanic. 74% of patients had left-sided breast cancer, 5% bilateral, and 21% right-sided. DEXA scan was normal in 20%, showed osteopenia in 34%, osteoporosis in 6%, and not performed in 40%. 57% of patients received antiendocrine therapy with an aromatase inhibitor. For 16% of patients, the breast +/- internal mammary nodes (IMN) were treated, while 32% underwent proton therapy to treat the breast and comprehensive regional lymphatics. 1% of patients had chest wall +/- IMN treated, while 51% underwent proton therapy to treat the chest wall and comprehensive regional lymphatics. 41% of patients were treated with passive scatter proton therapy (n=92); 52% of these had mastectomy. 58% of patients received treatment with pencil beam scanning (PBS) proton

therapy (n=131); 53% of these had mastectomy. A combination of passive scatter and PBS was used for 2 patients (1%). 85% of patients received a boost. Median follow-up was 3.1 years (range, 0.2 – 9.1). 97% of patients had > 12 months of follow-up. The 3 year cumulative incidence of in-field rib fracture was 3.7% (95%CI: 1.6%-7.1%). In total, 8 patients developed in-field rib fractures, one symptomatic and 7 identified incidentally on surveillance imaging, for a 0.4% rate of symptomatic rib fracture. Median time from completion of radiation to identification of rib fracture was 1.8 years (range, 0.4-7.4 years). Rib fractures occurred within 2.2 years from radiotherapy completion for seven of the eight patients who experienced this side effect. Three patients developed rib fractures outside of the radiation field, for a cumulative incidence of out-of-field rib fracture of 0.9% (95%CI: 0.2-3.0%). No variables were associated with rib fracture on univariate analysis. Of those with in-field rib fractures, 3 had low and 3 had normal bone density while 2 had not undergone testing; of those with out-of-field rib fractures, 2 had osteopenia and 1 did not have testing. Conclusions: Although a proton beam has higher biological dose deposition at end-of-range than the assumed constant RBE=1.1, the 3 year rate of any in-field rib fractures in our series remains low at 3.7%, with a 0.4% rate of symptomatic rib fracture. Contouring ribs as an OAR and establishing a dose constraint warrants further investigation as a means to maintaining a low rate of rib fracture with proton therapy.

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AQP4 inhibition prevents cytotoxic edema of AQP4+ astrocytes but promotes tumor growth of AQP4+ breast cancer brain metastasis

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Brain edema is a complication of radiation used to treat brain metastasis (BM) in which the brain parenchyma accumulates fluid and ions, often leading to the suspension of systemic anticancer treatment. While brain edema is often attributed to disruption of the Blood Brain Barrier (BBB), RTx induces cytotoxic-edema, a premorbid cellular process whereby extracellular Na⁺ and other cations enter into neurons and astrocytes and accumulate intracellularly, resulting in osmotic expansion of the cells and necrotic cell death. Aquaporin 4 (AQP4) is a main regulator of osmotic expansion (water intake) in astrocytes and we have shown that RTx upregulates AQP4 in astrocytes and leads to astrocytic swelling in vitro. However, whether pharmacological modulation of AQP4 could be used to prevent cytotoxic brain edema in RTx-treated BM and its impact on metastatic tumor progression remains unknown. Goal: To determine if the FDA-approved drug Topiramate (TPM), an anti-epileptic drug able to inhibit AQP4) can prevent astrocytic swelling in vitro, reduce RTx-induced brain edema and modulate brain metastatic progression. Results: Electron microscopy of brain cortex from mice treated with 35 Gy RTx showed acute astrocytic end-feet swelling and increase in AQP4 expression compared with non-irradiated mice. A single 8 Gy dose increased astrocytic cell area of human astrocytes by 4.8 fold compared with non-irradiated cells 24 h after RTx. This increased cell-swelling did not result from senescence-associated cellular hypertrophy, as staining of senescent β -galactosidase positive (SA- β -Gal+) cells showed that Rtx-induced astrocytic area only increased significantly in non-senescent (SA- β -Gal- cells). shAQP4s reduced AQP4 levels by 60% and 50%, respectively, and significantly reduced RTx-induced

astrocytic swelling. Since there are no FDA-approved AQP4 inhibitors, we tested whether the AQP4-blocking function of TPM could be sufficient to prevent cytotoxic edema, prevent BBB dysfunction and protect from necrotic cell death in vitro. TPM pretreatment did not alter radiation-induced ERK1/2 or AKT activation (a known maker of radioprotection) in astrocytes, but TPM decreased radiation-induced PARP-cleavage, pP38 and pJNK levels. TPM prevented loss of Trans-electric epithelial resistance (TEER) of Rtx-treated astrocytes, but was not able to protect astrocytes from ultimate cell death. Immunohistochemical analysis of a cohort of breast cancer BM showed heterogeneous AQP4 expression in cancer cells ranging from 1.6% to 91% AQP4+ tumoral areas and from 0.6% to 86.9% in stroma. AQP4 inhibition using shRNAs decreased proliferation and survival of AQP4 + 231BR, and EO711 cells in vitro. However, TPM did not alter survival of AQP4+ or AQP4- cells in vitro, suggesting that while AQP4 expression is important for survival of AQP4+ cells in vitro, the inhibition of AQP4 function by TPM is not sufficient to decrease their growth. To determine if TPM could decrease brain edema without negatively impacting tumor progression, female NSG mice were injected intracardially with JmT1BR3 AQP4-cells and ten days later randomized to (1) RTx + vehicle, (2) RTx + TPM (2 days prior to irradiation), (3) Non-RTx + vehicle, and (4) Non-RTx + TPM. TPM decreased brain-water content (a marker of brain edema) in irradiated mice as compared with vehicle-treated mice, without alteration of metastatic burden 21 days post-injection. However, a similar study using AQP4+ E0711 cells in C57Bl6 mice showed TPM was less effective in decreasing brain water content and resulted in a significant increase in extracranial metastatic tumor burden, suggesting that TPM can promote tumor progression by non-tumor intrinsic mechanisms. Conclusions: while TPM shows promise in preventing RTx-induced brain edema, our results show a potential pro-tumorigenic mechanism for TPM that warrants further investigation.

Disclosure(s):

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5:00 PM - 6:15 PM

P1-10-10

Radiation Treatment Patterns for Elderly Women with Breast Cancer Brain Metastases

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Background Breast cancer is the second most common cause of brain metastases (BM). Despite increasing incidence of BM in elderly patients, there is limited data on the optimal management of BM in this age group. In this study, we assessed the survival outcomes and treatment patterns of elderly breast cancer patients with BM (≥ 65 yo) treated at our institution and compared them to younger patients. **Methods** An IRB-approved single-institutional review of biopsy-proven breast cancer patients with BM treated with 1 to 5-fraction stereotactic radiation therapy (SRT) from 2015 to 2020 was performed. Primary endpoint was intracranial progression free survival (PFS) defined as time interval between end of SRT to date of first CNS progression. Secondary endpoints were overall survival (OS) from end of SRT, and radiation treatment patterns. Kaplan-Meier estimates, and Cox proportional hazard regression method were used for survival analyses. SPSS v26.0 was used for statistical analysis and p -value < 0.05 was considered significant. **Results** A total of 115 metastatic breast cancer patients with BMs were included of which $N=29$ were ≥ 65 yo and $N=86$ were < 65 yo. They received a total of 43 and 143 courses of stereotactic linac-based radiation therapy (RT) respectively to a mean number of 4.3 BM lesions (range 1-22). Median age at RT was 70 years (range 65-84) compared to 50.5 years (31-64) in younger patients. About 55.2% of elderly patients were ER/PR positive/Her2 negative (vs 24.4% in younger cohort), 31% were Her2 positive (vs 41.9%) and 13.8% were triple negative (vs 33.7%). Among patient characteristics, there was significant difference among elderly and young patients in hormone receptor status ($p = 0.016$); CNS only oligometastatic disease (0% vs 11.2%, $p = 0.005$); and the presence of extracranial disease at SRS (97.7% vs 79.7%, $p < 0.001$). There was no significant difference between the two age groups in Karnofsky performance score (KPS) (62.7% vs 45.5% with $KPS \leq 80$, $p = 0.131$), number of brain lesions treated (23.2% vs 30.1% with ≥ 5 BMs, $p = 0.445$), number of patients receiving prior whole brain radiotherapy (WBRT) (10.3% vs 19.8%, $p = 0.062$), surgery (23.2% vs 30.1%, $p = 0.592$), systemic therapy (including chemotherapy, targeted therapy and endocrine therapy) after SRT (86% vs 86.7%, $p = 0.543$), and salvage WBRT (10.3% vs 19.8%, $p = 0.134$). Median OS after RT was poorer in patients ≥ 65 yo compared to younger patients (7.9 months vs 14.4 months, $p = 0.020$), while intracranial PFS from RT was similar (8.5m vs 6.5m, $p = 0.345$). The rates of freedom from neurological death and leptomeningeal disease (LMD) at 1 year were similar between the two groups (83.3% vs 87%, $p = 0.780$ and 87.6% vs 73.3%, $p = 0.627$, respectively). On univariate analysis, significant predictors of survival were age ≥ 65 yo (hazard risk, HR = 1.56), $KPS < 80$ (HR = 1.69), extracranial progression at RT (HR = 2.44), systemic therapy after RT (HR = 0.28) and LMD (HR = 1.57). On multivariate analysis, age was not a significant factor for survival after adjusting for KPS, extracranial progression and systemic therapy. **Conclusions** Although elderly women had poorer OS than younger women, OS was similar after adjusting for KPS, extracranial progression and systemic therapy; and there was no difference in rates of intracranial PFS, neurological deaths and LMD in the different age groups. This study suggests that age alone may not play an independent role in treatment-selection and outcomes for breast cancer patients with BMs and personalized decision making including other clinical factors

should be considered. Future studies are warranted to assess neurocognitive outcomes and other radiation treatment toxicities in elderly patients.

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P1-10-11

Optical stimulated luminescence dosimeters for skin dose measurements during accelerated partial breast brachytherapy: In vivo dosimetric validation and clinical outcomes

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BACKGROUND:

The role of multi-lumen catheter devices in the delivery of high dose rate (HDR) brachytherapy for adjuvant accelerated partial breast irradiation (APBI) for women with DCIS or early-stage breast cancer has been well established. In vivo dosimetry (IVD) using optically stimulating luminescence dosimeters (OSLD) is a feasible way to detect applicator instability that may cause translational and rotational inaccuracies during HDR brachytherapy delivery. Herein, we evaluate the accuracy and effectiveness of IVD to improve patient outcomes following APBI brachytherapy using the Strut Adjusted Volume Irradiation (SAVI) device.

METHODS:

Single-institution cohort study piloting the use of OSLD on the patient's skin during HDR brachytherapy APBI to assess the estimated maximum skin dose (skin D_{max}) and the achievable accuracy of OSLD for skin D_{max} measurements. Women treated with SAVI-based APBI between November 1, 2018 and October 1, 2021 were eligible to enroll in our study. All patients met the American Society for Radiation Oncology "suitable" or "cautionary" criteria and were treated according to the American Brachytherapy Society consensus treatment planning guidelines. A SAVI preplan was created to estimate the probable point of skin D_{max}. During CT simulation, a radiopaque marker was placed on the skin for visualization during treatment planning. Correction factors were applied to account for the OSLD tissue-air interface that is not present in the TG-43 expected dose calculations. Measured and calculated IVD doses were

analyzed to assess agreement and cause for discrepancies found. Breast phantom IVD measurements repeated seven times with two independent dose points were analyzed to assess the best accuracy achievable under ideal conditions.

RESULTS:

We enrolled 41 patients with an average age of 68 years. Table 1 details the brachytherapy treatment delivery and dosimetry data. Higher skin Dmax as a percentage of the radiation prescription was associated with the occurrence of breast volume loss noted on subsequent clinical breast exams (OR 1.84 per each 5% increase in skin Dmax; 95% CI 1.21 – 3.32; p=0.016). The graphically estimated skin Dmax threshold was 80% with all cases of noted breast volume loss occurring above this threshold. The overall level of achievable IVD accuracy was $\pm 3.32\%$ based on breast phantom measurements. Under ideal conditions, all measurements were in the $\pm 7\%$ range. Three of 14 phantom measurement exceeded the 6% discrepancy range. Clinical IVD measurements detected 5 true positive cases (12.2% of cohort) that required intervention due to rotations in the SAVI applicator. For a $\pm 7\%$ tolerance criteria, 90.2% of the patients tested passed IVD. Of the eight patients that failed at the 7% level, IVD detected 3 OSLD placement errors, 2 rotational discrepancy cases, and 1 large air-gap at the point of measurement.

CONCLUSIONS:

Accuracy and reproducibility are imperative tenets of HDR brachytherapy APBI. IVD utilizing OSLD is an effective method for detecting treatment set-up and delivery errors for patients receiving SAVI-based APBI with dose accuracy within $\pm 3.32\%$. Errors requiring intervention due to SAVI device rotation were detected in 12.2% of our cohort, and these errors would have likely gone undetected without IVD. Using OSLD as IVD to measure skin Dmax doses that may increase the risk of breast cosmetic defects should be investigated further.

Table 1. Brachytherapy treatment delivery and dosimetry data

SAVI Applicator Size	Total, no. (n=41)
6-1	16
8-1	23
10-1	2
Skin bridge thickness (mm)	
Mean	17.1
Median	15.6
Range	2.1 – 57.1
Air or seroma percentage of cavity (%)	
Mean	4.0
Median	3.0
Range	0.1 – 13.2
Treatment regimen	
34 Gy / 10 fractions BID	34
33.3 Gy / 9 fractions BID	2
32 Gy / 8 fractions BID	5
PTV-Eval Volume* (cc)	
Mean	73.8
Median	76.2
Range	44.1 – 105.1
PTV-Eval V100 (%)	
Mean	96.7
Median	96.9
Range	94.5 – 99.7
PTV-Eval V150 (cc)	
Mean	35.9
Median	36.6
Range	23.3 – 45.9
PTV-Eval V200 (cc)	
Mean	17.7
Median	18.3
Range	12.6 – 20.0
Skin Dmax as % of prescription (%)	
Mean	77.0
Median	80.7
Range	26.8 – 107.4
Rib Dmax as % of prescription (%)	
Mean	78.2
Median	85.8
Range	24.6 – 122.0
*Percent dose discrepancy	
Mean	-1.02%
Median	-0.54%
Range	-27.7% to 29.9%

*PTV-Eval is a uniform 10 mm expansion on the CTV with exclusion of PTV within 5 mm of skin or chest wall.

+Percent dose discrepancy refers to difference in dose between APBI plan calculations and IVD measurements.

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5:00 PM - 6:15 PM

P1-10-12

AI-based cardiac sub-structures segmentation for safer radiotherapy planning

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Purpose

Whilst radiotherapy increases cure rates in breast cancer, lung cancer, among others, it may also involve some cardiac exposure, which in turn may increase the risk of different heart diseases. The heart is a complex anatomical organ that involves many different structures making it difficult to contour cardiac sub-structures reproducibly. Contouring, especially for these cases, suffers from inter- and intra-expert variability while being time consuming. Cardiac atlases have been developed to aid in the delineation of cardiac substructures. However, these methods have many shortcomings, including the inability to overcome variations in patient anatomy. In this study, a deep learning based commercial solution for automatic OAR delineation was trained following international guidelines for heart substructures delineation and tested on an unseen cohort of lung and breast patients to evaluate its clinical acceptability.

Methods

ART-Net, a CE-marked, FDA-cleared anatomically preserving deep-learning ensemble architecture for automatic annotation of OAR was evaluated using data of 20 breast/lung patients from 2 centers. Automatic annotation of 27 different structures (Ventricles (left and right), atria (left and right), left ventricle (anterior, apical, inferior, lateral, septal), LAD coronary (mid, proximal, distal, total), circumflex coronary (distal, proximal, total), RCA (distal, mid, proximal, total), coronary sinus, left main coronary artery, ascending aorta, pulmonary arteries, vena cava inferior, vena cava superior and the heart) was performed and submitted to 2 experts across 2 centers for qualitative evaluation. Contours were scored as A/acceptable, B/ acceptable after minor corrections, and C/ not acceptable for clinical use. To avoid any bias, experts were blind to whether the contour were manually, or AI delineated. The DSC between automatic and manual (ground truth) contours of the heart sub-structures were evaluated and compared with interobserver variability from the literature [1,2] using average and min DSC scores.

Results

Automatic contours were generated in a mean time of 0.5s per scan slice. Out of the 27 structures, 20 were considered clinically acceptable in the qualitative study. In the inter-expert variability study, 12 structures passed the test successfully using initial acceptance criterion over an acceptable sample size and 9 other structures demonstrated performances above the minimal threshold of inter-expert variability, sometimes on smaller datasets due to lack of manual data. Overall, 16 structures were included in the final model. 13 structures were considered clinically acceptable in 100% of the cases with AI contours rated at the same level as manual contours. For the other 3 structures (coronary sinus, left main coronary artery and vena cava inferior), the performance of the AI contours was slightly below that of the manual contours (within 3.4% difference), with the least performing structure being the coronary sinus (84% for AI vs 87% manual).

Conclusion

We show first results for the evaluation of AI-based auto-contouring tool for annotation of the substructures of the heart. The results show very good clinical acceptance, highlighting the high usability of the commercial tool for cardiac cases and its clinical implementation feasibility. The use of this AI tool can facilitate and accelerate future research studies investigating relationships between substructure doses and cardiac outcomes. Future work will include improvement of the sub-structures (mid, proximal, distal) and a retrospective meta-analysis to assess heart sub-structures degree of importance in terms of toxicity.

References:

1. Lee J., et al. Development of delineation for the left anterior descending coronary artery region in left breast cancer radiotherapy: An optimized organ at risk. *Radiother Oncol.* 2017
2. Duane F, et al. A cardiac contouring atlas for radiotherapy. *Radiother Oncol.* 2017

Table 1 - Quantitative and qualitative results of the evaluation

Structure	Inter-expert Range DSC	ART-Plan	
		Mean DSC	Percentage A+B
Ascending aorta	[0.72;0.91] ¹	0.82	100%
Circumflex coronary total	[0.19;0.63] ¹	0.2	79%
Circumflex coronary distal	[0.04;0.65] ²	0.18	75%
Circumflex coronary proximal	[0.06;0.31] ²	0.22	79%
Coronary sinus	NA	0.41	84%*
Heart	[0.93;0.96] ¹	0.95	100%
Lad coronary total	[0.15;0.67] ¹	0.5	97%
Lad coronary distal	[0.03;0.39] ²	0.11	80%
Lad coronary mid	[0.23;0.53] ²	0.4	97%
Lad coronary proximal	[0.34;0.72] ²	0.4	95%
Left atrium	[0.78;0.93] ¹	0.84	100%
Left main coronary artery	[0.09;0.76] ²	0.3	93%
	[0.17;0.69] ¹		
Left ventricle	[0.89;0.94] ²	0.9	100%
	[0.84;0.97] ¹		
Left ventricle anterior	[0.6;0.78] ²	0.58	100%
Left ventricular apical	[0.65;0.78] ²	0.55	100%
Left ventricle inferior	[0.5;0.74] ²	0.56	100%
Left ventricle lateral	[0.67;0.77] ²	0.68	100%
Left ventricle septal	[0.45;0.76] ²	0.64	100%
Pulmonary arteries	[0.66;0.96] ¹	0.78	100%
Rca total	[0.2;0.69] ¹	0.19	84%
Rca distal	[0.3;0.55] ²	0.23	75%
Rca mid	[0;0.31] ²	0.19	85%
Rca proximal	[0;0.46] ²	0.28	82%
Right atrium	[0.75;0.93] ¹	0.85	100%
Right ventricle	[0.81;0.92] ¹	0.86	100%
Vena cava inferior	[0.54;0.9] ¹	0.7	97%
Vena cava superior	[0.6;0.93] ¹	0.54	100%

Heart sub-structures evaluated quantitatively with mean DSC compared to a range of DSC found in international guidelines and qualitatively as A or B (i.e. considered clinically acceptable). Highlighted are all structures that met the acceptance criterion of reaching a percentage of at least 85% of A or B, or that fell within the DICE range of interobserver variability found in the literature.

Disclosure(s):

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5:00 PM - 6:15 PM

P1-10-13

Economic comparison of standard external beam whole breast (WBI) versus accelerated partial breast irradiation (ABPI) in postmenopausal women with early-stage breast cancer. Results from the French SHARE randomized trial

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Purpose: The economic evaluation reports the incremental cost utility ratio and budget impact of APBI vs standard external beam WBI for the treatment of post-menopausal women with early stage breast cancer.

Methods and materials: We compared 488 women in the standard arm (1 fraction per day delivered 5 days per week over 3 or 6/6.5 weeks) to 490 women in the ABPI arm (ten fractions delivered twice per day over one week). We took the perspective of the healthcare system, a 3-year time horizon; the outcomes were quality adjusted life years (QALYs). QALYs were calculated from the EQ5D5L questionnaires at baseline, 3 months, 6 months, 12 months and yearly after irradiation; scores were converted into utilities using the French value set and QALYs computed with the area under the curve approach. Measures of within-trial use of hospital resources were based on routine hospital data via patient-level information. We used the itemized and DRG cost data from each individual patient. Transportation costs were added in a sensitivity analysis. A 2.5% discount rate was applied to costs and QALYs. An incremental analysis with differences in costs and QALYs was performed to calculate the cost utility ratio. Bootstrapping was used to quantify uncertainty on the joint distribution of costs and outcomes, and 1,000 paired estimates of mean differential costs and QALYs were reported on a cost-effectiveness plane. A budget impact analysis based on incidence of breast cancer estimates was added. All analyses followed the intent to treat principle.

Results:

Cost and utilities were available for the entire population. Costs and QALY results are presented in table 1. The 2 925 € (95% IC, -3 364 €; - 2 452 €) significant difference in total costs favoring ABPI was driven by the difference in radiotherapy costs and partly by lower transportation costs. No significant difference was found in QALYs.

Figure 1 shows the uncertainty of the joint distribution of costs and QALYs. All replication are in the lower half of the plane indicating that ABPI is cost saving with QALYs distributed on each side of the vertical axis indicating equal distribution of QALYs.

would be eligible for treatment with ABPI. The uptake of ABPI for 16% of these women would result in a 16 million€ cost saving.

Conclusions

At three years, ABPI for the treatment of postmenopausal women with early-stage breast cancer was found to be cost saving, with no difference in outcome measured by QALYs.

Table 1:

	ABPI N=490	Standard of care N=488	P value
Radiotherapy (€)	2 369 (±1 300)	4 323 (±1 228)	< 0.001
Transportation (€)	657 (± 854)	1 663 (± 1 312)	< 0.001
Subsequent admissions(€)	180 (± 1 494)	145 (± 1 137)	0.678
Total 3-year costs (€)	3 206 (± 2 465)	6 131 (± 2 315)	< 0.001
QALYs	2,383	2,377	0.964

Figure 1:

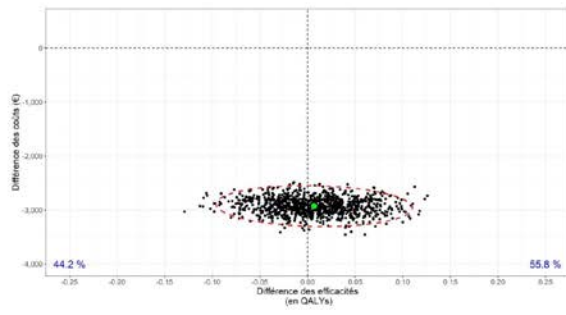
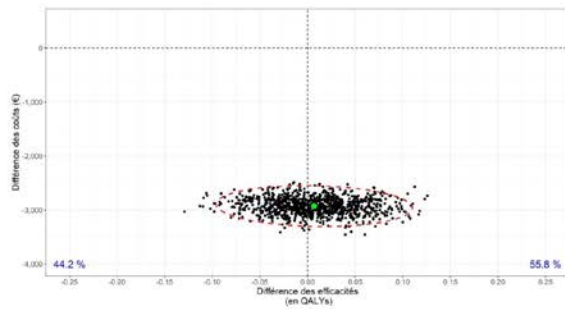


Figure 1:



Disclosure(s):

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5:00 PM - 6:15 PM

P1-10-14

Higher radiation dose to the heart in left sided breast cancer; anatomy versus dosimetry.

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Abstract: Background: There is assumption that omitting the internal mammary chain radiotherapy (IMC RT) in patients with breast cancer (BC) will significantly reduce the cardiac exposure for all patients regardless the cardiac anatomy of each patient. Aim: to evaluate the impact of IMC RT on the dose received by the heart and its chambers in patients with favorable versus unfavorable cardiac anatomy. Patients and methods: CT scans were obtained of 20 patients with left-sided BC, 10 with favorable and 10 with unfavorable cardiac anatomy. Three plans were generated for each patient, one treating only the breast with tangents, and one treating the breast and IMC with wide photon tangents, and one treating the breast and IMC to 50Gy with photon tangent fields and a matching medial electron field. Dose volume histograms (DVHs) were generated for the heart and chambers. The equivalent uniform doses (EUDs) were calculated for each DVH, and the mean EUDs for plans with unfavorable and favorable cardiac anatomy were compared using a two-sided two-sample T-test Results: The mean dose received by the heart from plans with tangents plus IMC fields in patients with favorable cardiac anatomy was significantly lower than that received from plans with tangents only or wide tangents in patients with unfavorable anatomy ($P < .0001$). The average EUD for plans with tangents and IMC fields in the favorable group was 16 Gy (SD = 4.5) as compared to 36 Gy (SD = 3.6) and 37 Gy (SD = 5.1) for plans with tangents only and wide tangents in the unfavorable group, respectively ($P < .0001$). The doses to the right ventricle were not significantly different. Conclusions: Treatment plans should be individualized based on the cardiac anatomy of each patient.

Disclosure(s):

Mohamed Alm El-Din, MD: No financial relationships to disclose

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P1-10-15

Conscious sparing of contralateral thyroid lobe in Ca Breast patients receiving post mastectomy radiotherapy by IMRT technique – A single institution dosimetric study

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Concious sparing of contralateral thyroid lobe in Ca Breast patients receiving post mastectomy radiotherapy by IMRT technique – A single institution dosimetric study

Purpose/Objective(s):

The purpose of this paper is to report the dosimetric effects of conscious sparing of contralateral lobe of thyroid gland in carcinoma breast patient receiving locoregional radiation by tangential beam Intensity Modulated radiotherapy technique.

Materials/Methods:

Treatment plans of 20 Ca Breast patients , who received post mastectomy adjuvant locoregional radiotherapy, were evaluated. Since October 2021 we adopted a department protocol of conscious sparing of contralateral thyroid in breast radiotherapy. 10 of these had conscious sparing of contralateral thyroid (group A) whereas 10 of old plans were evaluated when C/L thyroid were not given constraints & are being passively spared due to location on contralateral/non treatment side of neck (group B). Treatment planning was done using tangential beam (6 MV) IMRT in Eclipse 13.7 TPS in all of these patients. All of these patients received treatment to chest wall & SCF. RTOG contouring guidelines were followed in all the patients. Prescription Dose was 40Gy in 15# for both groups. The best treatment plans were selected ensuring 95% PTV dose coverage and acceptable dose to OARs. Uniform contouring, plan optimization & evaluation protocols were followed for all of these patients.

Results:

The mean thyroid volume in group A is 4.30cc & in group B is 3.99cc which is not statistically

different (P value -0.639)

The mean dose of thyroid in group A is 7.98Gy whereas in group B it is 17.00Gy which is spastically significant (P value – 0.000003).

Comparison of mean dose to contralateral lobe (in Gy) between the two groups

Groups No. Mean ± SD 't' value P value

Thyroid dose with constraint 10 7.98±1.46 -6.702, df=18 0.000003*

Thyroid dose without constraint 10 17.00±3.99

Unpaired 't' test applied. P value = 0.000003, Significant

Conclusion:

OARs present on contralateral side are passively spared due to the location. This often results in a tendency of not actively prescribing constraints to these. This study emphasizes that conscious sparing of contralateral Thyroid lobe can further reduce the dose to significant levels. This reduction can preserve thyroid function further. Further clinical trials are required to corroborate this dosimetric gain with clinical thyroid function preservation.

Groups	No.	Mean ± SD	't' value	P value
Thyroid dose with constraint	10	7.98±1.46	-6.702, df=18	0.000003*
Thyroid dose without constraint	10	17.00±3.99		

Unpaired 't' test applied. P value = 0.000003, Significant

Disclosure(s):

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P1-10-16

Cardiac conduction system exposure with modern radiotherapy techniques for breast cancer irradiation

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Introduction: Exposition of cardiac conduction system during breast radiotherapy has never been studied, despite increasing use of intensity modulated radiotherapy which expose larger volume to low dose bath. We evaluated conduction node exposure during breast irradiation with volumetric modulated arctherapy (VMAT) and estimated the potential dosimetric benefit with intensity modulated protontherapy (IMPT). Materials and methods: Atrioventricular (AVN) and sinoatrial (SAN) nodes were retrospectively delineated according to published guidelines on the simulation CT scans of twelve breast cancer patients having undergone conserving surgery and adjuvant locoregional VMAT. IMPT treatment was re-planned on the simulation CT scans for all breast cancer patients. Mean and maximum doses to the SAN and the AVN were retrieved and compared. Correlation coefficients were calculated between doses to the SAN or the AVN and to the whole heart. Results: Average mean doses to the SAN and to the AVN were 2.8 Gy and 2.3 Gy respectively for left-sided irradiation and 9.6 Gy and 3.6 Gy respectively for right-sided irradiation. Average maximum doses to the SAN and to the AVN were 3.5 Gy and 2.8 Gy respectively for left-sided irradiation and 13.1 Gy and 4.6 Gy respectively for right-sided irradiation. IMPT significantly reduces doses to conduction nodes. Correlations between doses to the SAN or the AVN and the whole heart were usually significant. Conclusion: SAN and AVN can be substantially exposed during breast VMAT, especially for right-sided irradiation. Cardiotoxicity studies evaluating conduction node exposure might define dose constraints and criteria for additional cardiac sparing techniques, such as respiratory techniques or proton therapy, which could be beneficial to patients with underlying rhythmic or conduction disorders.

Disclosure(s):

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P1-10-17

Axillary radiotherapy in selected patients with a preoperative diagnosis of lymph node involvement is a safe alternative to axillary lymph node dissection.

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Axillary radiotherapy in selected patients with a preoperative diagnosis of lymph node involvement is a safe alternative to axillary lymph node dissection.

Introduction

Axillary lymph node dissection (ALND) is associated with significant morbidity. Randomised data [1,2] suggest that axillary radiotherapy (RT), or no further axillary treatment beyond sentinel node biopsy (SNB) may be safe. There are very few studies to guide the management of preoperatively diagnosed lymph node metastases either in the context of neoadjuvant

chemotherapy (NACT) or direct to surgery. The current UK recommendation is for ALND. In 2015 our policy changed to RT for carefully selected patients after MDT discussion. These data look at axillary recurrence for those patients having axillary RT

Methods

Data were retrospectively collected on patients with preoperatively diagnosed lymph node metastases between January 2016 and December 2020. Patients undergoing surgery with a curative intent were included. The decision to offer axillary RT was made in the MDT based on clinical and radiological findings and the burden of disease in the axillary sample. Axillary recurrence was defined as disease recurring in the axilla with no distant disease.

Results

Data were collected on 132 patients. Demographics and tumour status are outlined in Table 1. 55% of patients had neoadjuvant chemotherapy with a 52% path CR in the axilla. Table 2 gives the results for the axillary RT group. During the same time period 25 patients had ALND. Of those 2 (8%) had isolated LN recurrence. 18 patients had axillary RT following positive SLN after NACT. There was a single patient with axillary recurrence in this group.

Conclusion:

In the absence of randomised data to guide practice, these data show that in selected patients axillary radiotherapy is safe after axillary node sampling. The decision should be based on axillary burden, tumour biology, MDT and patient discussion. We await with interest the results of the Alliance A011202 trial to guide practice in patients having NACT in N1 disease.

[1] Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJ, Mansel RE, Cataliotti L, Westenberg AH, Klinkenbijn JH, Orzalesi L, Bouma WH, van der Mijle HC, Nieuwenhuijzen GA, Veltkamp SC, Slaets L, Duez NJ, de Graaf PW, van Dalen T, Marinelli A, Rijna H, Snoj M, Bundred NJ, Merkus JW, Belkacemi Y, Petignat P, Schinagel DA, Coens C, Messina CG, Bogaerts J, Rutgers EJ. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. *Lancet Oncol.* 2014 Nov;15(12):1303-10. doi: 10.1016/S1470-2045(14)70460-7.

[2] Giuliano, A.E.; Ballman, K.; McCall, L.; Beitsch, P.; Whitworth, P.W.; Blumencranz, P.; Leitch, A.M.; Saha, S.; Morrow, M.; Hunt, K.K. Locoregional Recurrence After Sentinel Lymph Node Dissection With or Without Axillary Dissection in Patients With Sentinel Lymph Node Metastases: Long-term Follow-up From the American College of Surgeons Oncology Group (Alliance) ACOSOG Z0011 Randomized Trial. *Ann. Surg.* 2016, 264, 413–420

Table 1: Demographics and tumour status

	n / mean	%
Number of patients	132	
Mean age	62.38	
Grade 1 and 2	65	49.24
Grade 3	64	48.48
ER positive	89	67.43
HER2 positive	25	18.94
NACT	73	55.30
Mean size	30.77	

Table 2: Patients having Axillary RT

	n / median	%
Number of patients	77	
Nodes taken at SLN	4	
Nodes involved	1	
Axillary Recurrence	2	2.60

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Duncan Wheatley, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing)

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5:00 PM - 6:15 PM

P1-10-18

Impact of Adjuvant Chemoradiation on cardiopulmonary function and Quality of Life in Breast Cancer

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Aims and Objectives – To evaluate the safety of adjuvant chemo-radiation (CTRT) for breast cancer. We report the cardio-pulmonary safety and quality of life outcome of this regimen.

Methods – Stage II-III invasive breast cancer patients planned for adjuvant taxane-based chemotherapy and adjuvant radiotherapy (RT) between April 2019 to December 2020 were eligible irrespective of prior neo-adjuvant therapy. Patients received standard 3D conformal radiotherapy (40 Gy in 15 fractions over 3 weeks ± boost for breast conservation) along with the third cycle of adjuvant taxanes in a 3- weekly schedule or the eighth cycle in a weekly schedule. Troponin T, echo cardiography and pulmonary function test were done pre-RT and repeated at 6 months from RT conclusion while quality of life was evaluated pre-RT, at RT conclusion and after 6 months using EORTC QLQ C30 and BR23.

Results – Sixty patients were analysed. The median ejection fraction pre and post CTRT was 60% (p=0.177). The median value of Troponin T at baseline was 37 which decreased to 20 post CTRT (p=0.009). Of the 54 patients who underwent the PFT, the functional vital capacity (FCV) was 2.29 litres at baseline which was 2.2 litres post CTRT (p=0.375). No significant difference was seen for forced expiratory volume (FEV) at 1 second (1.86 vs. 1.82; p=0.365), FEV1/FVC (81.5 vs. 81.43; p=0.9) and diffusing capacity for carbon monoxide (DLCO) (88.3 vs. 87.6; p=0.62) at baseline and post CTRT respectively. There was a significant improvement in QOL scores for nausea, vomiting, pain, constipation, loss of appetite and hair loss post RT 6 months.

Conclusion- Patients treated with taxane-based adjuvant CTRT had stable cardio-pulmonary profile at 6 months compared to pre-RT. Quality of life scores improved after treatment for most of the domains compared to the pre-RT scores.

Table 1: Calculated scores of EORTC QLQ-C30 and BR23 scales for breast cancer patients at baseline, post CRT and at first follow up of six months.

Scales/Visit	Mean (SD)			P value baseline vs conclusion	P value Baseline Vs 6 months post RT
	Baseline	Post CRT	6 months		
QLQ-C30					
Global quality of life	72.08 (17.00))	70.97 (22.94)	76.39 (23.58)	0.752	0.287
Physical functioning	81.78 (17.99)	82.67 (18.94)	84.67 (15.05)	0.808	0.309
Role functioning	86.11 (23.20)	84.17 (22.00)	90.83 (13.87)	0.643	0.191
Emotional functioning	78.75 (24.52)	82.50 (17.94)	81.67 (16.58)	0.337	0.436
Cognitive functioning	88.05 (20.37)	89.17 (18.11)	84.72 (17.97)	0.753	0.328
Social functioning	89.72 (19.91)	86.39 (22.86)	84.17 (20.22)	0.341	0.105
Fatigue	30.00 (27.85)	28.52 (24.58)	23.33 (17.08)	0.774	0.131
Nausea/Vomiting	9.44 (13.15)	12.22 (18.88)	4.72 (14.09)	0.301	0.043
Pain	25.56 (28.03)	21.11 (23.14)	16.11 (17.62)	0.377	0.026
Dyspnea	10.00 (18.71)	11.11 (16.99)	7.78 (18.78)	0.748	0.551
Insomnia	21.11 (30.66)	18.89 (24.83)	14.44 (21.58)	0.658	0.171
Appetite loss	18.89 (24.06)	23.89 (24.62)	10.00 (18.71)	0.282	0.028
Constipation	20.00 (31.41)	15.00 (24.87)	9.44 (24.62)	0.380	0.048
Diarrhea	8.89 (16.08)	5.56 (13.95)	5.56 (17.54)	0.203	0.307
Financial problems	22.78 (32.18)	20.00 (32.59)	19.44 (30.25)	0.608	0.540
QLQ-BR23					
Body image	78.05 (27.99)	80.56 (24.96)	83.19 (23.94)	0.583	0.265
Sexual functioning	10.83 (18.37)	8.05 (13.54)	11.67 (15.74)	0.254	0.274
Sexual enjoyment	13.33 (25.45)	6.67 (13.44)	11.67 (20.19)	0.057	0.709
Future perspective	67.78 (41.15)	74.44 (32.69)	74.44 (32.69)	0.367	0.356
Systemic therapy side effects	25.95 (21.27)	23.97 (20.50)	11.90 (13.85)	0.592	0.9
Breast symptoms	10.69 (12.83)	11.11 (14.69)	12.92 (15.45)	0.871	0.383
Arm symptoms	17.96 (17.49)	14.81 (17.32)	15.00 (15.01)	0.353	0.319
Upset by hair loss	37.22 (45.14)	26.11 (38.37)	10.56 (27.78)	0.128	0.0003

All positive scores improved except cognitive and social domains while most of the negative scores except breast and arm symptoms reduced suggesting improved temporal scores.

Disclosure(s):

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Trastuzumab deruxtecan vs treatment of physician's choice in patients with HER2-low unresectable and/or metastatic breast cancer: Subgroup analyses from DESTINY-Breast04

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Background

DESTINY-Breast04 demonstrated that the HER2 targeting antibody–drug conjugate trastuzumab deruxtecan (T-DXd) significantly prolonged progression-free survival (PFS) and overall survival (OS) vs treatment of physician’s choice (TPC) in patients (pts) with HER2-low

(immunohistochemistry [IHC] 1+ or IHC 2+/in situ hybridization negative) metastatic breast cancer (mBC) in pts in the hormone receptor-positive (HR+) cohort and all pts (HR+ and HR-; median PFS, 9.9 vs 5.1 months [mo], hazard ratio: 0.50; median OS, 23.4 vs 16.8 mo, hazard ratio: 0.64; both $P < 0.0001$; Modi et al. N Engl J Med 2022). Objective response rate (ORR) with T-DXd was $\geq 50\%$ across cohorts. These subgroup analyses examine pt history and disease characteristics that may correlate with response to therapy.

Methods

N = 557 pts with centrally confirmed HER2-low mBC were randomized 2:1 to T-DXd or TPC. Randomization was stratified by HER2 status (IHC 1+ vs 2+), 1 vs 2 prior lines of chemotherapy, and HR+ (with vs without prior treatment with cyclin-dependent kinase 4/6 inhibitor [CDK4/6i]) vs HR-. With the exception of the PFS and OS analyses by prior CDK4/6i use, all other described efficacy analyses were assessed post-hoc.

Results

Benefit of T-DXd vs TPC was consistent in pts with or without prior CDK4/6i use (Table 1). Pts with high disease burden (ie, ≥ 3 metastatic sites) also benefited from T-DXd vs TPC (Table 2). There was a small subgroup (n = 22) among all pts (HR+ [n = 18] and HR- disease [n = 4]) with rapid progression prior to enrollment (disease progression within 6 mo of concluding a prior course of chemotherapy in early breast cancer). T-DXd showed responses in 7/14 (50%) pts in this subgroup vs 0/8 with TPC; this subgroup also had prolonged median PFS with T-DXd vs TPC (Table 3). Efficacy data for HER2 IHC 1+ vs 2+ and prior chemotherapy subgroups will be presented. Median OS was not reached for many subgroups (insufficient events in each group [data not shown]); however, subgroups in general showed OS benefit consistent with the primary analysis. With T-DXd, rates of interstitial lung disease/pneumonitis were similar in pts with/without prior CDK4/6i use.

Conclusions

T-DXd treatment for HER2-low mBC in the phase 3 study DESTINY-Breast04 showed consistent efficacy independent of disease burden, prior CDK4/6i treatment, or rapid progression status. ILD is an important identified risk and requires proactive monitoring and management. These data continue to support the use of T-DXd as the new standard of care across subgroups of pts with HER2-low mBC.

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Table 1. Efficacy by Prior CDK4/6i Treatment in Pts With HER2-Low Breast Cancer, HR+ Cohort

	Prior CDK4/6i		No prior CDK4/6i	
	T-DXd (n = 233)	TPC (n = 115)	T-DXd (n = 96)	TPC (n = 47)
Confirmed ORR, n (% [95% CI]) ^a	118 (50.6 [44.0-57.2])	15 (13.0 [7.5- 20.6])	56 (58.3 [47.8-68.3])	12 (25.5 [13.9-40.3])
Median PFS, months (95% CI) ^b	10.0 (8.3-11.4)	5.4 (4.0-7.8)	11.7 (9.5-17.7)	5.9 (4.3-8.2)
Hazard ratio (95% CI) ^c	0.55 (0.42-0.74)		0.42 (0.28-0.64)	

^aCI based on Clopper-Pearson method.

^bMedian PFS is from Kaplan-Meier analysis. CI for median was computed using the Brookmeyer-Crowley method.

^cHazard ratio is from unstratified Cox proportional hazards model with treatment as the only covariate.

Table 2. Efficacy by Disease Burden^a in Pts With HER2-Low Breast Cancer, ITT

	Low disease burden		High disease burden	
	T-DXd (n = 150)	TPC (n = 85)	T-DXd (n = 223)	TPC (n = 99)
Confirmed ORR, n (% [95% CI])	81 (54.0 [45.7-62.2])	13 (15.3 [8.4- 24.7])	114 (51.1 [44.4-57.9])	17 (17.2 [10.3-45.6])
Median PFS, months (95% CI)	11.4 (9.8- 16.2)	5.1 (3.1-7.3)	9.5 (7.5-10.1)	4.8 (2.9-6.9)
Hazard ratio (95% CI)	0.41 (0.30-0.58)		0.58 (0.43-0.78)	

ITT, intent-to-treat.

^aDisease burden was defined by the number of metastatic disease sites at baseline (low = 0-2; high = 3+).

Table 3. Efficacy by Rapid Progressor Status^a in Pts With HER2-Low Breast Cancer, ITT

	Rapid progression		No rapid progression	
	T-DXd (n = 14)	TPC (n = 8)	T-DXd (n = 359)	TPC (n = 176)
Confirmed ORR, n (% [95% CI])	7 (50.0 [23.0- 77.0])	0	188 (52.4 [47.1-57.6])	30 (17.0 [11.8-23.4])
Median PFS, months (95% CI)	8.2 (1.4-NE)	2.2 (0.6-NE)	9.9 (9.0-11.3)	5.3 (4.2-6.9)
Hazard ratio (95% CI)	0.38 (0.12-1.21)		0.51 (0.41-0.64)	

ITT, intent-to-treat; NE, not estimable.

^aRapid progressor status was defined as disease progression within 6 mo of concluding a prior course of chemotherapy in early breast cancer.

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5:00 PM - 6:15 PM

P1-11-03

VRN101099, Brain Permeable HER2 Kinase Inhibitor, Shows the Anti-tumor Activity in Preclinical Models of HER2-positive Cancers

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The brain is a common target organ for breast cancer metastasis, and the risk of brain metastasis is usually high for patients with HER2-positive breast cancer. While T-DXd showed positive results in HER2-positive breast cancer brain metastasis (BCBM), its activity and blood-brain barrier (BBB) permeability in active BCBM need to be further validated (TUXEDO-1 included 15 patients with active brain metastasis). Tucatinib plus Trastuzumab and Capecitabine triplet showed efficacy in patients with brain metastasis, but Tucatinib alone has

poor BBB penetration. There is still an unmet medical need for active HER2-positive BCBM. VRN101099 is a highly selective kinase inhibitor of HER2 (Eurofins scanMAX Kinase Profiling, S-score (35) of 0.01). VRN101099 has single- to double-digit nanomolar (IC50) cellular potency in HER2-dependent cancer cells, and Ba/F3 cells expressing HER2 wild type or mutations with selectivity over wildtype EGFR. VRN101099 inhibited proliferation of BT474 with 3.6 nM IC50 but HaCaT with 829.2 nM IC50. VRN101099 binds HER2 kinase by forming a covalent bond to the Cys805 and its irreversible inhibition resulted in a longer target resident time than Tucatinib, confirmed by in vitro washout experiments. Robust in vivo activity of VRN101099 was observed in HER2-positive BT474 xenograft models. Moreover, once daily oral administration of VRN101099 significantly regressed intracranial BT474 tumor, demonstrating greater efficacy than twice daily oral administration of Tucatinib. These results were well explained by the superior brain to plasma exposure of VRN101099 to Tucatinib. Also, VRN101099 showed high exposure in the target organ, the fat pad, which potentiated better clinical translation. These anti-tumor efficacies are correlated with pharmacodynamic responses, as confirmed by decreased HER2, AKT, and ERK phosphorylation. In summary, VRN101099 is a brain penetrant, orally bioavailable, irreversible, and highly selective inhibitor of HER2 with therapeutic potential in HER2-positive BCBM. These data support the clinical development of VRN101099 in HER2-driven cancers.

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Assessing the clinico-pathological characteristics of HER2 positive metastatic breast cancer patients experiencing radiologic complete response in a nationwide cohort

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Background: Up to 6% of patients (pts) with HER2 positive (pos) metastatic breast cancer (MBC) experience a radiologic complete response (rCR) to a first line of therapy, but these results mostly derive from dated and/or limited cohorts. Aim of this study was to define the clinico-pathological characteristics of HER2 positive (pos) MBC pts experiencing a rCR. Methods: Pts were selected from the database of the GIM14 study (NCT02284581) and classified according to the best radiologic response obtained to the first line chemotherapy (CT) and upon time-to-treatment-failure (TTF). rCR was defined as complete response (CR) with a TTF > 3 months. The association across variables was tested through logistic regression and their prognostic impact in terms of overall survival (OS) was estimated using the Kaplan-Meier method and compared using the log-rank test. Results: Of the 3,423 pts included in the GIM14 study, 814 had HER2 pos MBC. After exclusion of pts treated with first line endocrine therapy and/or with TTF < 3 months, 656 pts were included in the present analysis, of which 96 (14.6%) experienced a rCR. Instead, the best response was a partial response for 295 pts (45.0%), stable disease for 221 pts (33.7%), and progression for 44 pts (6.7%). Most pts (59.8%) presented de novo MBC; 379 pts (57.8%) had visceral metastases (mets), 609 pts (92.8%) did not have central nervous system (CNS) involvement and 318 pts (48.5%) had only 1 site of distant mets. Also, 445 pts (67.9%) had hormone receptor (HR) pos disease, a HER2 3+ score at immunohistochemistry (IHC) was present in 59.8% of cases versus 40.2% with HER2 2+ at IHC and in situ hybridization (ISH) + disease. Taxanes were the main CT backbone (489 pts, 74.5%), 341 pts (52.0%) had received a Trastuzumab-Pertuzumab doublet. At multivariable analysis, higher odds of experiencing a rCR were reported for presence of non-visceral mets (OR 1.87, 95%CI 1.10-3.17), low number of metastatic sites (OR 2.42, 95%CI 0.80-7.33 for 1 site only) and HER2 3+ score at IHC (OR 1.80, 95%CI 1.09-2.98). Disease-free interval (DFI) was associated to rCR at univariable but not at multivariable analysis. HR status, CT backbone and type of anti-HER2 regimen were not associated with rCR neither at univariable nor at multivariable analysis. Median follow-up was 76.2 months. Amongst pts with TTF>12 months, those with rCR had a significantly higher OS compared to those not experiencing a rCR (median OS 133 and 90 months, respectively; p=0.0191). OS rates in pts with TTF ≥ 12 months were 97.8% at 2-year follow-up and 59.4% at 5-year follow-up. Instead, in pts with TTF ≥ 60

months, OS rates were 76.7% at 10-year follow-up. Amongst the 96 pts experiencing a CR, 38 had a rCR with TTF between 12 and 60 months, while 22 pts had a rCR with a TTF \geq 60 months. The remaining pts had a CR with a TTF < 12 months. Pts with HR negative (neg) disease were found to be more likely to experience a rCR with a TTF between 12 and 60 months, whilst pts with HR pos disease had a higher probability to experience a rCR with a TTF \geq 60 months ($p=0.0074$). Pts with HER2 3+ score at IHC had a higher probability to achieve a rCR with a TTF \geq 12 months compared to pts with HER2 2+ score at IHC and ISH + ($p=0.0216$). Age at diagnosis, menopausal status, DFI, number and site of mets, CT backbone and anti-HER2 therapy did not influence the duration of the rCR obtained. Conclusions: This study characterized a real-world cohort of HER2 positive MBC patients experiencing radiologic complete response to a first line treatment. Based on these results a clinical trial focused on liquid biopsy-based minimal residual disease is being designed. Novel anti-HER2 agents are gaining momentum as ever increasingly effective treatments and future de-escalation strategies after complete response will represent a growing need.

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5:00 PM - 6:15 PM

P1-11-05

Provider perceptions of DESTINY-Breast04, HER2-low directed treatment, and interstitial lung disease

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Background: Human epidermal growth factor receptor 2 (HER2)-targeted therapies are an established treatment for patients with HER2-positive breast cancer, however, these therapies have not proven effective in the HER2-negative setting. Until recently, HER2 status was used to guide treatment decisions based on a binary classification of positive or negative. A new pathological category, HER2-low, has emerged as a subtype of interest within the breast cancer treatment landscape. HER2-low status is defined as a HER2 immunohistochemistry score of 1+ or 2+ and a negative in-situ hybridization result. DESTINY-Breast04 (DB04) was the first trial to evaluate a HER2-targeted agent within the metastatic HER2-low breast cancer setting. The anti-HER2 agent trastuzumab deruxtecan (T-DXd) demonstrated promising clinical activity in HER2-low expressing tumors. However, development of T-DXd-related interstitial lung disease (ILD) remains a concern when using this therapy. This survey-based study aimed to evaluate community oncologists' perceptions of the DB04 data, HER2-low directed treatment, and management of ILD. Methods: U.S.-based oncologists (n=83) convened at two live meetings in June 2022 to review clinical updates presented at ASCO 2022. Participant characteristics and demographic data were collected via an online survey prior to the respective meetings. Perceptions/reactions to clinical updates were captured in real-time via electronic keypad. Data were summarized using descriptive statistics. Results: Among respondents, 83.1% identified as community providers, with an average experience of 20.7 years in practice. On average, participants reported that 88.2% of their time is allocated towards direct patient care, with roughly 18 patients seen per clinic day. Nearly half of respondents (49.4%) reported awareness of HER2-low as a distinct pathological category prior to the presentation of DB04 at ASCO 2022, however, less than 10% of respondents had previously used this sub-category to determine therapy. Increased T-DXd-related ILD, which occurred in 12% of trial participants, was cited as the greatest limitation of the DB04 trial by over one-third (37.3%) of respondents. After reviewing real-world evidence data of ILD incidence in metastatic breast cancer, nearly one-third (31%) of respondents reported that their observed ILD rates are less than DB04, but more (36%) said that ILD can be hard to quantify because patients are not always symptomatic. When asked if the ILD rate associated with T-DXd would limit their selection of this agent for their patients with breast cancer, approximately one-quarter (24.1%) of respondents indicated

that they would reserve T-DXd use for patients without symptomatic pulmonary disease. However, the majority of respondents (60.2%) indicated that they would not limit their use of T-DXd based on ILD rates, with most (55.4%) opting for a risk-management approach involving increased monitoring for the development of ILD-related adverse events. Conclusions: Advancements in assay interpretation have made it possible to differentiate gradients of HER2 expression, creating a space for pathological sub-categories within a formerly binary paradigm. Among providers who reported awareness of HER2-low as a distinct pathological sub-category, few had used this as a benchmark to guide their treatment decisions prior to the presentation of DB04 at ASCO 2022. Newer anti-HER2 agents, such as T-DXd, provide a potential new standard of care for patients with HER2-low expressing tumors. Despite the concern of ILD rates associated with T-DXd use, the majority of providers do not view this as a limiting factor due to the ability to closely monitor patients for the development of adverse events coupled with appropriate provider/patient education.

Disclosure(s):

Brooke Leon, BA: Cardinal Health Specialty Solutions: Salary (Ongoing)

Robert Bone, PhD: Cardinal Health Specialty Solutions: Salary (Ongoing)

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5:00 PM - 6:15 PM

P1-11-06

Multi-omics profiling of HER2-low breast cancer reveals clinically relevant subgroups and therapeutic pathways

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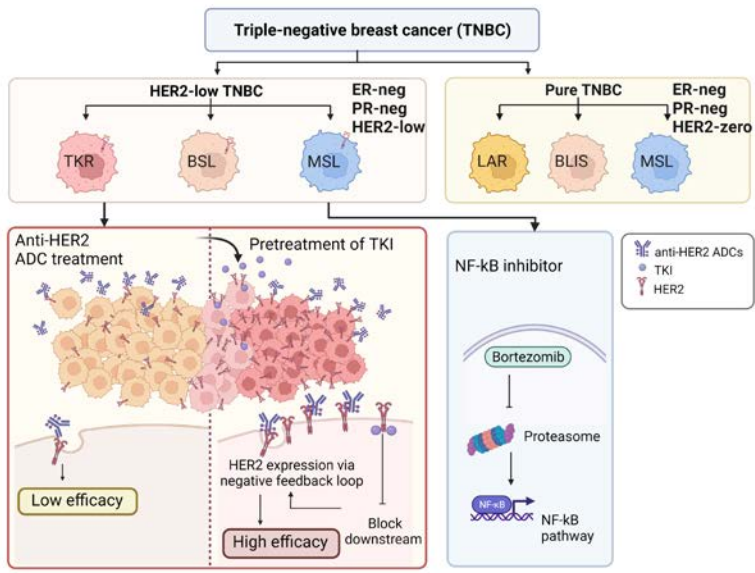
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The current HER2 testing algorithm can distinguish tumors that are completely negative for HER2 (IHC 0, HER2-zero) from HER2-low tumors [low (IHC 1+) or moderate expression (IHC 2+, ISH-)]. Because HER2-zero cases have often been combined with HER2-low cases, the clinical and biological understanding of HER2-low tumors is limited. To provide complementary information and shed light on the molecular characteristics and therapeutic insights of HER2-low breast cancer, we performed this multi-omics study of hormone receptor (HR)-negative and HER2-low breast cancer, also known as HER2-low triple-negative breast cancer (TNBC), and identified three subgroups: basal-like (BSL), receptor tyrosine kinase relevant (TKR), and mesenchymal stem-like (MSL). These three subgroups had distinct features and potential therapeutic targets and were validated in external datasets. Interestingly, the TKR subgroup (which exists in both HR-positive and HR-negative breast cancer) had activated HER2 and downstream MAPK signaling. In vitro and in vivo patient-derived xenograft experiments revealed that pretreatment with tyrosine kinase inhibitor (Lapatinib or Tucatinib) could inhibit HER2-signaling and induce accumulated expression of nonfunctional HER2 via a feedback loop, resulting in increased sensitivity to sequential HER2-targeting antibody-drug conjugate DS-8201. Our findings identify clinically relevant subgroups and provide potential therapeutic strategies for the previously targetless HER2-low TNBC subtype.

GRAPH ABSTRACT



Highlights of characteristics of HR-negative and HER2-low breast cancer subgroups

Table S1. Highlights of characteristics of HR-negative and HER2-low breast cancer subgroups

Subgroup	BSL	TKR	MSL
Clinical	5-years RFS: 87.1%	5-years RFS: 89.7%; high prevalence in Chinese	5-years RFS: 78.8%
Mutation	TP53 (62.5%); low PI3KCA (5.4%); low FOXA1 (0); HRDs high	TP53 (48.7%); high PI3KCA (43.6%); high FOXA1 (10.3%)	TP53 (71.4%); Middle PI3KCA (14.3%); high FOXA1 (14.3%)
Activated pathway	mTOR and mTORC1 signaling	ERBB2 signaling; Receptor tyrosine kinase; MAPK signaling	NF- κ B signaling
Potential therapy	mTOR and mTORC1 signaling inhibitor	Pre-treatment f Lapatinib or Tucatinib and followed by sequential DS-8201; Targeting MAPK signaling inhibitor	Bortezomib; Targeting CSCs

BSL, basal like; TKR, receptor tyrosine kinase relevant; MSL, mesenchymal stem-like; RFS, relapse-free survival; HRD, homologous recombination deficiency.

DS-8201, antibody-drug conjugates (ADC).

Lapatinib and Tucatinib, the small-molecule tyrosine kinase inhibitors (TKIs).

Bortezomib, NF- κ B pathway inhibitor.

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Lie Chen, M.D.: No financial relationships to disclose

Cui-Cui Liu, M.D.: No financial relationships to disclose

Jing-Yu Ge, M.D.: No financial relationships to disclose

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5:00 PM - 6:15 PM

P1-11-09

Five year follow up of a randomized phase II comparison of neo-adjuvant docetaxel, carboplatin, trastuzumab with or without lapatinib in HER-2 positive breast cancer.

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Background: The addition of trastuzumab (H) to pre-operative chemotherapy in HER2+ breast cancer (H+BC) increases the rate of pathological complete response (pCR). TCH is a widely used adjuvant regimen in early stage H+BC. Lapatinib (L) is a small molecule HER2 antagonist that produces responses following H failure, and has been reported to augment H activity in combination in vitro. We compared neo-adjuvant docetaxel, carboplatin (TC) + H v TCL v TCHL in pts with H+BC.

Methods: Pts with stages Ic–III H+BC were randomized to receive neo-adjuvant TCH, TCL or TCHL (ICORG/TRIAL-IE 10-05, NCT01485926 www.clinicaltrials.gov). Pts subsequently underwent surgery and received H post-operatively for 1 year from the first dose of H. The primary endpoint of the trial was pCR. Secondary objectives were overall survival (OS) and relapse-free survival (RFS) and molecular and pharmacological markers of response. This study was supported by GSK, Novartis, The Cancer Clinical Research Trust and The Caroline Foundation.

Results: When the NCIC CTG MA.31 trial reported inferior outcomes for L compared to H, we discontinued the TCL arm. This abstract reports data on the 76 pts recruited to the TCH and TCHL arms only, who included stage II (69.7%; n=53) or stage III disease (21.1%; n=16, with stage unknown for 9.2% (n=7)). The final analysis set numbered 75 pts. Clinicopathological characteristics were well balanced between arms. The pCR rate of the two arms TCHL and TCH were virtually identical at 51.6% and 52.8% respectively (Fisher's test p-value: 1.000). TCHL pts had significantly superior 5 year relapse-free survival (relative risk (RR) 0.171, 95% CI 0.041 – 0.713; log-rank test p-value = 0.009). OS was comparable between the TCH and TCHL groups (RR 0.205, 95% CI 0.025 – 1.675); log-rank test p-value = 0.2). Median RFS and OS were not reached. The most frequent serious adverse event was diarrhoea which occurred in 21.3% (n=16/75) pts (Grade 3 diarrhoea 13/16). One pt (TCH arm) who did not have protocol-mandated prophylactic G-CSF had a Grade 5 toxicity. One TCHL pt had a self-limiting diverticular perforation. There was a significantly higher frequency of severe diarrhoea in pts who received the TCHL regimen (Grade 3+, 32.4% vs 10.5%, p=0.038). The use of prophylactic loperamide reduced the frequency of diarrhoea in both the TCHL arm (86.2% vs

44.4%, p=0.004) and in the TCH arm (58.8% vs 24%, p=0.009). A post lock audit with minimum 9-year follow-up showed relapse rates of 15% TCHL vs 33% TCH.

Conclusions: The study did not meet its primary pCR endpoint possibly due to a high TCH pCR rate, and small numbers. TCHL produced a statistically significant improvement in RFS compared to TCH. TCHL produced a higher rate of gastro-intestinal toxicity, but the use of loperamide significantly reduced the frequency of diarrhoea. These data suggest that anti-HER2 TKIs merit further investigation in the neo-adjuvant treatment of early stage H+BC.

Table 1. pCR rates, 5 year RFS and OS results for ICORG/TRIAL-IE 10-05 (NCT01485926) study pts. * significant, p<0.05

Treatment arm	pCR	pCR Rate	p-value Fisher's test	Relapse Rate	5 year Relapse Rate (%)	p-value log-rank test for RFS	Relative Risk For Relapse	Death Rate	5 year Death Rate (%)	p-value log-rank test for OS	Relative Risk For Survival
TCH	19/36	52.8%	1.0	12/38	31.6%	0.009*	TCHL RR 0.171; 95% CI 0.041 – 0.713	5/38	13.2%	0.2	TCHL RR 0.205; 95% CI 0.025 – 1.675
TCHL	16/31	51.6%		2/37	5.4%			1/37	2.7%		

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John Crown, MB BCh BAO BSc MBA: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Travel (Ongoing); Cepheid: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi Sankyo: Conference registration fees (Ongoing); MSD: Advisory Board Conference registration fees/Travel (Ongoing); Novartis: Advisory Board Conference registration fees (Ongoing); Oncoassure: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Oncomark: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing); Pfizer: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Travel and honoraria (Ongoing); Pierre Fabre: Honorarium (Ongoing); Puma Biotechnology: Contracted Research (Ongoing); Roche: Conference registration fees (Ongoing); Sanofi: Compound for use in laboratory studies (Ongoing)

Denis M. Collins, PhD: Genentech: Supply of compound for research purposes under MTA. (Ongoing); Puma Biotechnology: Contracted Research (Ongoing); Sanofi: Supply of compound for research purposes under MTA. (Ongoing)

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P1-11-10

Reversible versus irreversible tyrosine kinase inhibitors (TKIs) combined with antibody-drug conjugates (ADCs) in HER2-positive (HER2+) breast cancer (BC) cell lines

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Background: Targeting the human epidermal growth factor receptor (HER) family of tyrosine kinase receptors with small molecule TKIs lapatinib, neratinib and tucatinib, monoclonal antibodies like trastuzumab and more recently with ADCs like T-DM1 and T-DXd has resulted in improved survival rates for patients with HER2+ BC. TKIs are primarily utilised in trastuzumab-refractory disease. Neratinib, and the pan-HER TKI afatinib, bind irreversibly to all members of the HER family, while lapatinib binds reversibly to HER2 and EGFR, and tucatinib binds reversibly to HER2 alone. Previous work in our lab has shown that TKIs like lapatinib are capable of modulating tumour surface HER2 levels and increasing trastuzumab load on tumours. Thus, there is a rationale for the use of TKI/ADC combinations in HER2+ BC. Using innately trastuzumab-resistant HER2+ BC cell lines, this in vitro study aims to assess the anti-proliferative potential of HER2-targeting ADCs T-DM1 or T-DXd in combination with the TKIs afatinib, lapatinib, neratinib or tucatinib.

Methods: HCC1569 and HCC1954 cells (HER2+, estrogen receptor (ER)-negative; innately trastuzumab-resistant) were grown in RPMI1640/10% FBS at 37°C and 5% CO₂. The anti-proliferative effects of afatinib, lapatinib, neratinib and tucatinib; of T-DM1 and T-DXd; and of each TKI/ADC combination thereof were assessed in these cells via 5-day acid phosphatase. ADCs were obtained from Saint Vincent's University Hospital, Dublin, and TKIs were purchased from commercial sources. Calcsyn software was used to generate IC₅₀ values and

combination index (CI) values at ED50. CI values > 1 represent an antagonistic combination, CI values = 1 are additive, and CI values < 1 are synergistic. All assays were carried out in triplicate.

Results: The HCC1569 cell line was more sensitive to all four TKIs (IC50 values were 12.8 ± 0.3 , 453.8 ± 47.1 nM, 4.7 ± 1.4 and 381.5 ± 37.3 nM for afatinib, lapatinib, neratinib and tucatinib respectively) compared to the HCC1954 cell line (IC50 22.3 ± 2.8 , 652.4 ± 36.0 , 57.0 ± 6.3 and 2365.1 ± 185.3 nM for afatinib, lapatinib, neratinib and tucatinib respectively). Despite their innate trastuzumab resistance, both cell lines displayed high sensitivity to T-DM1 (IC50 25.2 ± 8.7 ng/mL for HCC1569 and IC50 30.4 ± 3.2 ng/mL for HCC1954) and to T-DXd (IC50 16.0 ± 3.2 ng/mL for HCC1569 and IC50 36.8 ± 8.7 ng/mL for HCC1954). In both cell lines, co-treatment with ADCs and the irreversible TKIs afatinib and neratinib resulted in additive or synergistic responses, while the combination of the ADCs with the reversible TKIs lapatinib and tucatinib resulted in mild to moderate antagonism (Table 1).

Conclusions: In this pre-clinical study, T-DM1 and T-DXd consistently exhibited antagonistic interactions with reversible HER2-targeting TKIs, and synergy/additivity in combination with the irreversible TKIs tested. Future work will explore the underlying mechanisms of this observed synergy and antagonism, including impacts of TKIs on HER2 expression and real-time ADC internalisation rates.

Table 1

	Drug Combination	HCC1569 CI values	HCC1954 CI values
Irreversible	Afatinib + T-DM1	0.87 ± 0.10	0.73 ± 0.13
	Afatinib + T-DXd	0.85 ± 0.07	0.98 ± 0.11
	Neratinib + T-DM1	0.77 ± 0.07	0.87 ± 0.12
	Neratinib + T-DXd	0.85 ± 0.06	0.85 ± 0.11
Reversible	Lapatinib + T-DM1	1.21 ± 0.14	1.11 ± 0.05
	Lapatinib + T-DXd	1.38 ± 0.22	1.64 ± 0.32
	Tucatinib + T-DM1	1.37 ± 0.16	1.31 ± 0.34
	Tucatinib + T-DXd	1.28 ± 0.11	1.44 ± 0.20

CI values +/- Std Dev for each TKI/ADC treatment combination in HCC1569 and HCC1954 cells

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Niall Ashfield, n/a: Sanofi: Compound for research purposes (Ongoing)

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5:00 PM - 6:15 PM

P1-11-11

HER2-directed therapy in early breast cancer – improvement over 20 years

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Introduction:

HER2-positive breast cancer is considered aggressive, but due to the development of targeted drugs in the past 20 years, a substantial improvement of therapy results can be postulated. Proven evidence is provided by data of randomized clinical trials. The present study aimed at demonstrating the improvement of therapy results over time using single-center real world data.

Material and Methods:

In our center, we prospectively built a consecutive tumor and data base from 2000 to 2020 and identified patients with early HER2-positive breast cancer (n=396). The cohort was divided in four groups by year of diagnosis according to the changing therapy concepts: A) 2000-2004 (no HER2-directed therapy, n=83), B) 2005-2011 (trastuzumab, n=96), C) 2012-2017 (trastuzumab/pertuzumab, n=135), D) 2018-2020 (T-DM1 in patients with non-pCR), n=55). HER2 was measured by IHC and ISH corresponding to the ASCO-CAP guidelines. HER2-directed therapy was indicated according to the respective national guidelines (AGO). The

median follow-up was 58 months in the entire cohort (1-266), group A 84 months (10-266), group B 94 months (2-201), group C 56 months (1-118), group D 32 months (8-53). The primary endpoint was overall survival (OS), and secondary endpoint was iDFS. Kaplan-Meier estimates were calculated and multivariate analyses were performed using SPSS 28 (IBM, Armonk, NY, USA).

Results:

Overall, 57% of the 396 patients had an age of 50 years or more, 85% had a NST histology, 54% of the tumors were larger than 2cm, 45% were node-positive; 34% were steroid hormone receptor negative. HER2-directed therapy was delivered to 7 of 83 pts in group A (8.4%), to 62 of 96 pts in group B (64.6%), to 119 of 135 in group C (88.15%), and to 50 of 55 pts in group D (90.91%), resp.. Overall, in the first 3 years we observed 19 deaths and the probability for OS was 89.7 % for group A, 92.2 % for group B, 96.4 % for group C and 100% for group D, resp.; iDFS was 77.4% in A, 86.8% in B, 94.9% in C and 95.2% in D, resp.. After adjustment for nodal status, grading and steroid hormone receptor status, we calculated the effect size of the incremental improvement of treatment for OS and iDFS as HRs referred to group A (Table 1).

Conclusion:

With this prospectively established single center cohort, we are able to confirm a significant improvement of the treatment results in patients with HER2-positive early breast cancer over the last 20 years applying individualized HER2-directed therapies.

Table 1. Multivariate analyses of OS and iDFS adjusted for nodal status, grading and hormone receptor status.

	sample size (n=369)	events (n=56)	Hazard ratio multivariate OS	95% CI	p-value	events (n=81)	Hazard ratio multivariate iDFS	95% CI	p-value
Treatment period									
Group A (2000-2004)	83	23	1			32	1		
Group B (2005-2011)	96	23	0.824	0.454-1.495	0.524	30	0.688	0.412-1.147	0.152
Group C (2012-2017)	135	10	0.484	0.225-1.040	0.063	16	0.412	0.223-0.760	0.005
Group D (2018-2020)	55	0	-	-	-	3	0.311	0.093-1.035	0.057

Disclosure(s):

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P1-11-12

Soluble TNF α blockade enhances trastuzumab deruxtecan antitumor effect in HER2-positive breast cancer model

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Background. Clinical trials have demonstrated that trastuzumab deruxtecan (T-DXd) provides a durable responses for patients with HER2-positive and HER2 low metastatic breast cancer (BC). With T-DXd treatment, approximately 50% of patients with HER2+ metastatic BC were still alive and progression-free at 24 months (DESTINY-Breast03). We previously shown that mucin 4 (MUC4) expression is an independent predictor of poor response to trastuzumab in HER2-positive BC patients. We also showed that MUC4 is upregulated by soluble TNF α (sTNF α) secreted by the tumor, which confers primary trastuzumab resistance since it hides trastuzumab epitope on the HER2 molecule, reducing its binding and diminishing its therapeutic effects. In preclinical models of de novo trastuzumab-resistant tumors, we proved that administration of the sTNF α blocking agent INB03 (DN) together with trastuzumab inhibited tumor growth and induced an innate immune response in the tumor microenvironment (TME). DN is a dominant-negative inhibitor of sTNF α that is not immunosuppressive because it does not affect transmembrane TNF α . Our goal is to study whether neutralizing sTNF α can improve T-DXd effects in a multiple HER2-targeted therapy-resistant model. Methods JIMT-1 is a HER2-positive BC cell line resistant to trastuzumab, pertuzumab and lapatinib, which expresses MUC4. JIMT-1 tumor-bearing nude mice were treated with (1) IgG 5 mg/kg, (2) T-DXd 5 mg/kg, (3) T-DXd 2.5 mg/kg, (4) T-DXd 1.25 mg/kg, (5) DN 10 mg/kg, (6) T-DXd 5 mg/kg +DN, (7) T-DXd 2.5 mg/kg +DN and (8) T-DXd 1.25 mg/kg +DN. T-DXd and IgG were administered i.v. on days 0, 7 and 14. DN was administered i.p. twice a week for 3 weeks. Tumor growth was monitored regularly. Tumor-infiltrating macrophages, NK cells and myeloid-derived suppressor cells (MDSCs) were evaluated by immunofluorescence and flow cytometry. Results The dose-response curve of T-DXd exhibited tumor growth inhibitions of 83% (5 mg/kg), 61% (2.5 mg/kg) and 37% (1.25 mg/kg) vs IgG-treated tumors. DN alone had no antitumor effect. Combination of T-DXd with DN resulted in a reinforced antitumor effect, as the tumor growth inhibition escalated to 98% (T-DXd 5 mg/kg+ DN), 81% (T-DXd 2.5 mg/kg+DN) and 73% (T-DXd 1.25 mg/kg+DN). Moreover, we observed that addition of DN to T-DXd 1.25 and 5 mg/kg enhances the infiltration of resident macrophages ($p < 0.05$ and $p < 0.01$, respectively) and promotes polarization to the M1-like phenotype ($p < 0.05$ and $p < 0.001$, respectively). While T-DXd 2.5 and 5 mg/kg alone achieved a decrease in M2-like macrophages ($p < 0.05$), combination of T-

DXd 1.25mg/kg+DN impaired M2-like polarization at similar levels of that observed with 2.5 and 5 mg/kg T-DXd ($p < 0.05$). Notably, the M1/M2 ratio escalated from 10.9% to 51.5% when DN was added to the lowest T-DXd dose ($p < 0.01$). In addition, T-DXd 2.5 and 5 mg/kg induce an increase in the proportion of NK cells in TME ($p < 0.001$ and $p < 0.05$, respectively), which T-DXd 1.25 mg/kg+ DN treatment mimicked ($p < 0.05$). Although an increase in NK cell activation was observed with 1.25 and 2.5 mg/kg treatments ($p < 0.05$ and $p < 0.001$, respectively), adding DN did not further improve this effect. Only the highest dose of T-DXd in combination with DN was able to increase NK cell degranulation ($p < 0.05$), compared to T-DXd alone. Finally, the percentage of MDSCs population decreases with the addition of DN to the T-DXd 2.5 and 5 mg/kg. Conclusions Our results suggest that sTNF α blockade is able to enhance T-DXd effect in a multiple HER2-targeted therapy resistant model. Notably, the administration of T-DXd 1.25 mg/kg+DN achieved a similar antitumor effect to T-DXd 5 mg/kg alone and also transforms the TME to an antitumor one with a reinforced immune response. This finding highlights that sTNF α and MUC4 expression are important variables in the response to T-DXd. Neutralization of sTNF α may open new therapeutic strategies for treatment of patients who present with MUC4 expression or have progression on T-DXd therapy.

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P1-11-13

DE-REAL: ITALIAN MULTICENTER EXPERIENCE OF TRASTUZUMAB DERUXTECAN IN A REAL WORLD SETTING

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INTRODUCTION: Trastuzumab Deruxtecan (TDXd) is an innovative antibody drug conjugate (ADC) comprising an anti-HER2 antibody, a cleavable tetrapeptide-based linker and a potent topoisomerase I inhibitor. TDXd has demonstrated promising clinical efficacy in previously treated HER2-positive metastatic breast cancer patients (pts). Drug-drug interactions (DDIs) can influence drug activity and potentially affect treatment efficacy or determine increased toxicity. Drug-PIN® (Personalized Interactions Network) is a tool able to identify interactions between drugs and combine them with demographic, clinical and biochemical patient data. In this multicentric retrospective study, we aim to describe clinical outcomes, toxicities and drug-drug interactions (DDIs) of TDXd in a real-world population. **METHODS:** Pts with histological and radiological confirmed HER2+ mBC (defined as HER2 3+ or HER2 2+ with an amplification detected in SISH/FISH) who received TDXd were included in the study. The availability of complete data about clinical outcomes, toxicities and concurrent medications was needed. Pts who received at least one month of treatment were eligible. Radiological response and toxicities were evaluated following RECIST 1.1 and CTCAE v5 criteria. Drug-PIN® was used to define DDis, Drug-PIN® score and Drug-PIN® tier (green for no significant DDis and yellow, dark yellow, orange, red for increasing DDis) for each pts. Clinical and pathological features were collected from the referral hospital in an anonymous database and analyzed with R-package. Univariate analysis was conducted calculating the AUC of ROC or the PFS using the Kaplan and Meier curves and log-rank test as appropriate. Multivariate analysis was conducted using logistic or Cox proportional hazard regression model as appropriate. **RESULTS:** One hundred forty-three pts were enrolled from 11 Italian oncological hospitals. Median age was 56 years (33-84). Estrogen receptor (HR) status was positive in 108 (75%) pts and negative in 35 (25%) pts. TDXd was administered as the first, second, third or subsequent line in 4 (3%), 17 (12%), 41 (29%) and 81 (56%) pts, respectively, with an average of 4 treatments received (range 1-11). Among 114 pts with measurable disease, the ORR was 68% (6% of complete response). Eight (7%) pts had a primary resistance to TDXd. Median PFS was not reached and the milestone-1 year PFS was 56.7% in the overall population. PFS at 12 months was 100% vs 54.1 % in pts receiving upfront or second versus subsequent lines ($p=0.094$). A toxicity of any grade was registered in 80 pts (56%). Most common toxicities were nausea (43, 30%), neutropenia (28, 19%) and asthenia (19, 13%). Severe tox was reported in 21 (15%) pts. Most common severe tox were neutropenia, nausea/vomiting and interstitial lung disease (ILD) observed in 14, 2 and 2 pts, respectively. Concomitant medications were taken by 63 pts, with 8 pts receiving more than 5 drugs. Among pts taking any medications, median Drug-PIN® score was 6.3 (range 1.7-190). 127, 11, 3 and 2 pts were in the green, yellow, dark yellow and red Drug-PIN® tier, respectively. Sixteen pts (11%) had a relevant DDI. The median PFS was not reached vs 12 months in pts with green Drug-PIN® tier compared to yellow or more, however the difference did not reach statistical significance and a longer follow up is needed. Asthenia of any grade was associated with an elevated Drug-PIN® score (AUC 0,681; $P=0.011$). Severe ILD was reported in 2/16 pts with DDis while no cases (0/124) occurred in pts with no DDis (threshold Drug-PIN® score: 19.4/ Drug-PIN® tier: >yellow, $P=0.0061$). **CONCLUSIONS:** TDXd demonstrated to be effective and safe in our unselected real world

population, even in heavily pretreated pts. No new safety concerns were reported. DDIs seems to be associated with specific toxicities such as asthenia and ILD.

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5:00 PM - 6:15 PM

P1-11-16

Treatment with tyrosine kinase inhibitors (TKIs) in HER2-positive metastatic breast cancer after trastuzumab emtansine (T-DM1) failure: A real-world study

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Background Trastuzumab emtansine (T-DM1) has shown great effectiveness in treating HER2-positive metastatic breast cancer, but therapies subsequent to T-DM1 failure remain controversial. Here, we investigated efficacy and safety of tyrosine kinase inhibitors (TKIs) based therapy in T-DM1 resistant HER2-positive metastatic breast cancer. Methods From August 2019 to April 2022, 53 HER2-positive metastatic breast cancer patients received TKIs-based therapy after T-DM1 failure in Jiangsu Province Hospital. Progression-free survival (PFS), overall survival (OS), objective response rate (ORR), clinical benefit rate (CBR), and safety profiles were reported. Results 53 patients received TKIs-based therapies as a second or later line therapy. 51 (96.2%) patients received a combined therapy, including TKIs plus capecitabine, vinorelbine or trastuzumab. 2 (3.7%) patients received TKIs alone. The median follow-up time was 19.7 months (95%CI 15.4-24.0). The median PFS was 11.9 months (95%CI 7.9-15.9). OS has not reached. ORR was 19.6% and CBR was 72.5%. For patients who had brain metastasis (n=12), the median PFS was 10.5 months (95%CI 7.5-13.5) and intracranial ORR was 33.3%. Compared with lapatinib (n=30), pyrotinib (n=21) provided a better PFS after T-DM1 progression (8.0 months vs. 19.0 months, P=0.033). The most common adverse events were thrombocytopenia (12, 23.6%), diarrhea (8, 15.7%), leucopenia (8, 15.7%) and hand-foot syndrome (8, 15.7%). Conclusion TKIs-based therapy could prolong the survival of HER2-positive metastatic breast cancer patients after T-DM1 failure, including those with brain metastases. Compared with lapatinib, pyrotinib might provide better outcomes for overcoming T-DM1 resistance.

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P1-11-17

The real-world outcome of human epidermal growth factor type-2 positive breast cancer patients receiving neoadjuvant therapy with or without pertuzumab

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Background Standard treatment in early HER2 positive BC involves the use of neoadjuvant chemotherapy (NACT) with Trastuzumab (T) plus Pertuzumab (P). Dual blockade increases pathological complete response (pCR) and improves disease free survival (DFS). However, Chilean public health system does not include P use in the NACT schedule, while private insurers only provide partial coverage. Here, we aim to compare pCR, Distant DFS (DDFS) and site of recurrence in HER2 positive BC patients treated in the neoadjuvant setting with the use of T with or without P, in the largest BC Chilean registry. Methods We conducted a retrospective population-cohort study involving females with stage I-III HER2 positive BC

treated with NACT in a public and academic private centre between 2012 to 2021. CT regimens for comparison included anthracyclines, taxanes, T and P. pCR was defined as the absence of residual invasive disease in the breast and in the axillary lymph nodes (ypT0/is N0) at the completion of the NACT. DDFS was measured from the time of diagnosis to the event or lost to follow-up. We performed Cox regression analysis to identify factors associated with prognosis and a logistic regression to identify factors related to the first metastasis site. Results 372 patients with HER2 positive BC were included. Median age was 51 years (24 – 79), 57.5% were classified as Hormone Receptor positive (HR), and 4.5% were stage I, 48.2% stage II and 47.3% stage III. 65.8% were treated in a Public Hospital (PH) and 34.2% in an Academic Private Centre (AC). 85.2% received both anthracyclines and taxanes, 10.0% only taxanes and 4.8% only anthracyclines-based CT. 55 patients (14.8%) received both T and P, while 3.3% did not receive any HER2 directed therapy as NA treatment. Median T doses before surgery were 6 (1 – 12). pCR rate was 46.5% which varied according to HR expression: 61.0% in HR-positive BC vs. 36.2% in HR-negative disease ($p=0.0001$). pCR according to treatment were as follows: no-T no-P 22.2%, only-T 49.4%, both T-P 60.0% ($p=0.02$). We found no difference in pCR rate between anthracycline and non-anthracycline based CT (49.1% vs. 45.9%, $p=0.72$). With a median follow-up of 36 months, DDFS at 3 and 5 years differed regarding pathological response: 94.8% vs. 77.1% and 86.3% vs. 69.1% ($p=0.0006$), for pCR and non-pCR group, respectively. In a multivariate analysis, stage III vs. I-II (HR 2.5, $p=0.005$), non-pCR vs. pCR (HR 2.6, $p=0.01$) and not receiving NA anti-HER2 treatment (HR 2.6, $p=0.01$) were associated with higher risk of distant metastasis. Regarding recurrence, 7 out of 198 non-pCR tumors and 6 out of 174 pCR tumors presented brain metastasis (BM) as the first site of distant recurrence($p=0.96$). In contrast, visceral metastasis (VM) as the first site of recurrence, were more frequent in non-pCR (21/198) than pCR patients (3/174, $p=0.001$). In a multivariate analysis, the only factor associated with BM was stage III (HR 5.8 vs stage I-II, $p=0.02$) and with VM was not achieving pCR (HR 6.3, $p=0.02$) and not using T nor P (HR 5.1, $p=0.008$). Conclusion The use of anti-HER2 treatment in a NA scheme is critical in HER2 positive disease. Although P is associated with increased pCR, we found no survival benefit with its use. Retrospective analysis, few events, post-surgical treatment might have influenced these results. Achieving pCR is associated with better prognosis by reducing distant recurrence but not BM. New strategies are needed to prevent the occurrence of this event.

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P1-11-18

The efficacy and safety of trastuzumab and pertuzumab in combination with different chemotherapy regimens for neoadjuvant treatment of HER2-positive breast cancer: a multi-center real-world study in China

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Background: Dual HER2 targeted therapy with trastuzumab (H) and pertuzumab (P) has been approved as neoadjuvant therapy for patients with HER2-positive breast cancer in China in 2019 based on the results from NeoSphere and PEONY study. However, the real-world efficacy and safety data are currently lack of evidence in China. Therefore, this multi-center real-world study aims to retrospectively analyze the efficacy and safety of neoadjuvant trastuzumab and pertuzumab combined with different chemotherapy regimens of HER2-positive early breast cancer. Methods: Patients received trastuzumab and pertuzumab in combination with different chemotherapy regimens, including taxanes (T), cyclophosphamide (C), anthracyclines (A) were collected retrospectively from 12 centers. The primary endpoint was total pathological complete response (tpCR, ypT0/is ypN0) rate. Results: A total of 357 patients were enrolled, among which 204 (57.5%) received TCbHP, 92 (25.9%) received EC-THP, and 51 (14.4%) received THP as chemotherapy regimens. The median age was 48 years old (range, 22-76), 142 (39.8%) of patients were classified as hormone receptor (HR)-positive, and 215 (60.2%) were HR-negative. The overall tpCR rate was 58.5% (95%CI, 53.2%-63.7%). tpCR rate for HR-negative patients was significantly higher than HR-positive patients (65.6% vs. 47.9%, $p=0.001$) and there was not any statistical difference according to chemotherapy regimens (56.9% for TCbHP, 56.5% for EC-THP, and 66.7% for THP, $p=0.445$). The most common adverse events included anemia (40.1%), white blood cell count decreased (34.3%), ejection fraction decreased (19.5%), Alanine aminotransferase increased (18.9%), platelet count decreased (12.8%) and neutrophil count decreased (12.0%). There was not any toxicity leading to death. Conclusions: Multi-center real-world data show satisfactory tpCR rate and tolerable adverse events of trastuzumab and pertuzumab in combination with different chemotherapy regimens in China.

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A real-world evidence study of treatment patterns in patients with HER2-positive metastatic breast cancer who have received at least 2-lines of therapy

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Background. Standard-of-care treatment for HER2-positive metastatic breast cancer (HER2+ mBC) patients has traditionally included targeted therapies such as trastuzumab and/or pertuzumab in first line (1L) and ado-trastuzumab emtansine (T-DM1) in the second line (2L). In 2021, fam-trastuzumab deruxtecan-nxki (T-DXd, Enhertu®) was approved following DESTINY-Breast 03 trial results, demonstrating a significant reduction in the risk of progression compared to T-DM1 in 2L. Contemporary data on treatment patterns and clinical outcomes for HER2+ mBC patients after their 1L therapy in a real-world setting is limited and would help understand whether all eligible patients receive optimal and timely targeted therapies. This study aimed to report 2L treatment patterns and outcomes among HER2+ mBC patients in the United States (US). Methods. Adult HER2+ mBC patients with ≥2 lines of therapy were identified from the Syapse Learning Health Network (LHN) database; a longitudinal US oncology database integrating data from community health systems, labs and other external sources. Included patients initiated 2L treatment for metastatic disease between January 2014-February 2021 (index date), allowing for 12-months of follow-up. Descriptive statistics for patient characteristics, treatment patterns including prior metastatic treatments, time to treatment discontinuation (TTD), and reasons for 2L discontinuation were reported. Results. Of the 15,241 breast cancer patients in the LHN with abstracted data, 312 HER2+ mBC patients received ≥2L treatment. The patients were mostly White (69%) or African American (21%), median age of 59 years (interquartile range [IQR], 50-66) at start of 2L. The African American population was typically diagnosed young (median age 50 [IQR, 44-61] vs. 54 [IQR, 46-62] years) with stage IV disease at initial diagnosis (69% vs 62%) versus Whites. Majority of the 312 patients had stage IV disease at initial diagnosis (62%); most common sites of metastasis

at mBC diagnosis were bone (52%), distant lymph node(s) (38%), liver (36%) and brain (10%). The median length of follow-up was 22 months (IQR, 13-37), 54% had initiated their 2L therapy since 2018. Majority of the 312 patients had received a trastuzumab-based (T-based) regimen in 1L (78%). Among the 312 patients, 37% had received only 2 lines of therapy in the metastatic setting, 28% received 3 and 35% received ≥ 4 lines of therapy. In 2L, 89% of the 312 patients received a HER2-targeted treatment (monotherapy or combination); the most frequent 2L regimens included T-DM1 monotherapy (29%), trastuzumab/pertuzumab/taxane (10%) and T-DM1/trastuzumab (8%). Subsequently, 197 of the 312 patients (63%) received 3L therapy. Among these 197 patients, T-DM1 monotherapy (19%), T-DXd monotherapy (10%) and capecitabine/lapatinib (8%) were the most frequently reported 3L regimens. Around 88% (n=274) of the 312 patients discontinued their 2L therapy. Median TTD of 2L from index date was 7.2 months (95% CI, 6.5-8.9); median TTD was 10.6 months (95% CI, 7.4-14.0) among a sub-group of patients who received a T-based regimen in their 2L (N=116). Approximately 47% of patients discontinued their 2L regimen due to progression/worsening of cancer, 17% discontinued from intolerance/toxicity in the absence of progression. Conclusions. This study suggests the treatment trajectory of US HER2+ mBC patients is variable in the real world clinical practice. Approximately two-thirds of the 2L patients had to receive a subsequent therapy and disease progression was the most common reason for 2L treatment discontinuation, reflecting a remaining need to improve outcomes for patients in 2L HER2+ disease.

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Trastuzumab (HLX02) plus Pertuzumab as Dual-target Neoadjuvant Therapy for HER2-positive Breast Cancer: A Real-World Study

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Background: The effect of neoadjuvant therapy on tumor downstaging and breast-conserving during surgery is well documented. Pathologic complete response (pCR) after neoadjuvant treatment was associated with long-term survival. HLX02 (Zercepac®), a biosimilar of trastuzumab, showed the same efficacy, safety, and immunogenicity as the reference drug in human epidermal growth factor receptor-2 (HER2)-positive patients. Despite this, real-world evidence of its effectiveness when combined with pertuzumab in neoadjuvant treatment of HER-2 positive breast cancer still lacks.

Methods: In this retrospective real-world study, women with confirmed invasive HER2-positive breast cancer who have received chemotherapy plus HLX02 and pertuzumab (Perjeta®) as neoadjuvant therapy were enrolled. Patients must be over 18 years old, have an Eastern Cooperative Oncology Group performance status score of 0 or 1, and have a baseline left ventricular ejection fraction of $\geq 55\%$. Patients without pathological assessment after neoadjuvant therapy were excluded. Pathologic complete response (pCR) was defined as no residual invasive tumors in mammary glands and axillary lymph nodes. Clinical response was assessed using RECIST1.1. To investigate the factors associated with pCR, univariate and multivariate logistic regression (forward stepwise) analyses were conducted.

Results: A total of 85 patients were enrolled in this study, and 55 patients (64.71%) achieved pCR after neoadjuvant therapy. There were 84 (98.82%) patients with partial response (PR), one (1.18%) patient with stable disease (SD). According to the univariable analysis, when compared to those with a tumor diameter ≤ 5 cm, patients with a tumor diameter > 5 cm at baseline showed a lower pCR rate (odds ratio [OR] = 0.286; 95% confidence interval [CI]:

0.108-0.758, P = 0.01). Patients with preoperative PR positivity > 10% showed lower pCR rate than those with preoperative PR positivity < 1% (OR = 0.115, 95% CI 0.036-0.372, P = 0.02). Besides, pCR was more common in patients with preoperative hormone receptor (HR)-negative than in those with preoperative HR-positive (ER or PR positivity > 10%) (OR = 4.452, 95% CI 1.679-11.804, P < 0.01). Multivariable analyses showed that patients with tumor diameter > 5 cm had a lower pCR rate than those with tumor diameter ≤ 5cm (OR = 0.213; 95% CI 0.070-0.644, P = 0.01). Patients with preoperative HR-negative tumors were more likely to achieve pCR than those with preoperative HR-positive tumors (OR =5.649, 95% CI 1.927-16.556, P < 0.01) (Table 1). The treatment were well tolerated by patients, and no additional adverse events were reported.

Conclusion: According to this real-world study, HLX02 in combination with pertuzumab as neoadjuvant therapy for HER2-positive breast cancer patients showed a similar pCR rate to that of dual-target neoadjuvant therapy reported in previous clinical trials. The treatment showed an encouraging effectiveness, and may become a novel neoadjuvant option for patients with HER2-positive breast cancer.

The study was supported by the Natural Science Foundation of Shanghai (21ZR1414700).

Table 1. Logistic regression for pCR

Variables	Univariable			Multivariable		
	OR	95% CI	P	OR	95% CI	P
Tumor size, cm						
>5 vs ≤5	0.286	0.108-0.758	0.01	0.213	0.070-0.644	0.01
ER						
1-10% vs <1%	0.193	0.036-1.021	0.22			
>10% vs <1%	0.257	0.095-0.695	0.32			
PR						
1-10% vs <1%	0.208	0.054-0.810	0.46			
>10% vs <1%	0.115	0.036-0.372	0.02			
HR						
- vs +	4.452	1.679-11.804	<0.01	5.649	1.927-16.556	<0.01

Disclosure(s):

Yin Liu, n/a: No financial relationships to disclose

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Impact of Anti-Estrogen Therapy on Early Vascular Referrals, Tests and Medications in Premenopausal Women with Operable Breast Cancer

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Introduction: Premenopausal women with high-risk hormone receptor-positive (HR+) breast cancer (BC) undergo abrupt menopause induction with anti-estrogen therapy (AE) and ovarian function suppression (OFS). This treatment improves recurrence-free survival but may increase cardiovascular (CV) risk associated with early hypoestrogenemia, as observed in women with non-cancerous reasons for premature menopause. We sought to identify patterns of CV actions including referrals, tests and medication by type of AE therapy in premenopausal women in early follow-up for operable BC as a possible surrogate for early CV disease.

Methods: Consecutive premenopausal women ≤ 50 years (mean age 42.6 years; sd 5.9) with Stage I-III HR+ or triple negative breast cancer (TNBC) diagnosed between 02/2013-06/2020 were identified by retrospective review. Mean follow-up was 4.9 years (sd 2.1 years.) Women were placed into 3 treatment groups based on initial AE approach: HR+ on OFS+AE (HR+OFS), HR+ not on OFS (HRnoOFS), and TNBC. Patient demographics, cancer treatment and CV risk factors as well as post-diagnosis adverse CV events (myocardial infarction, transient ischemic attack) and CV-related clinical actions (CV actions) including referrals, (cardiology, neurology (vascular)), tests (stress test, angiogram, ECHO, EKG, Carotid US) and medications (statin, ACEi, ARB, betablocker, calcium channel blocker, antiarrhythmic, and anti-platelet agents) were recorded. For each CV outcome (events, total actions, referrals, tests,

medications) we created an “any” vs “none” dichotomous variable as well as a variable for number of CV outcome per year of follow-up. Categorical variables were compared among the 3 groups using chi-square and Fisher’s exact tests; continuous outcomes (including the “per year” variables) were compared among the 3 groups using ANOVA. For the ANOVAs we report the global null hypothesis p-value. A two-tailed alpha of 0.05 was used throughout.

Results: 80, 78, and 48 (total n=206) women were identified in the HR+OFS, HRnoOFS and TNBC groups respectively. Mean follow-up was longest in the HRnoOFS group (Table 1). Mean number of CV actions per year were highest in the HR+OFS group compared with HRnoOFS and TNBC (0.41 vs 0.22 and 0.35, respectively; p=0.008.) The HR+OFS group had significantly more referrals during follow-up, as well as more referrals per year than the other two groups. This group also had significantly more tests per year than the other two groups. CV medication initiation did not differ among the groups. The proportion with >3 CV actions during follow-up was 62% higher in women in the HR+OFS group compared to other groups. Experiencing >3 CV actions was associated with having diabetes, hypertension, and hyperlipidemia, being a current smoker, and receipt of left-sided radiation (Table 2).

Conclusions: In this early follow-up period, women on OFS+AE experienced more CV actions per year suggesting concern for CV sequela in this patient group. Future work should seek to further understand the impact of OFS+AE on the CV health of premenopausal women, try to identify who is at greatest risk and test strategies to mitigate cardiotoxicity.

Table 1: Patient Characteristics and CV outcomes by Breast Cancer Treatment Group

Table 1: Patient Characteristics and CV outcomes by Breast Cancer Treatment Group

	HR+OFS (80)	HRnoOFS (78)	TNBC (48)	p*
	N (%) or mean (sd)	N (%) or mean (sd)	N (%) or mean (sd)	
Age (years)	42.9 (5.9)	44.9 (4.1)	39.5 (7.0)	<0.0001
Mean length of follow-up (years)	4.1 (1.8)	6.0 (2.0)	4.5 (2.1)	<0.0001
BMI (SD) kg/m ²	29.1(6.3)	29.0 (7.1)	30.1 (6.8)	0.65
Race N (%)				0.03
White	56 (69.1)	60 (76.9)	26 (54.2)	
Black	19 (23.5)	12 (15.4)	12(25.0)	
Other	5 (6.3)	6 (7.7)	10 (20.8)	
Ethnicity				0.006
Hispanic	2 (2.5)	1 (1.3)	6 (12.5)	
Non-Hispanic	78 (97.5)	77 (98.7)	42 (87.5)	
CV Event (Any)	1 (1.3)	1 (1.3)	0 (0.0)	1.0
CV Action				
CV Action (Any)	53 (66.3)	48 (61.5)	30 (62.5)	0.81
Mean CV actions per year	0.41 (0.45)	0.22 (0.30)	0.35 (0.38)	0.008
Referrals (Any)	28 (35.0)	10 (12.8)	14 (29.2)	0.005
Mean referrals per year	0.11 (0.17)	0.03 (0.09)	0.09 (0.16)	0.001
Tests (Any)	41 (51.3)	36 (46.2)	25 (52.1)	0.75
Mean tests per year	0.20 (0.25)	0.10 (0.16)	0.18 (0.22)	0.02
Medications (Any)	23 (28.8)	30 (38.5)	13 (27.1)	0.30
Mean medications per year	0.11 (0.22)	0.09 (0.14)	0.08 (0.16)	0.79
≥3 CV actions	18 (22.5%)	11 (14.1%)	7(14.6%)	0.32

*Differences between the groups

Table 2. Patient Characteristics by number of CV Actions

Table 2. Patient Characteristics by number of CV Actions

	<3 CV Actions	≥3 CV Actions	p
N (%)	170 (82.5)	36 (17.5)	
Age (SD) yrs	42.5 (6.0)	42.9 (5.5)	0.91
BMI (SD) kg/m ²	29.1 (6.8)	30.1 (6.2)	0.40
Race N (%)			0.68
White	119 (70.0)	23 (63.9)	
Black	35 (20.6)	8 (22.2)	
Other	16 (9.4)	5 (13.9)	
Ethnicity			0.36
Hispanic	9 (5.3)	0 (0)	
Non-Hispanic	161 (94.7)	36 (100)	
Cardiovascular Risk Factors			
Diabetes Mellitus	9 (5.3)	6 (16.7)	0.03
Hypertension	39 (22.9)	16 (44.4)	0.008
Hyperlipidemia	12 (7.1)	7 (19.4)	0.02
Current tobacco use	13 (7.7)	8 (22.2)	0.032
Breast Cancer Treatment			
Anthracycline	66 (38.8)	15 (41.7)	0.75
Radiation	107 (62.9)	26 (72.2)	0.29
Left Sided	47 (27.7)	17 (47.2)	0.02
Right Sided	64 (37.7)	9 (25.0)	0.15

Disclosure(s):

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P1-12-02

Unusual hepatotoxicity with the use of Ribociclib in a premenopausal patient

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BACKGROUND The introduction of cyclin inhibitors in the treatment of metastatic breast cancer has completely changed the natural history of this disease. In the case of premenopausal women, the use of ovarian suppression + aromatase inhibitor or tamoxifen associated with ribociclib demonstrated not only a gain in disease-free survival, but also in overall survival, making it the first choice of treatment for premenopausal women with HER2 negative hormone receptor-positive metastatic breast cancer. Ribociclib is a very well tolerated drug. Neutropenia, the main side effect, is easily manageable in clinical practice. However, one study showed elevation of ALT and AST grade 3 or 4 in 9.3% of patients, while other studies observed that liver dysfunction was dose-limited, and therefore should always be evaluated when using this drug. The pathophysiology of liver injury, not yet fully understood, is attributed to hepatotoxic metabolites or immunogenic effects with damage to hepatocytes similar to the ones triggered by autoimmune hepatitis. There are successful case reports with re-exposure to either the same drug or another CDK4/6 inhibitor. **METHODS** We describe a case of a premenopausal woman with metastatic breast cancer who experienced severe hepatotoxicity with ribociclib use. When her liver function was back to normal, she did a rechallenge with a lower dose of ribociclib and had another liver disfunction. **RESULTS** A 34-year-old premenopausal and nulliparous woman, was diagnosed in 2020 with a hepatic and lymph nodes metastatic HER2 negative hormone receptor-positive invasive breast carcinoma, (ER 90%, PR 90%, HER2 negative, KI-67: 20%). Genetic evaluation showed pathogenic mutation in ATM and VUS in RET, and positive PIK3CA in the tumor. Her first-line treatment was according to the Monaleesa-7 trial with goserelin 3.6 mg every 28 days + letrozole 2.5 mg daily + ribociclib 600 mg/day for 21 days and a break for 7 days, without delays or dose reductions. After 3 months of treatment, with monthly laboratory tests showing normal results, a new PET-CT was performed, which showed a complete metabolic response, both in lymph nodes and in liver lesions (attached figures). In the 4th month of treatment, the patient presented symptoms of malaise, nausea, vomiting, epigastric pain, and jaundice. Laboratory tests showed: ALT 1439 (Reference value – RV: 13-35); AST 1946 (RV:10-49), Total Bilirubin 5 (RV: 1.1), INR 1.8, GGT

500 (RV< 38), ALP 651 (RV: 46-116). After extensive laboratory investigation, the hypothesis of toxicity by ribociclib was raised, which was suspended. She was started with prednisone 60 mg daily associated with ursodeoxycholic acid 300 mg BID with normalization of the hepatic profile after 2 months, when PET-CT was repeated, maintaining response in all lesion foci. It was decided to reintroduce ribociclib, this time at a dose of 200 mg daily, with further laboratory worsening after 2 weeks and definitive suspension of the drug. The patient is currently with non-evidence of disease, using goserelin 3.6 mg every 28 days associated with letrozole 2.5 mg daily. Last PET-CT was performed 15 months after ribociclib discontinuation, maintaining response in all lesions. **CONCLUSION** Ribociclib is a great therapeutic option for the treatment of HER 2 negative HR+ metastatic breast cancer. It is generally well tolerated, however laboratory monitoring should be performed throughout the treatment period. Hepatotoxicity, although rare, may occur, with improvement after discontinuation of the drug.

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P1-12-03

Antidiarrheal prophylaxis with loperamide for patients with lymph node-negative (N0) or micrometastatic (N1mi), HER2-positive breast cancer who received adjuvant pyrotinib plus nab-paclitaxel: a randomized sub-study of PHAEDRA

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Background: Diarrhea is the most common adverse event of pan-HER tyrosine kinase inhibitors. There is no consensus on therapeutic or prophylactic strategy of pyrotinib-related diarrhea. PHAEDRA is an ongoing multicenter, single-arm, phase II trial conducted to evaluate adjuvant pyrotinib plus nab-paclitaxel for patients with low-risk HER2-positive breast cancer. Here, we reported the results from the sub-study of PHAEDRA, which investigated the effect of

different prophylactic strategies with loperamide for diarrhea. Methods: In PHAEDRA, patients with N0/N1mi, HER2-positive invasive breast cancer and primary tumor ≤ 3 cm received nab-paclitaxel 260 mg/m² once every 3 weeks for 12 weeks and pyrotinib 400 mg once daily for one year within 90 days after surgery. In the sub-study, patients were randomly assigned to receive loperamide 4 mg three times a day on days 1-7 and twice a day on days 8-21 (cohort A) or days 8-42 (cohort B) since the initiation of adjuvant therapy. The primary endpoint of the sub-study was the incidence of grade ≥ 3 diarrhea. Results: Between January 2021 and May 2022, the enrollment of 120 patients in the sub-study was completed. Grade ≥ 3 diarrhea was reported in 18 (30%) of 60 patients in cohort A and 19 (32%) of 60 patients in cohort B. The median time to first grade ≥ 3 diarrhea was 4.5 days (IQR, 1.0-6.5) in cohort A and 4 days (IQR, 1.0-6.0) in cohort B. The median number of grade ≥ 3 diarrhea episodes was 1 (IQR, 1-1) in both cohorts. Three (5%) patients in each cohort had constipation events, respectively, which were all grade 1 or 2. One (2%) patient in cohort A and two (3%) in cohort B had dose reductions of loperamide due to constipation, and no patients discontinued loperamide. One (2%) patient in cohort A had dose reduction of pyrotinib and one (2%) in each cohort discontinued pyrotinib due to diarrhea. Conclusions: The effects of both loperamide regimens on antidiarrheal prophylaxis were consistent with that of loperamide prophylaxis in the CONTROL trial, but with extremely fewer constipation events. Long-course and short-course loperamide prophylaxis showed numerically similar incidence of grade ≥ 3 diarrhea. Proactive diarrhea management can promote the full-dose and full-course treatment with pyrotinib. It is still necessary to develop more effective antidiarrheal prophylaxis regimens for pan-HER tyrosine kinase inhibitors.

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Side Effects of the mRNA COVID-19 Vaccines in Women Treated for Breast Cancer

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Background

The introduction of the novel COVID-19 vaccination raised concerns regarding side effects from patients who had undergone breast cancer treatment. Lymph node swelling after the mRNA vaccines (Moderna, Pfizer) is a distressing side effect for women treated for breast cancer as it may indicate cancer progression or recurrence. Patients at risk of breast cancer-related lymphedema (BCRL) are fearful that lymph node swelling from the vaccine could incite or worsen BCRL. Data investigating associated side effects in this population is essential for patient education and future self-advocacy.

Purpose

The purpose of this study was to elicit side effects associated with the COVID vaccine in women treated for breast cancer.

Methods

4,945 surveys were sent to women over the age of 18 who had received breast cancer treatment and had been prospectively screened for BCRL with perometry. 621 participants who received an mRNA vaccine and responded to the survey were included in analysis, 469 of whom completed booster dose surveys. Participants were asked about type and duration of side effects after each vaccine dose. Solicited side effects included injection site soreness, swelling, or redness; swelling, numbness, or heaviness of the arm; generalized muscle soreness (GMS); fatigue; headache; joint pain; chills; nausea; vomiting; fever; Bell's palsy; axillary or supraclavicular lymph node swelling; other; or none of the above. We computed frequencies and the median duration of side effects for each dose. To investigate predictors of side effects, we fit multivariable logistic regression models separately for each side effect, with random effects for participants to account for clustered responses. We considered significant predictors those with $p < 0.05$.

Results

Of the 621 participants, the median follow-up time between breast surgery and date of first vaccine dose was 69 months. The distribution of the top 5 side effects is presented in Table 1. Of note, the majority of participants who reported lymph node swelling (9.8% dose 1, 12.9% dose 2, 11.3% dose 3) reported it in the axilla ipsilateral to the vaccine (54.1% D1, 61.3% D2, 71.7% D3). Lymph node swelling was also reported in the axilla contralateral to the vaccine (45.9% D1, 45% D2, 24.5% D3), supraclavicular region ipsilateral (29.5% D1, 26.3% D2, 32.1% D3) and contralateral (18% D1, 18.8% D2, 9.4% D3) to the vaccine. Older patients reported each side effect significantly less frequently. Those who had received neoadjuvant chemotherapy reported significantly more GMS and headache than those who did not. Those who had received regional lymph node radiation were less likely to report GMS, as were patients who had sentinel lymph node biopsies (vs. no lymph node surgery). The median duration of side effects for all three doses was 48 hours or less, with the plurality (41.0% D1, 38.7% D2, 44.1% D3) of participants reporting side effects lasting 24 hours or less. While all side effects apart from injection site soreness were significantly more common in the second than the first doses, the duration of side effects only increased for 28.1% of participants.

Conclusion

Over 86% of women treated for breast cancer may experience at least one side effect after any dose of the COVID-19 vaccine. This data, collected specifically for patients with breast cancer, will help enhance guidelines for structured and universal education regarding additional doses of the vaccine in the future. This will allow patients to better understand COVID vaccine side effect profiles after breast cancer treatment and self-advocate prior to future doses.

Table 1. Top 5 Side Effects Reported

	Injection site soreness	Fatigue	Generalized muscle soreness (GMS)	Headache	Chills
Dose 1	76.0% (472/621)	42.7% (265/621)	23.0% (143/621)	18.4% (114/621)	9.5% (59/621)
Dose 2	76.2% (473/621)	59.3% (368/621)	31.9% (198/621)	32.4% (201/621)	23.7% (147/621)
Dose 3	69.9% (328/469)	44.3% (208/469)	24.5% (115/469)	21.5% (101/469)	19.2% (90/469)

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Brooke Juhel, BS: No financial relationships to disclose

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The Impact of Adjuvant Chemotherapy, Including Taxanes, on Breast Cancer-Related Lymphedema Risk

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BACKGROUND: Adjuvant chemotherapy, particularly taxane-based chemotherapies, which are used to treat high-risk breast cancers, has been shown to be efficacious in prolonging overall survival. However, the impact of such therapies on risk of breast cancer-related lymphedema (BCRL) is yet to be fully understood. Available studies have contradictory findings as to whether or not taxanes increase BCRL risk. Unfortunately, methodological flaws, such as not incorporating a preoperative baseline arm volume measurement or utilizing flawed measurement techniques and diagnostic criteria, result in misdiagnosis of the primary outcome of BCRL and it is therefore difficult to draw conclusions from these studies. As such, a more comprehensive understanding of the potential risks associated with these treatment modalities can improve quality of care as patients are better prepared to face a potentially devastating sequela of breast cancer treatment. **PURPOSE:** The purpose of this study is to determine if chemotherapy administered in the adjuvant setting is an independent risk factor of BCRL, as well as to assess any specific risks of taxane-based chemotherapy on BCRL. **METHODS:** From

2005 to 2021, 2049 patients treated for breast cancer were enrolled in a prospective BCRL screening trial and screened from preoperative baseline through last follow-up. Screening included objective arm volume measurements via perometry. Chemotherapy data and clinicopathological and demographic characteristics were collected directly from the electronic medical record. Patients who had not received neoadjuvant chemotherapy were eligible for the current study; they were classified based on whether they had received taxane-based chemotherapy, non-taxane chemotherapy only, or no chemotherapy. Relative volume change (RVC) increase $\geq 10\%$ from preoperative baseline >3 months postoperatively was used to define BCRL. Patients were censored at cancer recurrence or most recent clinic visit. We fit a Cox regression model to estimate adjusted hazard ratios (aHR) for BCRL. The model was adjusted for baseline BMI, axillary lymph node dissection (ALND), regional lymph node radiation (RLNR), age at diagnosis, and smoking history. RESULTS: The eligible cohort included 1759 patients, including 564 (32%) who received taxane-based chemotherapy and 104 (6%) who received non-taxane chemotherapy only. The median follow-up time for the entire cohort was 58 months. 141/1759 (8%) of patients developed BCRL. The median time to develop BCRL was 21 months post-operatively. Compared to no chemotherapy, the aHR associated with taxane-based chemotherapy was 1.04 (95% CI 0.37, 1.8; $p = 0.62$). Compared to no chemotherapy, the aHR for non-taxane chemotherapy was 0.82 (95% CI 0.67, 1.6; $p = 0.86$). There was no significant difference between taxane and non-taxane therapies in terms of BCRL risk ($p = 0.55$). ALND, RLNR, and high BMI remained independent risk factors for BCRL, consistent with the published literature. CONCLUSION: The receipt of adjuvant chemotherapy and specifically adjuvant taxane-based chemotherapy were not associated with increased risk of BCRL in this cohort of 1759 patients at risk of and prospectively screened for BCRL.

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5:00 PM - 6:15 PM

P1-12-06

Prevalence and Spectrum of Manifestations of Tamoxifen Retinopathy as Assessed by Multimodal and Ultra-widefield Retinal Imaging

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Introduction Tamoxifen, a selective estrogen antagonist, is part of standard adjuvant therapy for hormone receptor-positive breast cancer. In addition to known systemic toxicities, well-described retinotoxic effects include peripheral and macular crystalline deposits, pseudocystic foveal cavitations, as well as an increased risk of developing punctate pigmentary changes. However, the true prevalence of retinal toxicity is unclear, with the literature reporting rates between 1.5% and 11%, with significant geographic and temporal discrepancies depending on choice of screening modality. Advances in retinal imaging, specifically spectral domain and swept-source optical coherence tomography (OCT), have led to more sensitive diagnosis of toxicity. However, the field of view of commercially available OCT is limited 30 degrees, whereas ultra-widefield (UWF) imaging can image up to 200 degrees of the retina, albeit with a superficial rather than a cross-sectional view. Therefore, UWF imaging may visualize previously underreported signs of toxicity in the peripheral retina such as pigmentary changes better than macula-focused imaging alone like OCT. As such, the goals of the present study were to: 1) determine the prevalence of tamoxifen retinopathy in our cohort, a major northeastern metropolitan area, based on multimodal retinal imaging including macular OCT, fundus photos, and autofluorescence; 2) determine whether the additional field of view captured in UWF imaging contributes to the diagnosis of tamoxifen retinopathy by assessing for peripheral findings, most specifically pigmentary retinopathy. **Methods** This is a retrospective study of patients who visited the retina service of a single academic tertiary referral center between September 2012 and November 2021. Female patients initiated on tamoxifen for at least 6 months before their first retinal exam were identified. Patients with poor image quality, prior vitreoretinal surgery, retinal laser, or confounding pathology such as severe diabetic retinopathy were excluded. Two independent graders performed blinded review of OCT images for evidence of macular toxicity and UWF images for signs of central and peripheral toxicity, and the prevalence of the latter was compared to age- and gender-matched controls. A two-tailed t-test was used to compare ages of patients in the two cohorts. A one-tailed two proportion Z-test was used to determine if eyes in the tamoxifen cohort exhibited a greater rate of peripheral pigmentary changes. **Results** 252 eyes from 128 patients were included in the tamoxifen cohort, and 244 eyes from 125 patients in the control cohort. The average age at first retinal imaging in the tamoxifen cohort (61.1 ± 1.1 , $n=128$) versus the control cohort (61.0 ± 1.3 , $n = 125$) was not significantly different ($p=0.95$). 4 eyes (1.6%) from 2 patients (1.6%) had evidence of definitive tamoxifen retinopathy. One patient had crystalline maculopathy bilaterally visible on OCT and UWF imaging and another had macular pseudocystic cavitations bilaterally on OCT. Neither patient had peripheral findings on UWF. 31 eyes (12.4%) among 16 (12.5%) patients in the tamoxifen cohort displayed peripheral reticular pigmentary changes, compared to 59 eyes (24.2%) among 30 patients (24.0%) in the control group. The rate of peripheral pigmentary change in the tamoxifen cohort was not significantly greater than in the control group ($p=0.99$). **Conclusion** Only 2 patients had definitive tamoxifen retinopathy findings, which were both

concentrated in the macula and clearly visible on OCT imaging. Given the absence of meaningful UWF changes, macular OCT may be the most valuable tool in diagnosing tamoxifen retinopathy. Our prevalence (1.6%) diverges from higher prevalences reported by studies screening with advanced retinal imaging (10-12%), though notably reflects a very different ethnic and geographic population compared with other work. Further large population studies are needed.

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P1-12-07

Management of genitourinary symptoms in breast cancer patients: An updated systematic review of available evidence from randomized trials

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Background: Genitourinary symptoms (GUS) such as vaginal dryness, dyspareunia, itching, urinary incontinence, urinary tract infections and discharge are common in patients with breast cancer (BC). Optimal management of GUS remains unclear. Our group previously published a systematic review (SR) on GUS management in 2014 which showed a paucity of RCT evidence addressing this knowledge gap (Mazzarello et al. 2015). We performed an updated SR to

assess if more prospective trial data had been published in the past 7 years to inform management of this common complication of BC. Methods: EMBASE, Ovid Medline and the Cochrane Library were searched for RCTs evaluating treatments for GUS in BC patients from September 2014 to December 2021. A PICOS (population, intervention/comparators, outcomes and study design) framework was utilized. Population: women with breast cancer. Intervention/comparators: all forms of oral, intra-vaginal and topical hormonal and non-hormonal treatments. Outcomes of interest: improvements in vaginal symptoms (e.g., dryness, pain, dyspareunia, itching); vaginal hormone response, measured by validated scales [e.g., Vaginal Health Index (VHI) and Vaginal Maturation Index (VMI)] and quality of life [e.g., Female Sexual Function Index (FSFI)]. Study design: only RCTs were included. Two independent reviewers performed the tasks of study selection, data collection, and risk of bias assessment. Results: Of 842 unique citations identified (412 from this update, 430 from previous SR), eight studies (n = 539 patients) met inclusion criteria. Interventions included 0.005% estriol gel (EG; n=50 patients), intravaginal testosterone (IVT; n=21), intravaginal prebiotic (n=13), hyaluronic acid (HA; n=12), polyacrylic acid (PA; n=25), pH-balanced gel (two studies; n=118), Replens[®] (n=24) and Lidocaine gel (n=22). These interventions were compared to placebo/saline/usual care (n=254). One study had three arms comparing prebiotics, HA and usual care. Study sample sizes ranged from 44 to 136 patients. Given the heterogeneity of the studies, a narrative synthesis was performed. Compared to placebo, FSFI total score was significantly improved by all interventions except IVT (which demonstrated significant improvement in only the satisfaction domain) and 4% aqueous lidocaine before vaginal penetration (which improved significantly all domains except for orgasm). FSFI changes were not reported for Replens[®]. Significant improvements in vaginal hormone responses (VHI and VMI) were reported for 0.005% EG and pH-balanced gel; however, no significant effects were found for IVT, HA or prebiotics. Vaginal symptoms (vaginal dryness, dyspareunia and pruritis) were significantly improved by EG, IVT, and PA. Vaginal symptoms were significantly improved in the single study of pH-balanced gel that reported this outcome. Conclusion: GUS is reported in 75% of BC patients but despite its frequency, the management of GUS remains a challenging issue for patients and health care providers. Due to study heterogeneity, there remains insufficient RCT evidence to define optimal therapy. More prospective trials comparing commonly used interventions are needed. Keywords: Genitourinary symptoms, Topical moisturizers, Intra-vaginal testosterone

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P1-12-08

Biomarker analysis of hepatotoxicity in a Phase II study of nivolumab, abemaciclib and endocrine therapy in patients with HR-positive, HER2-negative breast cancer:

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Background Previously, we reported the clinical outcomes of the combination of anti-PD-1 Ab, cyclin-dependent kinase 4/6 inhibitors, and endocrine therapy (ET) in patients with ER positive/HER2 negative advanced breast cancer in SABCs2020; biomarker analysis has been performed to provide insight into the hepatotoxicity frequently observed in the study. Methods Subjects received 240 mg nivolumab IV on days 1 and 15, 150 mg abemaciclib PO twice daily, and either 500 mg fulvestrant (FUL) on days 1, 15, 29, and every 4 weeks thereafter (FUL cohort) or 2.5 mg letrozole (LET) once daily (LET cohort). The primary endpoint was objective response rate and secondary endpoints included toxicity evaluated in the CTCAE along with an exploratory endpoint as related to the biomarker analysis. Archival tumor tissues were collected before study entry and blood and stool samples were collected at baseline and on cycle3 day1. Tumor tissues were subjected to IHC analysis and RNA sequencing followed by subtyping using NGS. High throughput cytokine analysis using ELISA-based assay were performed with serum samples and cell sorting analysis of PBMC was performed with FACS. Results From June 2019 to December 2019, 17 subjects were enrolled (FUL cohort [n = 12], LET cohort [n = 5]). The study was prematurely closed due to safety concerns such as hepatotoxicity and interstitial lung disease. AEs \geq Grade 3 were observed in 91.7% and 100% of patients in the FUL and LET cohorts, respectively. The most frequent AEs \geq Grade 3 were elevated liver function tests (LFT; FUL cohort: 50.0%, LET cohort: 60.0%). Serum cytokine analysis from the subjects with severe hepatotoxicity indicated cytokine storm with elevations of sCD30/TNFRSF8, IL-11, -34, Pentraxin-3, sTNF-R1, -R2, TSLP, which was supported by the findings of reduction of effector regulatory T cells in PBMC. IHC study in liver biopsy from three subjects with the toxicity revealed infiltration of CD8+ T cells and FOXP3+ T reg into the liver, suggesting the immune related liver injury upon the treatment with nivolumab and abemaciclib. HLA typing was performed in the 17 patients but no association between HLA type and ILD or hepatotoxicity were observed. Conclusions The frequent and severe immune related hepatotoxicity induced by the combination of anti-DD-1 and CDK 4/6 inhibitors might have been

an immune-boosting therapy as suggested in the preclinical studies. This study was supported by the Ono Pharmaceutical Co., LTD. The registration number of the study is UMIN000036970.

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P1-12-09

WITHDRAWN - An Evaluation of CDK4/6 Inhibitors Administered in the Adjuvant Setting and Risk of Breast Cancer-Related Lymphedema

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BACKGROUND: Breast cancer-related lymphedema (BCRL) affects approximately 1 in 5 women treated for breast cancer in the United States. Well determined risk factors include axillary lymph node dissection (ALND), regional lymph node radiation (RLNR), and BMI > 25 at diagnosis. The monarchE trial showed benefits of the CDK4/6 inhibitor, abemaciclib, given in the adjuvant setting for patients with high-risk HR+/HER2- early breast cancer. We have previously demonstrated that CDK4/6 inhibitors can be associated with lymphedema in the metastatic setting. However, the impact of adjuvant CDK4/6 inhibitors on development of BCRL is not known. **PURPOSE:** The purpose of this study is to investigate the impact of CDK4/6 inhibitors on BCRL risk in a prospectively screened cohort of patients treated with these agents in the adjuvant setting compared to those who did not receive CDK4/6 inhibitors. **METHODS:** Patients treated for breast cancer were screened prospectively from preoperative baseline for the control group and pre-drug baseline for the study cohort receiving CDK4/6 inhibitors through last follow-up. Screening included objective arm volume measurements via perometry. CDK4/6 inhibitor data and clinicopathological and demographic characteristics were collected directly from the electronic medical record. The control cohort, which did not receive CDK4/6 inhibitors, consisted of patients with ER/PR+, HER2- breast cancer, 3+ malignant lymph nodes, arm measurement data at least 1-year after surgery, and had surgery in 2014 or later. Patients with arm measurement data before and after drug start date were eligible for the current study. Relative volume change (RVC) increase $\geq 10\%$ from preoperative or pre-drug baseline was used to define BCRL. Patients were censored at cancer recurrence, most recent clinic visit, or first follow up date that BCRL was detected. We fit a Cox regression model to estimate adjusted hazard ratios (aHR) for BCRL. The model was adjusted for baseline BMI, ALND, and RLNR. **RESULTS:** The eligible cohort included 98 patients, including 46 (47%) who received CDK4/6 inhibitors and 52 (53%) who did not. The median follow-up time for the entire cohort was 30 months (range 0.36, 93.9 months). 24/98 (24.5%) of patients developed BCRL. The median time to develop BCRL was 16 months (range 0.36, 63.9 months) Compared to the control group, the aHR associated with CDK4/6 inhibitors was 2.08 (95% CI 0.82, 5.24; $p = 0.122$). **CONCLUSION:** The combination of endocrine therapy (ET) and CDK4/6 inhibitors may increase the risk of BCRL compared to ET alone. Further research in larger datasets is needed to validate these hypotheses generating findings, and further refine the efficacy/toxicity ratio of CDK4/6 inhibitors for patients with localized breast cancer.

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P1-12-10

Superior Effectiveness of Plinabulin (Plin) versus No-Treatment for Docetaxel (Doc)-Induced Neutropenia (N) and other Hematologic Complication in Breast Cancer (BC) Patients

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Introduction: Minimizing hematologic complications (HC) in breast cancer patients (pt) increases pt safety and convenience, minimizes financial toxicity and may lower risk for COVID-19 infection. Plin is a novel small molecule which protects bone marrow progenitor stem cells and is non-inferior to Peg for the prevention of chemotherapy-induced neutropenia (CIN) after Doc (Blayney, JAMA Open 2021). In contrast to pegfilgrastim (Peg), Plin (as a single dose per cycle), is given on the same day of chemotherapy, has minimal bone pain and thrombopenia, has anti-cancer efficacy, and could minimize healthcare system touches (Blayney, JAMA Onc 2020; Han, ESMO 2021). Doc 75 mg/m² in BC pts is typically used without G-CSF prophylaxis ('no treatment'). We evaluated Plin's HC preventive effects in comparison to no-treatment in BC patients receiving Doc from published studies.

Methods: The HC endpoints from the 27 early BC patients with at least one NCCN high FN risk factor (N=27) from the phase 3 CIN trial (PROTECTIVE-1, NCT03102606) were compared with No-Treatment (non-prophylactic Peg or G-CSF) in patients receiving 75 mg/m² Doc. Plin was given by 30 minute (min) IV infusion as a single dose each cycle, 30 min after Doc, over 4 cycles. Cycle 1 hematology measurements in Plin-treated pts were taken pre-dose and days 1, 2, 6, 7, 8, 9, 10, 15 and 21 (10 ANC values in cycle 1); and in cycles 2-4 on days 1, 8, 21 and at end of study and were then analyzed by Covance Central Laboratory. No treatment neutropenia data was obtained from published cancer trials with monotherapy Doc 75 mg/m² in two No-Treatment studies with at least weekly blood sampling (Harvey et al., JCO, 2006: ~3-4 draws in cycle 1), or twice-weekly (Dieras et al., Br J Ca, 1996: ~5-6 draws in cycle 1). The HC endpoints were all grade (Gr) N, Gr4N, Gr3/4N, Gr3/4 febrile N (FN), infections, anemia and thrombopenia. Other endpoints were adverse events (AEs) and Quality of Life (QoL with EORTC QLQ-C30).

Results: Baseline demographics were generally comparable between the Plin and No-Treatment literature studies for age, ECOG, and number of prior lines. Gr4N frequency with Plin was 44%, 11%, 3% and 0% in cycles 1, 2, 3 and 4 respectively, thus no added Gr4N was observed after cycle 4. Plin had significantly less neutropenia, and numerically less anemia and thrombopenia vs No-Treatment. QoL with plinabulin remained unchanged over 4 cycles.

Conclusion: Blood sampling in the No-Treatment studies (Harvey and Dieras) were infrequent, and likely underestimated the true Gr4N frequency. Despite a higher frequency of ANC sampling in cycle 1, Plin was superior vs No-Treatment for Doc-induced neutropenia and HC, while maintaining QoL and with minimal AE and bone pain burden. The same day dosing combined with the avoidance of AEs typically leading to healthcare touches, provides a distinct benefit with Plin for the prevention of Doc-induced neutropenia.

Hematologic Complications

	All GrN	Gr 3/4N	Gr4N	Gr3/4 FN	Gr3/4 Infections	Gr3/4 Anemia	Gr3/4 Thrombopenia
Plin (N=27)	88.9%	70.4%	48.1%	3.7%	0%	7.4%	0%
Dieras et al (N=39)	97%	95%	82%	7.7%	0%	13%	3%
<i>p-value Plin vs Dieras</i>	0.30	0.04*	0.004*	0.64	>0.999	0.70	>0.999
Harvey et al (N=190)	94%	83.7%	67.9%	7.4%	3.2%	8.9%	4.2%
<i>p-value Plin vs Harvey</i>	0.40	0.09	0.04*	0.70	>0.999	>0.999	0.60

*p-value is significant in favor of Plin

Disclosure(s):

Doug Blayney, n/a: BeyondSpring Pharmaceuticals, Inc.: Principle Investigator (Ongoing)

Jasmine Wells, n/a: BeyondSpring Pharmaceuticals, Inc.: Salary (Ongoing)

Stephen Duprez, n/a: BeyondSpring Pharmaceuticals, Inc.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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P1-12-11

Real-world incidence and management of diarrhea secondary to pyrotinib in patients with HER-2 positive breast cancer

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Objective: Pyrotinib, an oral irreversible pan-HER receptor tyrosine kinase inhibitor, showed promising efficacy and manageable safety profiles in the treatment of HER-2 positive breast cancer. Diarrhea is the most common adverse event associated with pyrotinib. This study aimed to evaluate the incidence and management of diarrhea secondary to pyrotinib in Chinese patients with HER-2 positive breast cancer.

Methods: In this prospective real-world study, consecutive patients aged over 18 with HER-2 positive breast cancer and an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0-2 who planned to receive pyrotinib-based regimens for at least 21 days were included. Pyrotinib-treated patients and those with preexisting gastrointestinal conditions were excluded. There were no planned management strategy or primary prophylaxis for diarrhea,

while loperamide, montmorillonite powder or Golden Bifid (a live combined Bifidobacterium, Lactobacillus and Streptococcus Thermophilus tablet) were recommended. Treatment was given in accordance with routine clinical practice by investigators. For patients developed grade 3 or higher diarrhea, pyrotinib was suspended until the diarrhea improving to grade 1 or less, and secondary prophylaxis (such as loperamide, loperamide plus montmorillonite powder, or loperamide plus Golden Bifid) was administrated before pyrotinib resumption. The baseline characteristics of patients and details of diarrhea (onset time, duration, severity according to the National Cancer Institute-Common Terminology Criteria for Adverse Events version 4.03, treatment and prognosis) were collected.

Results: Between August, 2020 and April, 2022, a total of 107 eligible patients were included, with a median age of 54 (range: 25-81) years old. Most patients (93.5%) had an ECOG PS of 0-1, and 51 patients (47.7%) were hormone receptor positive. A total of 46 patients (43.0%) received pyrotinib in the early stage and 61 (57.0%) in the advanced stage. Sixty-nine cases (64.5%) used pyrotinib-containing combination therapy (including 40 combined with capecitabine, 13 combined with trastuzumab, and 16 combined with other regimens), and 38 (35.5%) received pyrotinib alone. Ninety-eight cases (91.6%) reported diarrhea of any grade. Grade 1, 2 and 3 diarrhea occurred in 78 (72.9%), 9 (8.4%) and 11 (10.3%) patients, respectively. The median time to first onset of diarrhea of any grade was 2.5 (1-12) days, and the duration of first onset was 4 (1-24) days. The cumulative duration of diarrhea was 10 (1-60) days. Sixty-four, two, thirty, two patients used loperamide alone, montmorillonite powder alone, loperamide plus montmorillonite powder and loperamide plus Golden Bifid for the treatment of diarrhea, respectively. Eleven (10.3%) and seven (6.5%) patients experienced pyrotinib dose reduction and pyrotinib discontinuation. For 11 patients suffered grade 3 diarrhea, the median time to first onset of grade 3 diarrhea was 9 (4-14) days. Two, four and five patients administrated loperamide, loperamide plus Golden Bifid and loperamide plus montmorillonite powder as their secondary prophylaxis. Ten of eleven had grade 1 or 2 diarrhea after secondary prophylaxis, while one patient still suffered grade 3 diarrhea. All of them (11/11) held the pyrotinib dose. The incidence rate of constipation of all patients was 3.7%, which did not increase after treatment or secondary prophylaxis for diarrhea.

Conclusion: In this study, the majority of patients developed pyrotinib associated diarrhea, and most of them were grade 1. About 10% patients reported grade 3 diarrhea, which can be managed by loperamide-based treatment and secondary prophylaxis.

Table 1. Baseline characteristics of patients

Variables	All (n=107)	With grade 3 diarrhea (n=11)
Age (years), median (range)	54 (25-81)	52 (31-64)
ECOG PS, n (%)		
0-1	100 (93.5)	11 (100)
2	7 (6.5)	0
Hormone receptor status, n (%)		
Positive	51(47.7)	6 (54.5)
Negative	56 (52.3)	5 (45.5)
With visceral metastases, n (%)	29 (27.1)	0
With nonvisceral metastases, n (%)	71 (66.4)	6 (54.5)
Metastatic site, n (%)		
Lung	20 (18.7)	0
Liver	12 (11.2)	0
Brain	9 (8.4)	0
Bone	29 (27.1)	1 (9.1)
Lymph nodes	49 (45.8)	6 (54.5)
Others	14 (13.1)	2 (18.1)
Number of metastatic sites, n (%)		
1	37 (34.6)	4 (36.3)
2	20 (18.7)	1 (9.1)
≥3	21 (19.6)	1 (9.1)
Previous radiotherapy, n (%)	29 (27.1)	3 (27.3)
Previous (neo)adjuvant therapy, n (%)	69 (64.5)	10 (90.9)
Previous anti-HER2 therapy, n (%)		
Trastuzumab	39 (83.2)	9 (81.8)
Pertuzumab	62 (57.9)	9 (81.8)
Lapatinib	1 (0.9)	0
Treatment setting of pyrotinib, n (%)		
Early stage	46 (43.0)	9 (81.8)
Advanced stage	61 (57.0)	2 (18.2)
Treatment pattern, n (%)		
Pyrotinib-containing therapy	69 (64.5)	6 (54.5)
Combined with capecitabine	40 (37.4)	1 (9.1)
Combined with trastuzumab	13 (12.1)	4 (36.4)
Combined with others	16 (15.0)	1 (9.1)
Pyrotinib alone	38 (35.5)	5 (45.5)
Starting dose of pyrotinib, n (%)		
160mg	1 (0.9)	0
240mg	3 (2.8)	0
320mg	13 (12.1)	5 (45.5)
400mg	90 (84.1)	6 (54.5)

ECOG PS: Eastern Cooperative Oncology Group performance status; HER-2: human epidermal growth factor receptor 2.

Table 2. Summary of patients developed diarrhea

Variables	All (n=107)	Loperamide (n=64)	Montmorillonite powder (n=2)	Loperamide plus montmorillonite powder (n=30)	Loperamide plus Golden Bifid (n=2)
Patients developed diarrhea, n (%)	98 (91.6)	64 (100)	2 (100)	30 (100)	2 (100)
Maximum toxicity, n (%)					
Grade 1	78 (72.9)	55 (85.9)	2 (100)	21 (70)	0
Grade 2	9 (8.4)	3 (4.7)	0	5 (16.7)	1 (50.0)
Grade 3	11 (10.3)	6 (9.4)	0	4 (13.3)	1 (50.0)
Time to first onset of diarrhea, days, median (range)	2.5 (1-12)	3 (1-12)	2 (1-3)	2.5 (1-11)	1 (1-1)
Duration of first onset of diarrhea, days, median (range)	4 (1-24)	3 (1-15)	7 (6-8)	5 (2-24)	2.5 (3-5)
Cumulative duration of diarrhea, days, median (range)	10 (1-60)	8 (1-55)	22.5 (15-30)	14 (4-60)	17.5 (16-19)
Actions required due to diarrhea, n (%)					
Dose hold	89 (83.2)	57 (89.1)	0	22 (73.3)	1 (50.0)
Dose reduction	11 (10.3)	5 (7.8)	1 (50.0)	4 (13.3)	1 (50.0)
Treatment discontinuation	7 (6.5)	2 (3.1)	1 (50.0)	4 (13.3)	0

Table 3. Summary of patients developed grade 3 diarrhea

Variables	All (n=11)	Loperamide (n=2)	Loperamide plus Golden Bifid (n=4)	Loperamide plus montmorillonite powder (n=5)
Time to first onset of grade 3 diarrhea, days, median (range)	9 (4-14)	5 (4-6)	8.5 (8-14)	9 (8-11)
Dose hold, n (%)	11 (100)	2 (100)	4 (100)	5 (100)
Severity of diarrhea after secondary prophylaxis, n (%)				
Grade 1	8 (72.7%)	2 (100)	2 (50.0)	4 (80.0)
Grade 2	2 (18.2%)	0	1 (25.0)	1 (20.0)
Grade 3	1 (9.1%)	0	1 (25.0)	0
Time to first onset of diarrhea after secondary prophylaxis, days, median (range)	6 (2-12)	7.5 (3-12)	5.5 (3-7)	6 (2-9)
Cumulative duration of diarrhea after secondary prophylaxis, days, median (range)	7 (2-12)	5 (2-8)	4.5 (4-9)	8 (6-12)

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P1-13-01

Targeting RRM2 for the treatment of palbociclib resistant breast cancer

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Hormone receptor (HR) positive breast cancer (BC) is a prevalent disease accounting for almost 2 million new cases globally. Almost 70-80% of breast cancer patients are women with a positive score for the estrogen receptor (ER). HR positive BCs of all stages are selectively treated with endocrine therapy targeting ER activity. Intrinsic and acquired resistance are common phenomena, impacting patient outcomes negatively. Palbociclib is an FDA approved checkpoint inhibitor for the treatment of HR+/HER2- breast cancer in combination with aromatase inhibitors or selective estrogen receptor degraders. However, patients responding well to the therapy in the beginning, lose sensitivity to palbociclib with time. Ribonucleotide reductase (RR) is a rate limiting enzyme in DNA synthesis consisting of two subunits RRM1 and RRM2. In our previous study, we have shown that RRM2 is upregulated in ER positive tamoxifen resistant BC. Previously, we have also reported that didox (DDX) which is a unique RRM2 enzyme inhibitor can significantly halt malignant breast cancer cell division in combination with an anthracycline drug doxorubicin by targeting RRM2, mutant p53 and NFkB regulatory proteins. In this study, we target palbociclib resistant BC with DDX to circumvent palbociclib resistance. For this purpose, we have developed palbociclib resistant ER positive MCF7 and ER negative MDA-MB-468 breast cancer cell lines. Here, we report morphological changes in parental as compared to palbociclib resistant cells after treatment with palbociclib alone, DDX alone or with palbociclib as compared to non-treated cells. Cell proliferation studies confirm the synergistic combinatorial effect of palbociclib and DDX compared to palbociclib or DDX alone. We also report that DDX alone or in combination with palbociclib downregulates cell cycle and NFkB proteins in palbociclib resistant ER positive MCF7 and ER negative MBA-MB-468 breast cancer cell lines.

Disclosure(s):

Nahid Sultana, n/a: University of the Pacific: University (Ongoing)

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The Aberrant Activity of Retrotransposon Elements Mediates the Chemo-tolerant Persister Cells Relapse in TNBC

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The emergence of acquired drug resistance through therapeutic treatment remains a critical threat to efficient chemotherapy, target therapy, or immune therapy. These resistant cancer cells most often lead to relapse or metastasis. The development of drug resistance is a multi-step evolutionary adaptation for cancer cells. Tumor heterogeneity, cancer cells' plasticity, and microenvironment contribute to the resistant clone's formation. Therefore, a time-lapse adaptation model is critical to define the mechanism of drug resistance evolution. Recently, several studies have revealed that the initial acquired drug resistance might be conferred by transient events, such as drug-tolerant persisters (DTP) that might occur in a subpopulation of the cancer cells at the early stage of the treatment, which were then followed by the transcriptomic reprogramming and secondary-wave genetic mutations in the progression of resistance development. In the clinic, chemotherapy is still the mainstream treatment for TNBC, and one of the primary chemo agents is doxorubicin. Although the initial responsive rate of doxorubicin-based chemotherapy is up to 70%, it is well recognized that TNBC cells usually generate an evolutionary adaptive response that can result in the acquired drug-resistance and multi-drug resistant phenotypes. To date, numerous different mechanisms of acquired chemo-resistance have been reported, but the vast majority of these results have been derived from the continuous-high-dose-exposure acquired resistant cell line models. Since the chemo-treatment dosage in these artificial models is well above what is physiologically achievable in patients, few of them can mimic the actual situation of resistance development or improve the clinical trial outcomes. Moreover, most of these studies only characterized the terminal resistant cells, which are challenging to be resensitized because of their dominant genetic mutations. In this study, we hypothesize that the TNBC chemo-resistant cells may derive from the early-stage reversible chemo-tolerant "DTP-like" (CTP) cells, and early-stage epigenetic landscape perturbation might determine the progression of chemo-resistance development. To test the

hypothesis and overcome the previous model limitations, based on the clinical drug exposure kinetics for doxorubicin, we developed an in vitro “pulsing-treatment CTPs regrowth” model (referred to as CTP model), which could mimic the clinical treatment and provide therapeutically relevant insights into the initial drug-induced stress response and resistance development. Leveraging this CTP model, we are able to define the early event for drug response, in which the doxorubicin-treated cells showed a senescence-like phenotype, and the interferon alpha (type I) pathway was activated. Furthermore, unexpectedly, we found that the expression of HERVs was significantly activated but LINE1s not. To further explore the TEs reactivation, we did the single cell RNA-seq for 0h, 2h, and 4 days samples. With a novel bioinformatic workflow, we integrated the TE expression information with coding genes mRNA profiling from the same single cell RNA-seq dataset and identified the IFN-enriched cluster had higher expression of HERVs. Herein, a subpopulation of HERV^{high} cells with IFN activation was identified as a “hot-cluster” which might be the early determinant in the resistance evolution.

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Xinluo Luo, PhD: No financial relationships to disclose

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Establishment and characterization of two T-DM1-resistant, ER+/HER2+ breast XPDX models developed sequentially from the same patient with differential in vivo sensitivity to trastuzumab deruxtecan (DS-8201a)

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Background: Trastuzumab deruxtecan (DS-8201a) is an antibody-drug conjugate (ADC), consisting of a humanized anti-HER2 (human epidermal growth factor receptor 2) monoclonal antibody linked to a topoisomerase I inhibitor payload using a cleavable tetrapeptide-based linker, approved for the treatment of HER2+ metastatic breast cancer patients refractory to anti-HER2 therapy including T-DM1. While some mechanisms for clinical T-DM1 resistance have been identified, less is known about innate or acquired resistance to DS-8201a. We established two XenoSTART Patient-Derived Xenograft (XPDX) models from tissue samples collected two years apart from a patient with ER+/HER2+ breast cancer before and after HER2 directed therapies. These models designated ST4565 and ST4565C were developed and characterized for receptor expression, genomic alterations, and in vivo drug sensitivities toward multiple chemotherapies and targeted agents, including T-DM1 and DS-8201a. Methods: Models ST4565 and ST4565C were established from breast samples collected from a Caucasian

female with ER+/HER2+ metastatic breast cancer; ST4565 was collected at age 35 prior to therapy and ST4564C at age 37 following several treatment regimens including 5-FU/doxorubicin/cyclophosphamide, docetaxel/trastuzumab/pertuzumab, and T-DM1/anastrozole. Both were grown subcutaneously in female athymic nude mice supplemented with exogenous estradiol. The resulting models were passaged, and receptor expression confirmed immunohistochemically; genomic analysis, including WES and RNAseq, was performed to further characterize the models. For in vivo studies, both models were evaluated using several chemotherapy and targeted agents alone and in combination including: trastuzumab, pertuzumab, T-DM1, DS-8201a, neratinib, tucatinib, fulvestrant, alpelisib, sacituzumab, and irinotecan. In vivo study endpoints included tumor volume and time from treatment initiation with %T/C values and tumor regression reported at study completion; a T/C of $\leq 20\%$ versus control was considered sensitive. Tumor regression ($\%T/C < 0$) versus Day 0 tumor volume was also reported. Results: ST4565 and ST4565C retained comparable receptor expression (ER=2+/HER2=3+) over tested passages with similar histology compared to archival clinical samples. DNA/RNA sequencing identified several conserved variants including loss of CDKN2A/B and MTAP and a CNV=14 for CCND1. In vivo, ST4565 and ST4565C were found resistant to T-DM1 at 3 mg/kg weekly with a T/C of 100% in both models. However, DS-8201a treatment at 3 mg/kg weekly resulted in partial tumor regressions in ST4565 (T/C=-51%) while ST4565C was found resistant (T/C=49%). Both models were found resistant to all tested chemotherapies and all other targeted therapies but reported similar sensitivity to fulvestrant (T/C= $\sim 40\%$). Conclusion: We established two XPDX models representing T-DM1-resistant, ER+/HER2+ breast cancer from breast samples collected two years apart from the same patient that were found differentially responsive to DS-8201a. These models can be utilized as a valuable tool in better understanding innate resistance to T-DM1 and acquired resistance to DS-8201a.

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Potentiating Alpelisib in PI3K Pathway Overactive Triple Negative Breast Cancers

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Potentiating Alpelisib in PI3K Pathway Overactive Triple Negative Breast Cancers David C. Boyd^{1,2}, Amy L. Olex³, Tess Leftwich¹, Nicole Hairr¹, Alex K. Duong¹, Narmeen S. Rashid^{1,3}, Mohammad A Alzubi^{1,2}, Holly Byers¹, Aaron D. Valentine¹, Julia E. Altman¹, Emily Zboril¹, Jacqueline M. Grible¹, Madelyn Esquivel¹, Scott A. Turner¹, Andrea Ferreira-Gonzalez¹, Mikhail G. Dozmorov⁵, J. Chuck Harrell^{1,2,6} ¹Department of Pathology, Virginia Commonwealth University; ²Integrative Life Sciences Program, VCU; ³Wright Center for Clinical and Translational Research, VCU; ⁴Department of Biology, University of Richmond; ⁵Department of Biostatistics, VCU; ⁶Massey Cancer Center, VCU. There is an urgent need for new therapeutic options for basal-like Triple Negative Breast Cancers (TNBC). To mirror the NCI-ComboMATCH study, and identify new synergistic drug combinations, we analyzed a set of 20 breast cancer patient-derived xenografts and 14 cell lines to identify targetable targets in each model. The OncoPrint Comprehensive Assay v3 was performed to assess 161 genes for hotspot mutations, focal copy number variants, amplification/deletions, and RNA-fusion genes. Next, each PDX and their isogenic drug-resistant sublines were analyzed with bulk RNA-sequencing (217 samples) and cell single-cell RNA-sequencing (~100,000 cells). Of all NCI-MATCH defined targetable mutations, 37% of the models contained pathogenic PIK3CA amplifications or mutations. PIK3CA is one of the most common oncogenic aberrations identified in patients and the PI3K pathway is overactive in the majority of TNBCs, therefore we sought to target it across all models and identify the most efficacious synergistic drug partner. Short-term cultures of each PDX model were screened with a library of >1,000 FDA-approved/experimental drugs to identify compounds that were cytotoxic. Synergistic drug screens were then performed with each drug in combination with the PI3K inhibitor byl-719 (alpelisib) a current standard-of-care drug used for PI3K mutant ER+ disease. Synergism was identified using coefficient of drug interaction (CDI) calculations and 10 drugs were identified as synergistic across several models. Using several criteria, including clinical status and pathway analysis, 3 drugs were selected for CompuSyn-based synergism testing and each was confirmed to be synergistic in vitro. Testing with in vivo models of each drug combination has thus far confirmed that each is synergistic per CDI metrics. Those combinations are currently being tested for efficacy in the metastatic setting with a set of basal-like PDXs.

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Extracellular vesicles-transported lncRNA BCDR1 promotes tumor cell proliferation and therapy resistance via upregulating G1/S-phase transition in breast cancer

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Background Extracellular vesicles (EVs), secreted by tumor cells for intercellular communication, play an important role in breast cancer progression. Previous studies have proved that lncRNA could use EVs to transmit signals and affect the progression and treatment of breast cancer. In addition, a previous study has found that, in HER2 therapy-resistant tumors, CDK4/6 activity and cell cycle progression genes were involved and might serve as treatment targets. However, recent clinical trials were not supportive of the use of CDK4/6 inhibitors in HER2 enriched internal subtypes of breast cancer. In this study, we aim to explore the role of EVs-transported long noncoding RNA BCDR1 in the promotion of cell cycle progression in HER2-positive breast cancer, exploring a new potential target in combination with CDK4/6 inhibitor and anti-HER2 treatment. Methods Samples were collected from patients with HER2 overexpression receiving neoadjuvant therapy. RNA-seq was performed to identify differentially expressed RNAs between pathological complete response (pCR) and non-pCR group. In addition, serum extracellular vesicles were collected and determined through RNA-seq. The drug response and proliferation rate of tumor cells were measured in breast cancer cells (HCC-1954, BT-474 and MCF-7). Quantitative RT-PCR (qRT-PCR) was used to detect the expression levels of BCDR1 and its potential target genes. RNA-seq and GSEA analysis was carried out to determine the target pathways regulated by BCDR1. DNA fiber assay, mass spectrometry, and flow cytometry were used to understand the underlying mechanism of BCDR1. Results Core needle biopsy tissues from HER2-positive breast cancer patients with any ER status were collected before NAC. Among genes differentially overexpressed, BCDR1 was found to be downregulated in pCR group compared with non-pCR group. BCDR1 was also elevated in plasma EVs in the non-pCR group. In addition, overexpression of BCDR1 in breast cancer cells promoted cell proliferation and HER2 treatment resistance. Through pathway analysis, we found BCDR1 could facilitate G1/S-phase transition. Flow cytometry confirmed these findings. We also noticed that proteins that regulate DNA licensing including

minichromosome maintenance proteins (MCMs) were enriched in BCDR1 overexpression cells. Through DNA fiber assay, we confirmed that BCDR1 could promote DNA replication initiation. Interestingly, under CDK4/6 inhibitor treatment, BCDR1 was induced, unrevealing an internal treatment-resistant mechanism in these tumor cells. Through EVs RT-qPCR, we found BCDR1 could transport from high expression cells to low, with the same biological function. We also explored antisense oligonucleotide (ASO) use in the inhibition of BCDR1 biological function and transportation. Conclusion BCDR1 promotes cell proliferation and therapy resistance via upregulating DNA licensing in breast cancer. BCDR1 could transported through EVs with same biological function. This study also suggests that BCDR1 could serve as a biomarker and therapeutic target in breast cancer.

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Jiong Wu, n/a: No financial relationships to disclose

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Loss of emerging tumor and metastasis suppressor RasGAPs mediates therapeutic resistance in HER2+ breast cancer

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Resistance to HER2 inhibitors remains a clinical challenge in HER2+ breast cancer. Therefore, there is an urgent need to 1) understand the mechanisms that underlie resistance to these current treatments and 2) develop improved, and more importantly, curative combination therapies. We recently discovered that two emerging tumor suppressor RasGAPs, DAB2IP and RASAL2, cooperatively drive metastatic breast cancer when lost or inactivated. Interestingly, we have now generated robust data demonstrating that the loss of these RasGAPs also induces resistance to HER2 inhibitors in breast cancer. First, we genetically ablated both RASAL2 and DAB2IP in multiple HER2+ breast cancer cell lines (SKBR3, EFM192A, SUM190, BT474) and performed manual counting experiments after 6 days of TKI (lapatinib, tucatinib) treatment. In all cell lines, RASAL2/DAB2IP knockdown conferred resistance to HER2 inhibitors. Moreover, loss of these RasGAPs prevented TKI-induced caspase-3/7 activation, measured by Incucyte live cell imaging, and enabled the regrowth of cells in long-term 10-day treatment and drug washout experiments, monitored by Incucyte or crystal violet staining. Next, we sought to investigate the individual contribution of each RasGAP to these phenotypes. Surprisingly, we found that RASAL2 and DAB2IP functioned quite differently in this context.

Specifically, while RASAL2 loss prevented apoptosis, DAB2IP loss prevented irreversible cell cycle arrest (measured by functional long-term experiments and EdU staining assays). Mechanistically, RASAL2 loss uniquely impaired BIM induction at both mRNA and protein levels, which is required for lapatinib-induced cell death of HER2+ cancer cells. By contrast, cell cycle progression pathways were uniquely enriched in DAB2IP-deficient cells on lapatinib treatment and immunoblots revealed higher residual levels of pRb and low levels of p27 in these cells. These data suggest that RASAL2 and DAB2IP (loss) mediate resistance to HER2 inhibitors by differentially deregulating unique pathways/phenotypes. We next evaluated the relevance of these findings in a SUM190 orthotopic xenograft model. Importantly, while control tumors (expressing both RASAL2 and DAB2IP) regressed upon lapatinib treatment, DAB2IP- and RASAL2-deficient tumors did not regress and grew with kinetics comparable to vehicle-treated tumors after few days on treatment. These data suggest that the unique phenotypes/pathways induced by both RASAL2 and DAB2IP are important mediators of resistance to HER2 inhibitors. Further understanding the contribution of these pathways to anti-HER2 resistance and determining how RASAL2 and DAB2IP differentially function will be essential for developing effective therapeutic strategies to bypass each type of resistance.

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Investigating NF1 Mutations in Circulating Tumor DNA of Patients with Hormone-receptor Positive (HR+) Breast Tumors Resistant to CDK4/6 Inhibition (CDK4/6i): A Retrospective Clinical Analysis

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Background: CDK4/6 inhibitors (CDK4/6i) are standard of care for the management of HR+/HER2- metastatic breast cancer (MBC). Genomic alterations that drive resistance to CDK4/6i are diverse, and while the molecular landscape is heterogeneous, several

mechanisms of CDK4/6i resistance converge on the RAS/MAPK and PI3K/AKT/mTOR signaling pathways. NF1 downregulates RAS and dampens cellular proliferation. Laboratory-based models demonstrate that loss of NF1 is associated with resistance to endocrine therapy (ET), and emergence of NF1 mutations (NF1m) are correlated with progressive disease (PD) in circulating tumor DNA (ctDNA). While NF1m may diminish CDK4/6i susceptibility, a clear relationship has not been elucidated. The primary objective of this study was to characterize patient (pt) response to CDK4/6i in NF1m HR+/HER2- MBC. Methods: We identified 47 pts with NF1m via a database with one or more ctDNA samples sequenced at variable time-points as part of routine care for MBC. NF1m were categorized as pathogenic (p)NF1m or variants of uncertain significance (VUS) based on their associated Guardant report. We identified 27 pts with HR+/HER2- MBC and NF1m that received at least 1 line of CDK4/6i in the metastatic setting. Intrinsic resistance was defined as PD < 6 months on a CDK4/6i regimen, and acquired resistance was defined as PD >6 months. Pts with intrinsic resistance or acquired resistance and NF1m detected post-PD were categorized as having a resistance phenotype potentially driven by NF1m. Pts with NF1m detected prior to therapy and >6 months clinical response on a CDK4/6i were categorized as having NF1m tumors sensitive to CDK4/6i. Results: The NF1m cohort (n = 27) had 9 pts with pNF1m, while 18 pts expressed VUS. The median age at MBC diagnosis was 54 years, and 67% had visceral metastasis at ctDNA collection. Pts received a median of 1 prior line (range: 0 - 6) of ET or chemotherapy in the metastatic setting before CDK4/6i. Amongst pts with pathogenic variants (n = 9), we found 3 pts with pNF1m were intrinsically resistant to CDK4/6i. Acquired resistance was seen in 1 pt with pNF1m detected post-PD, and 2 pts had evidence of both acquired and subsequent intrinsic resistance to a later line of CDK4/6i. Overall, 67% (6 / 9) of pNF1m pts demonstrated a CDK4/6i resistance phenotype; mutant allele fraction (AF) ranged from 0.2% - 29.9%, and the mean maximum allele fraction (MAF) was 6.0%. Pre- and post-treatment samples were available on 3 pts with pNF1m, and 1 of these pts had an AF rise from 2.7% to 12.3% when comparing ctDNA pre- and post-CDK4/6i. ctDNA from 4 of 6 resistant tumors harbored other putative drivers including alterations in FGFR, KRAS, PTEN, and RB. We identified 2 counter-examples of pNF1m tumors sensitive to CDK4/6i. These pts expressed relatively low NF1m AF, ranging 0.1% - 0.5% with a mean MAF 0.3%. Another pNF1m pt had intrinsic resistance to initial CDK4/6i but was sensitive to later-line CDK4/6i. In the subgroup of pts with VUS-NF1m (n = 18), a more mixed picture of resistance and sensitivity was seen. 8 pts had intrinsic or acquired resistance, 8 pts had NF1m tumors sensitive to CDK4/6i, and 1 pt had evidence of both; 61% (n = 11) of pts expressed alterations in other resistance mediating genes. 1 pt stopped therapy due to toxicity rather than PD. Conclusions: Our work demonstrates that tumor expression of pNF1m may be associated with CDK4/6i resistance in pts with HR+/HER2- MBC, and allele fraction could be predictive of drug susceptibility. Tumors harboring VUS had varied sensitivity, suggesting that some of these mutations may not be pathogenic, and counter-examples of pNF1m MBC benefiting from CDK4/6i plus ET highlight the complexities in predicting drug response based on single gene alteration. Future effort is warranted to explore the potential impact of NF1 on CDK4/6i resistance, as well as the potential role for therapies targeting the MAPK pathway in this patient population.

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5:00 PM - 6:15 PM

P1-13-08

Inhibition of RNA binding protein HuR function sensitizes the TNBC to chemotherapy

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The 5-year relative survival rate for triple-negative breast cancer (TNBC) is 77%, which is notably lower than 90%, the overall survival rate for breast cancer. The primary systemic treatment for TNBC remains to be chemotherapy. However, patients frequently develop resistance to conventional chemotherapy, greatly compromising the anti-tumor effects of chemodrugs. Therefore, this study is aimed to enhance the effects of chemotherapy. The RNA-binding protein Hu antigen R (HuR) plays an important role in chemotherapy resistance. HuR post-transcriptionally regulates the stability of the target mRNA by binding to the U- or AU-rich elements (ARE) mainly in the 3' untranslated region (UTR) of mRNA. In most cases, the binding stabilizes mRNA, thereby enhancing the translation of the encoded protein, many of which are implicated in multiple cancer hallmarks, including chemoresistance. The overexpression of HuR, and accumulated cytoplasmic expression, are reported to be related to chemoresistance in many types of cancer cells. We hypothesized that inhibition of HuR function by disrupting its interaction with mRNA can accelerate the decay of mRNA and thus reduce the translation of proteins contributing to chemoresistance. Previously, our lab reported a small molecule HuR inhibitor, KH-3, which potently inhibits HuR function by disrupting the HuR-

mRNA interactions. To test our hypothesis, we utilized KH-3 as a tool compound to assess whether HuR inhibition enhances the efficacy of chemotherapy for TNBC cells. We generated a cell sub-line (231-TR) derived from the human TNBC cell line MDA-MB-231 with acquired resistance against docetaxel (TXT). Compared with the parental cell line, 231-TR exhibited similar sensitivity to KH-3 in the MTT-based cytotoxicity assay and the colony formation assay. The in vitro and in vivo combination of KH-3 and TXT synergized in inhibiting cell proliferation and tumor growth of multiple TNBC cell lines. Regarding mechanisms of action, the apoptosis pathway was downregulated and the Wnt signaling pathway was upregulated in 231-TR cells. KH-3 treatment downregulated β -Catenin, involved in promoting cell proliferation, in a time and dose-dependent manner. KH-3 was also identified to induce apoptosis cell death via inhibiting the anti-apoptotic protein BCL2. The cell cycle analysis revealed that KH-3 treatment caused the S phase accumulation. Therefore, the cell proliferation inhibition by KH-3 results from a combination of apoptosis and cell cycle arrest. Furtherly, KH-3 restored the effects of docetaxel in inducing apoptotic cell death in 231-TR cells. Together, this study provides a new strategy to overcome chemotherapy resistance in TNBC cells by functional inhibiting HuR.

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P1-13-10

Deconvoluting dynamics of acquired chemoresistance in Triple Negative Breast Cancer tumors

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Background: BRCA deficient Triple negative breast cancers (TNBC) are effectively treated with platinum agents but, upon relapse, resistance is common. A number of genes have been shown to mediate chemoresistance in vitro, but none have been clinically useful due to the heterogeneous mechanisms of in vivo tumor chemo-resilience. Methods: We attacked this problem by recapitulating the generation of in vivo resistance to cisplatin in 50 mice bearing a platinum sensitive TNBC patient derived xenograft (PDX) TM00099, a BRCA1 deficient type 1 tandem duplicator phenotype tumor. Untreated tumors were compared to residual tumors that were sampled after the first cycle of cisplatin, upon recovery, and after the second cycle of drug which generated platinum resistant and sensitive tumors. Our earlier work on TM00099 suggested the existence of two major subspecies, designated A and B, with shifts observed in their proportions post treatment (1). We deconvoluted the bulk tumors into their clonal components to assess the precise numerical fluxes after each treatment cycle to gain insight into the cellular basis of the emergence of in vivo resistance. Results: 55 single cell derived clones isolated from bulk TM00099 tumors were genomically characterized identifying five subclonal populations: B, CCR, and variations of the original A: A25, A33 and A50. SNP analyses indicated that these five subclones comprised the vast majority (~93%) of all

TM00099 tumors. Lineage analysis revealed that all A clones were related but distinct from B. CCR however had both A and B SNP markers and relatively higher ploidy indicating that CCR is a fusion of ancestral A and B clones. We found that A50, A33, and CCR were ~1.9X more resistant to cisplatin (mean IC50=4.4 μ M) compared to the sensitive clones A25 and B (mean IC50=2.3 μ M; p=0.002) in vitro. Although B clones had similar IC50 to A25s, B had improved in vitro survival at higher concentrations of cisplatin suggesting a dormancy-like phenotype: the persistent B cells did not recover within 50 days after in vitro exposure to cisplatin. Using clonal markers in bulk tumors, we found excellent concordance with their in vitro phenotypic analysis: after the first cycle of cisplatin, there was a proportional decline in A25, an enrichment of B, and stable proportions of A50, A33, and CCR. After the second platinum cycle, the emerging resistant tumors were mostly devoid of A25, and had low proportions of B, but highly enriched for A50, A33, CCR and an uncharacterized resistant A clone. The sensitive tumor residuals after the second platinum dose were predominantly comprised of B. Genomic analysis of the clones did not reveal any genetic drivers of resistance. Transcriptionally, the sensitive B clones were characterized as mesenchymal or basal-like 1 TNBC subtypes, while the resistant As were categorized as basal-like 2, which have enhanced growth factor signaling and is associated with poorer response to chemotherapy. Correspondingly, the MAPK and stress associated NF- κ B signaling pathways were augmented in As which were indeed more sensitive to blockade of MEK, EGFR and NF- κ B than the platinum sensitive B clone. A25s which are sensitive revertants of the otherwise resistant A group use a mechanism to bypass resistance likely driven by ZNF350 and ZNF93. Conclusions: Our clonal reconstruction of TM00099 showed that acquired resistance can emerge by enrichment of not one but a composite of multiple preexisting resistant clones. The origins and characteristics of these clones are complex and include epigenetically driven resistance (A50 and A33), cell fusion mediated resistance (CCR), reversion to sensitivity (A25), and dormancy despite initial sensitivity (B). These nuances would not be discerned using bulk tumor assessments pointing to single cell genomic analyses as the most precise way to deconvolute the capacity of TNBC tumors to develop resistance. References: 1. H. Kim et al., Sci Rep. 8, 17937 (2018).

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P1-13-11

YES1 is a targetable vulnerability for improving taxane response in triple-negative breast cancer

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Triple-negative breast cancer (TNBC) is the most aggressive breast cancer subtype. Due to the lack of receptor expression, there are limited targeted therapies available for TNBC. As a result, TNBC patients are primarily treated with chemotherapies such as taxanes. Although TNBCs initially regress in response to taxane treatment, resistance is common. One mechanism of taxol unresponsiveness/resistance is an increase in chromosomal instability (CIN). Increased CIN can confer survival advantages to cancer cells and increase their aggressiveness. However, CIN levels can be leveraged using drugs that inhibit proteins important for chromosomal stability. Combining CIN-inducing drugs, such as taxanes, can improve treatment efficacy or re-sensitize tumor cells to certain drugs by shifting cells towards a state of maladaptive CIN that is incompatible with cell viability. We have found that the non-receptor SRC family kinase YES1 is crucial for chromosomal stability. YES1 is important for cell division, motility, adhesion, and survival in both normal and TNBC cells. Since taxol and YES1 silencing independently increase chromosomal instability, I hypothesized that combining a YES1 inhibitor (YES1i) with taxanes would shift cells toward an irreversible state of maladaptive CIN, decreasing their survival. I found that YES1 mRNA and protein are upregulated in taxane-resistant cells and that YES1 protein expression correlates with the paclitaxel IC50 in a panel of TNBC cell lines, suggesting that YES1 may drive taxane resistance. Furthermore, I found that a selective YES1 inhibitor (CH6953755) synergizes with paclitaxel and improves taxane response in both in vitro and in vivo TNBC models. In addition, the combination of YES1i and paclitaxel treatment increases phenotypes associated with chromosomal instability more than either drug alone. These data suggest that YES1 inhibition in combination with taxanes represents an innovative and novel drug treatment regimen that improves TNBC patient outcomes.

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P1-13-12

Targeting Dynamin-related protein 1 for the management of taxane-resistant triple-negative breast cancer

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The development of drug resistance is a primary cause of chemotherapy failure in the treatment of triple-negative breast cancer (TNBC). Some cancer cells are resistant to drugs with unrelated structures and mechanisms of action, a phenomenon known as multidrug resistance (MDR). Although taxanes such as docetaxel and paclitaxel are effective against non-metastatic and metastatic TNBC and other types of breast cancer, they eventually become ineffective due to development of drug resistance. Mitochondrial dynamics has gained significant attention as a means to treat MDR and non-MDR cancers. Mitochondrial dynamics determine the number, shape, and location of mitochondria within cells, which are fundamental to the health of the cell. Among its key components is the mitochondrial fission-promoting dynamin-related protein 1 (Drp1). There is mounting evidence indicating that both Drp1 and its phosphorylated form promote cancer survival, resistance to apoptosis, and chemoresistance. We observed increased phosphorylation of Drp1 at Ser616 as well as phosphorylation of its upstream kinase ERK1/2 in TNBC lines SUM159PT and its paclitaxel-resistant derivative that we developed called SUM159PT/PAC200 that displays more than an 80-fold increase in resistance to paclitaxel. Using CRISPR-Cas9 technology, we knocked out the gene encoding Drp1 in both lines. When Drp1 is genetically ablated, paclitaxel resistance in SUM159PT/PAC200 was significantly reversed. Furthermore, proliferation, migration, and invasion capabilities were decreased in both parental and paclitaxel-resistant Drp1 knockout lines. In SUM159PT/PAC200 Drp1-KO cells, a mesenchymal to epithelial transition (MET) was observed as indicated by downregulation of mesenchymal markers such as N-cadherin and β -catenin, and upregulation of the epithelial marker ZO-1. Interestingly, Drp1 knockout halted the ability of SUM159PT/PAC200 to form colonies in soft agar. SUM159PT/PAC200 cells strongly express the MDR pump P-glycoprotein (ABCB1), to which paclitaxel is a known substrate, and genetically targeting Drp1 reduced the expression to almost undetectable levels. Taken together, these findings suggest that Drp1 is both a resistance factor and a key protein in breast cancer proliferation and dissemination, making it a promising actionable molecular target in the treatment of TNBC. Further studies are in progress to understand the role of Drp1 in the development and maintenance of MDR phenotype, proliferation, and invasion.

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Nuclear envelope Expression of the Oncogene Adipocyte-Associated Methionine Domain Containing Conveys Inferior Prognosis but Increased Sensitivity to Statins and Fluorouracil-Based Therapy

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The sub-classification of invasive breast cancer into Integrated Clusters by a combined analysis of genomic change and expression profiling has revealed novel cancer drivers. The integrated Cluster 2 breast cancer sub-group represents a cohort with aggressive, largely estrogen receptor positive tumours with a high relapse rate. It is characterized by an amplification of chromosome 11 at the heart of which is a little studied gene which codes for the protein Adipocyte-Associated Methionine Domain Containing (AAMDC). Initial cell line and murine studies demonstrated oncogenic behaviours for AAMDC including increased proliferation and invasion, increased colony formation and anti-estrogen resistance. Downstream gene

expression analysis showed the protein to modulate cholesterol biosynthesis, one carbon metabolism and mTOR signaling. To assess the clinical impact of differing levels and sub-localizations of AAMDC, immunohistochemistry for AAMDC was carried out using tissue microarrays from a cohort of 420 patients with invasive breast cancer. Expression was noted in a number of sub-cellular localizations including diffuse cytoplasm, nucleus and nuclear envelope. Using both dichotomous and continuous scoring, no significant association for any expression site with standard prognostic factors was identified including size, lymph node status, grade or receptor statuses. However, both cytoplasmic and nuclear envelope expressions correlated with significantly worse overall survival ($p=0.04$ and $p=0.04$ respectively) whereas nuclear expression showed a trend to better survival ($p=0.06$). Distant relapse and breast cancer deaths were lowest where there was nuclear expression but no nuclear envelope expression (4.7% and 4.7% respectively) but significantly higher for the reverse expression pattern (18.9%, $p=0.02$ and 17.6%, $p=0.03$ respectively). Considering the pre-clinical impact of AAMDC on genes involved in cholesterol biosynthesis, we studied the effects of statin prescription in the early disease setting in the context of AAMDC expression. Statins were found to be generally protective of relapse across the group. Only nuclear envelope AAMDC expression interacted, with a hazard ratio (HR) of 0.33 for distant relapse with high expressors, compared to a HR of 0.90 in low expression ($p=0.02$ for difference). Similarly, considering one carbon metabolism, we explored the impact of the anti-metabolite drug capecitabine compared to other chemotherapy treatments, largely taxane-based, in the metastatic setting. Again, only nuclear envelope expression interacted with median progression-free survivals on capecitabine of 2.0 v 12.2 months for low and high nuclear envelope expression respectively, $p=0.03$. In summary, AAMDC nuclear envelope expression correlates with poor prognosis which may be mitigated by statin administration in the early disease setting. This expression pattern also confers sensitivity to flurouracil-based metastatic treatment.

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P1-13-14

Increased androgen receptor expression as a mechanism of acquired anti-androgen resistance in androgen receptor-positive triple negative breast cancer.

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Background: Triple negative breast cancer (TNBC) represents the most aggressive breast cancer subtype, and despite recent treatment advances, clinical outcomes remain poor, particularly in the metastatic setting. TNBC is a biologically heterogeneous entity, and up to 50% of TNBC express the androgen receptor (AR). Gene expression subtyping has identified a subset of AR-TNBC with a luminal AR-driven (LAR) phenotype. Consequently, there has been great interest in translating androgen receptor signaling inhibitors (ARSIs) approved for use in prostate cancer such as enzalutamide and bicalutamide into the management of LAR-TNBC. However, early phase clinical trials of anti-androgens in metastatic AR-TNBC have had modest results. While multiple mechanisms of anti-androgen resistance have been identified in prostate cancer, including AR amplification and over-expression, emergence of AR splice variants (AR-Vs), and transition to AR independent growth, molecular determinants of anti-androgen resistance in TNBC remain poorly understood, and pre-clinical models to study acquired ARSI resistance in LAR-TNBC have been limited. Methods: A novel pre-clinical model of acquired ARSI resistance was derived from the LAR subtype MDA-MB-453 cell line through serial passaging with increasing concentrations of enzalutamide. Celltiter Blue viability assays were used to determine enzalutamide IC50 of parental and enzalutamide-resistant (EnZR) cell lines.

RNA was extracted from the parental and resistant cells, reverse transcribed and expression of AR, splice-variants and canonical AR target genes were evaluated using RT-qPCR. Immunofluorescence was used to investigate the amount and nuclear localization of the AR protein within the parental and enzalutamide resistant cells. Results: EnzR MDA-MB-453 cells were derived through culture in increasing concentrations of enzalutamide for >6 months, and found to have a significant increase in enzalutamide IC50 compared to the parental cell line. EnzR MDA-MB-453 cells had a 4.5 fold increase in full-length AR expression at the transcriptional level compared to the parental cell line. AR protein expression and nuclear localization were also increased in EnzR cells compared to the parental cell line. Canonical AR targets including NKX3.1 were downregulated in response to enzalutamide in parental but not EnzR cells. While pathogenic AR splice variants (AR-Vs) implicated in ARSI resistance in prostate cancer were detected at low levels in MDA-MB-453 cells, no increase in AR-V expression was observed in the EnzR cell line. Conclusions: We have developed a novel pre-clinical model of anti-androgen/ARSI resistance in LAR-TNBC, and identified AR overexpression and persistent AR signaling associated with acquired enzalutamide resistance in LAR-TNBC. While pathogenic AR splice variants have been implicated in ARSI resistance in metastatic prostate cancer and are detected in the MDA-MB-453 cell line model, enzalutamide resistance was not associated with increased AR splice variant expression in this model. Future work will investigate mechanisms leading to AR overexpression as well as combination therapeutic strategies to overcome acquired ARSI resistance.

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5:00 PM - 6:15 PM

P1-13-15

Elevated TCEAL9 Expression Is Correlated With Trastuzumab-based Neoadjuvant Chemotherapy Resistance In HER2-positive Breast Cancer

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Background: -Trastuzumab-based neoadjuvant chemotherapy has shown to have remarkable clinical benefits for HER2-positive breast cancer patients who had higher tumor burden. - Patients who achieved pathological complete response (pCR) are known to have better prognosis. -However, certain patients have little response or are not sensitive to trastuzumab-based treatment regimens. -Understanding the mechanism of trastuzumab resistance is crucial for the development of new therapeutic strategy. Objectives: To investigate the role of TCEAL9 in developing trastuzumab resistance in HER2-positive breast cancer Methods: A total of 83 patients who received paclitaxel, carboplatin and trastuzumab neoadjuvant chemotherapy in Fudan University Shanghai Cancer Center(FUSCC) from 2016 to 2018 were enrolled in this study. After completed neoadjuvant chemotherapy and surgery, gene expressions were compared between the pCR and non-pCR groups. Total RNA from formalin-fixed paraffin-embedded tissue sections was isolated and RNA-sequencing was performed. Gene sets from GEO dataset GSE52707 were used to analyze TCEAL9 expression in resistant and non-resistant cell lines. Gene expression levels were converted into log2 values and row-wised standardized. BT-474 and SK-BR-3 cell lines were transduced with each expression lentivirus, followed by selection with puromycin for stable expression. TCEAL9 mRNA and protein level evaluation was evaluated by qPCR and western blot. The influence of TCEAL9 expression on proliferation and sensitivity to HER2-targeted therapy was evaluated by CCK8. BT-474 and SK-BR-3 transfected cells were plated in 96-well plates with 4,000 cells per well. After 3 or 5 days of incubation with trastuzumab, pertuzumab or lapatinib, the viability of cells was measured using Cell Proliferation Assay. Comparisons between Kaplan-Meier curves were performed using the long-rank test. Results: TCEAL9 was elevated significantly ($P < 0.05$) in non-pCR patients in the FUSCC cohort and was associated with lapatinib resistance in GSE52707 from GEO datasets. Patients with elevated TCEAL9 expression had worse recurrence-free survival (RFS), distant metastasis-free survival (DMFS) and progression-free survival (PPS) (all $P < 0.05$) by using KM-plotter. Overexpression of TCEAL9 was associated with lapatinib($IC_{50} = 5.56$ vs 10.90 nM) and trastuzumab + pertuzumab($IC_{50} = 745$ vs 635 nM) resistance in BT-474 and SK-BR-3 respectively, but has no influence in proliferation. In this study, we found that TCEAL9 could induce HER2-positive breast cancer cells resistance to HER2-targeted therapy through the activation of mTOR signaling pathway. After EGFR stimulation, TCEAL9 has a higher mTOR phosphorylation level in BT-474 cells. TCEAL9 elevation also increased HER2 and mTOR phosphorylation after lapatinib treatment in SK-BR-3 cells. In addition, the elevation of TCEAL9 has a positive correlation with HER2 signaling pathways such as EGFR , PIK3R1 , FOXO1 and AKT3 in TCGA datasets. Conclusions: TCEAL9 expression correlates with trastuzumab resistance and high TCEAL9 expression is associated with poor prognosis in HER2-positive breast cancer patients.

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Dissecting the biological activity of different CDK4/6 inhibitors (CDK4/6i) in hormone receptor-positive/HER2-negative (HR+/HER2-) breast cancer (BC)

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Background: Palbociclib might be less effective than ribociclib in HR+/HER2- and HER2-enriched BC. This hypothesis is currently being tested in the HARMONIA prospective phase III clinical trial (NCT05207709). Here, we evaluated the downstream biological effects of both drugs using cell lines and patient tumor samples. Methods: Three HR+ BC cell lines (i.e., MCF7, T47D and BT474) were treated at 2 different dose levels of palbociclib or ribociclib (i.e., 100 nM and 500 nM) +/- fulvestrant (1 nM) for 72 hours (h). PAM50 gene signatures were determined on the nCounter, as well as phosphorylation of RB (p-RB) by Western Blot and senescence-associated β -galactosidase activity by FACS. In vitro experiments were performed in triplicates. PAM50 gene signatures were obtained from 49 paired baseline versus week-2 samples and 49 paired baseline versus surgery samples of the CORALLEEN phase II study (Prat, *Lancet Oncol.* 2020), which treated 49 women with PAM50 Luminal B HR+/HER2- early BC with neoadjuvant ribociclib (600 mg daily) plus endocrine therapy (ET). PAM50 signature scores were also evaluated in publicly available data from 23 paired baseline versus week-2 samples and 16 paired baseline versus surgery samples of the NEOPALANA phase II trial (Ma, *Clin Cancer Res.* 2017) which treated 50 patients with HR+/HER2- early BC with palbociclib (125 mg daily) plus anastrozole. Changes in PAM50 signatures upon CDK4/6i were determined by paired t-tests and significant analysis of microarray (SAM). Results: Across all cell lines, both palbociclib and ribociclib statistically significantly reduced p-RB at 72h with both doses (i.e., 100 and 500 nM) compared to non-treated cells ($p < 0.001$). Senescence was also observed at 72h with both doses. Both drugs +/- ET significantly increased the Luminal A signature and decreased Luminal B and proliferation signatures with both doses. However, the HER2-enriched signature was only significantly reduced when both CDK4/6 inhibitors were given at 500 nM. In tumor samples from the CORALLEEN and NEOPALANA phase II studies, a similar change in PAM50 biology was observed with both drugs, namely an increase in Luminal A signature and a decrease in Luminal B and proliferation signatures after 2 weeks of treatment and at surgery. At 2 weeks of treatment, the HER2-enriched signature was significantly decreased in both studies with ribociclib ($p < 0.001$) and palbociclib ($p < 0.001$). However, the decrease in the HER2-enriched signature was only observed in surgical samples of patients treated with ribociclib ($p < 0.001$), but not palbociclib ($p = 0.194$). A difference in sample size could explain this result. Nevertheless, in CORALLEEN, the median number of days between the last dose of ribociclib and surgery was 13.1 days (range: 1-78). In NEOPALANA, the median number of days between the last dose of palbociclib and surgery was 29 days (range: 8-49), except for 8 patients who received additional 10-12 days of palbociclib immediately

before surgery (Ma, Clin Cancer Res. 2017). In patients who underwent surgery at 8 days or before, the HER2-enriched signature was significantly decreased for both ribociclib ($p < 0.001$) and palbociclib ($p = 0.013$). Interestingly, in patients that underwent surgery after >8 days from the last dose, a significant reduction of the HER2-enriched signature was only observed with ribociclib ($p < 0.001$), but not with palbociclib ($p = 0.500$). Conclusions: Both palbociclib and ribociclib have similar effects on PAM50 biology when given at the same dose. However, in clinical practice, palbociclib is given at a lower dose than ribociclib, and although HER2-enriched signature is significantly decreased in tumors after 2 weeks of CDK4/6i+ET, this effect is only maintained at later time points with ribociclib, indicating a dose-dependent efficacy of CDK4/6i in this biologically aggressive subtype.

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Hyperactivation of the EGFR pathway is associated with resistance to tucatinib in HER2-positive breast cancer models

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Background: The HER2-specific tyrosine kinase inhibitor (TKI) tucatinib (Tuca) recently approved for advanced HER2+ breast cancer is making a move towards the early setting. Given its growing use, resistance is inevitable, as observed in the HER2CLIMB study, where only one patient with brain metastasis remained progression free after 2 years on Tuca. Driven by the prevailing lack of knowledge about the mechanisms of resistance, in this study, we sought to define these mechanisms and identify treatment strategies to overcome them. We previously reported (SABCS 2021) that our BT474 TucaR models acquired EGFR amplification and showed elevated levels of phosphorylated (p) and total (t) EGFR, pHER2, pHER3, and downstream pAKT and pS6. Since the HER pathway is activated by ligands, here we aim to assess if hyperactivation of EGFR via high levels of its ligands is an alternative mechanism of Tuca resistance. Materials and Methods: Our recently developed HER2+ BT474 (ATCC and AZ) cell models with acquired resistance to Tuca (TucaR) developed through long-term exposure to gradually increasing doses of Tuca and their naïve parental (P) were used. Genomic (DNA-seq), transcriptomic (RNA-seq), and proteomic (western blot) characterization were performed. Changes in cell growth and migration were assessed by methylene blue and Incucyte wound healing assays, respectively. Results: RNA-seq analysis demonstrated that the levels of TGF α was significantly higher in our BT474 TucaR models compared to P cells. Our results now demonstrate that exogenous supplementation of EGF to BT474-P cells rescues the Tuca-mediated inhibition of pEGFR, pHER2, and the downstream pAKT, pERK, and pS6 levels. Exogenous EGF was also found to reduce the levels of apoptosis, as assessed by cleaved PARP, mitigating the Tuca-induced cell death. Exogenous EGF or TGF α rendered naïve BT474 and SKBR3 cells resistant to Tuca while neratinib, a pan-HER TKI, effectively inhibited this ligand-driven cell growth. We previously showed that the HER signaling reactivation observed in our EGFR-amplified TucaR cells was inhibited by the EGFR-specific TKI gefitinib (Gef) (SABCS 2021) and that the TucaR cells displayed enhanced migratory capabilities (AACR 2022). Here, we demonstrate that in addition to curbing the growth of TucaR cells, Gef, either alone or together with Tuca, also markedly reverts the migration of the TucaR cells. Knockdown (KD) of EGFR but not HER2 selectively and substantially inhibited the migration of the TucaR cells. KD of EGFR also had a marked cell killing effect on only the TucaR cells, whereas HER2 KD inhibited the growth of P but not TucaR cells. Our findings are consistent with the notion that while the P cells are functionally dependent on HER2, in TucaR cells the survival dependence could be rewired to rely primarily on the hyperactive EGFR signaling. Genomic analysis further revealed that in addition to EGFR amplification, the AZ TucaR cells also acquired a gain of YES1, a src family receptor tyrosine kinase implicated in cancer cell growth, invasion, and metastasis. Functional studies using 2 siRNAs, however, showed that YES1 KD had no effect on the growth of TucaR cells, and the migration of both TucaR and P cells was equally affected by YES1 KD, precluding the potential role of YES1 in driving the resistant and enhanced migratory phenotypes. Conclusions: Hyperactivation of the

EGFR pathway via amplification of EGFR or increased expression of its ligands confers resistance to Tuca, which may be overcome using dual/pan-HER TKIs or the combination of potent EGFR and HER2 inhibitors. Given the rapidly evolving treatment landscape of HER2+ breast cancer and biomarkers of resistance, our novel findings have potentially crucial therapeutic implications and suggest that rationally sequencing the currently available TKIs may be clinically important.

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5:00 PM - 6:15 PM

P1-13-18

EGFR signaling contributes to acquired resistance to CDK4/6 inhibitors in ER+ breast cancer cells in vitro and in vivo.

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Breast cancer driven by different hormone receptors, including estrogen receptor (ER+), is responsible for approximately 70-80% of cases among women. While endocrine therapy (ET) of ER+ primary tumors with antiestrogens or aromatase inhibitors is an effective first-line therapy, its success is limited by intrinsic and acquired resistance. Response to ET can be limited due to overexpression of cyclin D1, which promotes the activation of cyclin-dependent kinases 4 and 6 (CDK4/6). Selective inhibition of CDK4/6 and ER signaling is now standard-of-care therapy for ER+ metastatic breast cancer. CDK4/6 inhibitors (CDK4/6i), including palbociclib (PD), ribociclib, and abemaciclib, used in combination with ET, have shown improvement in progression-free survival compared to ET alone in the metastatic setting. However, the inevitable development of acquired resistance significantly limits the efficacy of this targeted therapy. Rewired signaling driven by different oncogenes, including the epidermal growth factor receptor (EGFR), overcomes the targeted inhibition of CDK4/6, which, in turn, allows cell cycle progression contributing to acquired resistance. We evaluated the expression and activity of EGFR in the panel of different matching pairs of ER- and ER+ CDK4/6i-sensitive (pS) and CDK4/6i-resistant (pR) breast cancer cell lines in vitro. Increased EGFR expression in ER+ MCF7/pR cells correlated with elevated ER phosphorylation, suggesting a direct cross-talk between EGFR and ER signaling in PD-resistant cells. Stimulation with EGF promoted ER activation, whereas estrogen stimulation promoted EGFR activation in ER+ pS and pR cell lines, indicating a direct cross-regulation between these molecular targets. Treatment of MCF7/pR cells with CDK4/6i resulted in elevated EGFR mRNA expression, confirming the dependency of resistant cells on EGFR signaling. Moreover, exposure to the EGFR inhibitors dramatically inhibited the proliferation of MCF7/pR cells compared to the parental cells, suggesting that EGFR could be an essential bypass signaling regulator contributing to resistance to CDK4/6i. We found that combined treatment with EGFRi and CDK4/6i significantly inhibited Rb phosphorylation in pR cells improving the effect of CDK4/6i on cell cycle arrest. We evaluated EGFR expression in MCF7/pS and pR mouse xenograft models in vivo. We observed a significant elevation in EGFR expression and phosphorylation in response to PD treatment, confirming the importance of EGFR signaling in maintaining the acquired resistance

to CDK4/6i in ER+ breast cancer cells. Taken together, our findings suggest that EGFR signaling plays an important role in acquired resistance to CDK4/6i in ER+ breast cancer cells in vitro and in vivo and targeting EGFR with small-molecule inhibitors (like erlotinib or gefitinib) or chimeric monoclonal antibodies (i.e. cetuximab) can be a promising approach to improve CDK4/6i efficacy in breast cancer patients.

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P1-13-19

ESAM reduces anti-HER2 therapy sensitivity by activating mTOR pathway in HER2 positive breast cancer

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Background: Trastuzumab combined with pertuzumab is the main therapy for HER2 positive breast cancer, but poor patient response due to drug resistance remains a clinical challenge. Organoids derived from tumor patients can highly maintain the heterogeneity of the original tumor, and have been used in drug sensitivity testing and new drug development. To screen for genes that associated with trastuzumab or pertuzumab drug resistance, this study used HER2-positive breast cancer organoids to establish a model of trastuzumab combined with pertuzumab and conducted high-throughput sequencing to screen the differential genes. We carried out further research to explore the effect of ESAM on drug sensitivity of HER2-targeted therapy and clarify the specific regulatory mechanisms and potential therapeutic targets of ESAM. Method: 8 HER2 positive breast cancer organoids were cultured. Immunohistochemistry, hematoxylin-eosin staining and Immunofluorescence were performed to identify the consistency between organoids and primitive tumors. According to drug sensitivity results of organoids to trastuzumab combined with pertuzumab, organoids were divided into a relatively sensitive group and a relatively insensitive group. Trastuzumab combined with pertuzumab was regularly used to stimulate the two groups. After 3 cycles, high-throughput transcriptome sequencing was used to evaluate their gene expression to find a gene responsible for trastuzumab and pertuzumab resistance. METABRIC and our center database were used to determine the prognostic value of ESAM. ESAM overexpression and knockdown stably transfected cell lines were constructed in SK-BR-3 and BT474 breast cancer cell lines by lentivirus. Colony formation assay, CCK-8 assay, organoid model and mouse xenograft model were conducted to examine the influence of ESAM on proliferation and trastuzumab or pertuzumab sensitization in vitro and in vivo. RNA-seq and GSEA analysis were performed to investigate the downstream pathways of ESAM. Western blot was used to confirm the relationship between ESAM and mTOR pathway. Small interfering RNA and mTOR/PI3K pathway inhibitors were used to confirm the function of mTOR in ESAM-induced drug

resistance of trastuzumab. Results: HER2 positive breast cancer organoids can maintain the pathological characteristics of primitive tumors. The results of high-throughput transcriptome show that ESAM is significantly up-regulated in the relatively insensitive group compared to the relatively sensitive group. METABRIC and our center database suggest that high ESAM mRNA expression was associated with poor OS, RFS, DFS and PFS of HER2-positive breast cancer patients. CCK-8 and cell colony formation assay confirm that ESAM can promote the proliferation of HER2-positive breast cancer cells and inhibit the drug sensitivity of HER2-positive breast cancer cells to trastuzumab and pertuzumab. GSEA analysis shows high ESAM can activate mTORC1 signaling pathway. Western blotting analysis proves the expression of ESAM is positively correlated with mTOR pathway. Inhibition of mTOR pathway in ESAM overexpression cells can suppress ESAM-mediated proliferation and reverse the drug sensitivity of cells to trastuzumab and pertuzumab. In vivo, overexpression of ESAM can promote the proliferation of mouse mammary tumors and reduce the sensitivity of mouse mammary tumors to trastuzumab, combined use of PI3K inhibitor could reverse drug sensitivity of mouse mammary tumors to trastuzumab. Conclusion: High ESAM expression is associated with poor prognosis in patients with HER2 positive breast cancer. ESAM can activate mTOR pathway, promote cell proliferation and reduce the sensitivity of HER2 positive breast cancer cells to trastuzumab and pertuzumab, which can be inhibited by the application of PI3K/mTOR inhibitors. Keywords: ESAM; HER2 positive breast cancer; HER2 targeted therapy; mTOR; drug sensitivity.

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Reprogramming of oncogenic signal pathways and metabolism during trastuzumab resistance formation of HER2 positive breast cancer

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Background The formation of resistance against trastuzumab deeply affects the treatment of HER2 positive breast cancer. Although studies have demonstrated several possible reasons that cause the trastuzumab resistance, the precise changes of cell process as well as the interaction between cancer cells and tumor microenvironment during the formation of resistance are still poorly understood. Here we figured out several crucial changes including oncogenic signal pathways as well as metabolism processes especially amino acids and polyunsaturated fatty acids (PUFAs) during the establishment of trastuzumab resistance. We further suggested that the inducers of ferroptosis may be promising reagents for trastuzumab resistant HER2 positive breast cancer. Methods The trastuzumab resistant cell was generated from a sensitive cell line SKBR3. To simulate the adaptation process of HER2 positive tumor to anti-tumor drug, the concentration of trastuzumab was changed gently to prevent cell death. After 8 weeks treatment, trastuzumab concentration in medium was raised from 1µg/ml to 6µg/ml, and a “persister” cell line SKBR3_HP was obtained. The original cell line SKBR3 was cultured for 8 weeks as well to exclude any changes that caused by culture condition. And each cell line includes 3 biological repeats. The viability of two cell lines is measured by CCK8 cell proliferation test with different concentration of trastuzumab. Total RNA of both SKBR3 and SKBR3_HP cells were prepared for sequencing. Activity scores of oncogenic signal pathways as well as metabolism processes were defined and calculated as the relative gene expression value averaged over all genes in this pathway in certain cell type. Flow cytometry was applied for reactive oxygen species measurement with BODIPY-C11. Results After 8 weeks treatment of trastuzumab, the persister cell line SKBR3_HP showed a significant higher viability than original sensitive cell line SKBR3. Oncogenic signal pathway analysis revealed that RTK-Ras, MYC and HIPPO pathways turn into a more active state in SKBR3_HP cells, as well as the upregulation of several cell cycle genes, which are all the response to the blockage of HER2 signal cascade and together maintains cell proliferation. Beside signal pathway, the reprogramming of metabolism is also the consequence of cell adaptation to trastuzumab. Minor changes in energy metabolism, such as glycolysis, citrate cycle and oxidative phosphorylation were observed in SKBR3_HP cells. However, amino acid metabolism, including the synthesis of phenylalanine, histidine, arginine, proline, cysteine and methionine, was largely enhanced in SKBR3_HP cells. Fatty acid, specifically the metabolism of PUFAs, such as linoleic acid, alpha-linolenic acid and arachidonic acid, was activated during the formation of trastuzumab resistance, which was confirmed by the lipid metabolomics data that most n-3/n-6 PUFAs decreased in SKBR3_HP cells. As cysteine and PUFAs metabolism might closely associate

with cellular redox balances, erastin and RSL3 were applied to interrupt the intake of cysteine and potentiate the lipid peroxidation process, respectively. A situation of higher ferroptosis sensitivity accompanies raising peroxidated lipids could be detected in SKBR3_HP cells. Conclusion By analyzing the transcriptome and metabolomics data of trastuzumab sensitive and persister cell lines, we pointed out that the changes of oncogenic signal pathway, together with metabolism variation, particularly amino acids and PUFAs, are all the cellular adaptations to high trastuzumab environment. And the higher ferroptosis sensitivity of persister cells could be a valuable treatment target.

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Loss of CDKN2B expression as a potential marker of resistance to CDK4/6 inhibitor in Luminal Breast Cancer cells

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Background Cyclin-Dependent Kinase (CDK) 4/6 inhibitors have significantly improved progression-free survival of Hormone Receptor positive (HR+), Human Epidermal Growth Factor Receptor type 2 negative (HER2-) luminal breast cancers (LBC). Several studies demonstrated that the addition of CDK4/6 inhibitors to endocrine therapy results in a significant prolongation of progression-free survival in patients with endocrine-sensitive or endocrine-resistant LBCs. However, the percentage of patients unresponsive or refractory to these

therapies is as high as 40%, and no reliable and reproducible biomarkers able to select a priori responder or resistant patients have been validated till now. The main cause of resistance is the selection of mutant clones in the target oncoprotein. Other mechanisms, like oncogene amplification/overexpression or mutations in other pathways, have been described in several models. Here, we focused on palbociclib, a selective inhibitor of CDK4/6. Methods: We generated and characterized human luminal breast cancer MCF-7 and T47D derived cell lines, able to survive and proliferate at different palbociclib concentrations, which also shows cross-resistance to abemaciclib. The resistant MCF7 cell line was characterized by RNA sequencing. Results: To confirm resistance, we performed cell viability assays in MCF-7 and T47D palbociclib sensitive cells (MCF-7pS and T47pS) versus MCF-7 and T47D palbociclib resistant cells (MCF-7pR5), showing a 10-fold increase of IC50 in MCF-7pR5 compared to parental MCF-7pS cells (16.7 vs 1.8 μ M) and a 3-fold increase of IC50 in T47DpR5 vs parental T47DpS. We also confirmed a significant cross resistance using abemaciclib in MCF-7pR5 with an IC50 equal to 6.8 vs 0.35 μ M and in T47DpR with an IC50 of 10.72 vs 0.5 μ M. RNA sequencing, qRT-qPCR and Western blot results demonstrated a dramatic downregulation of the CDK4 inhibitor CDKN2B in both cell lines and we found upregulation of an miR-31, a putative regulator of CDKN2B. This finding was further validated in a biopsy from a patient progressing on CDK4/6 inhibitor therapy. Conclusions: This study provides new relevant information regarding the mechanism of resistance to CDK4/6 inhibitors and suggests potential new markers to follow up patients during the treatment.

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Establishment and characterization of two ER+/HER2- XPDx models developed sequentially before and after acquired resistance to the CDK4/6 inhibitor palbociclib from a patient with metastatic breast cancer

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Background: Several CDK4/6 inhibitors have recently been approved in combination with letrozole or fulvestrant in hormone receptor-positive breast cancer. Although this combination therapy has been found effective in some patients, resistance often develops. To aid in developing new therapies for CDK4/6i-resistant breast cancer and better understand potential resistance mechanisms, we established two XenoSTART Patient-Derived Xenograft (XPDx) models representing ER+/HER2- breast cancer from tissue samples collected seventeen months apart from the same patient before and after palbociclib therapy. These models designated ST4887 and ST4887B were developed and characterized for receptor expression, genomic alterations, and in vivo drug sensitivities toward multiple chemotherapies and targeted agents, including CDK4/6i and fulvestrant. Methods: Models ST4887 and ST4887B were established from metastatic samples collected from a Caucasian female with ER+/HER2- metastatic breast cancer; ST4887 was collected at age 38 from a femur mass biopsy following several treatment regimens including paclitaxel/doxorubicin/cyclophosphamide, radiation and tamoxifen. ST4887B was collected at age 39 from a liver biopsy following treatment with palbociclib/letrozole then palbociclib/fulvestrant, and finally ixabepilone/capecitabine. Both were grown subcutaneously in female athymic nude mice supplemented with exogenous estradiol. The resulting models were passaged, and receptor expression confirmed immunohistochemically; genomic analysis, including WES and RNAseq, was performed to further characterize models. For in vivo studies, both models were evaluated using several

chemotherapy and targeted agents alone and in combination including cisplatin, docetaxel, CDK4/6i, fulvestrant, letrozole, olaparib, niraparib, and sacituzumab. In vivo study endpoints included tumor volume and time from treatment initiation with %T/C values and tumor regression reported at study completion; a T/C of $\leq 20\%$ versus control was considered sensitive. Tumor regression ($\%T/C \leq 0$) versus Day 0 tumor volume was also reported. Results: ST4887 and ST4887B retained comparable receptor expression (ER=3+/HER2=1+) over tested passages with similar histology compared to archival clinical samples. DNA/RNA sequencing identified several conserved variants including a somatic BRCA2 truncation (BRCA2Y2660*); transcriptomic analysis revealed upregulation of several related genes but no notable fusions. In vivo, both models were insensitive to cisplatin or docetaxel, however ST4887 but not ST4887B was sensitive to fulvestrant or CDK4/6i therapies, although abemaciclib demonstrated some activity toward ST4887B. PARP inhibitors were active toward ST4887 and to a lesser extent ST4887B, while sacituzumab did not have a significant effect on either model. Conclusion: We established and characterized two XPDX models from the same patient before and after acquired resistance to the CDK4/6i palbociclib. Both models were found to retain receptor status and drug sensitivities similar to the patient at the time of sample collection. These models can be utilized as a valuable tool in better understanding acquired resistance to palbociclib.

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5:00 PM - 6:15 PM

P1-13-23

Carboplatin resistance-associated changes in the 3D chromatin landscape of a triple-negative breast cancer Patient-Derived Xenograft

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Changes in the three-dimensional (3D) structure of the genome are an emerging hallmark of cancer. Cancer-associated copy number variants and single nucleotide polymorphisms promote rewiring of chromatin loops, disruption of topologically associating domains (TADs), active/inactive chromatin state switching, leading to oncogene expression and silencing of tumor suppressors. However, little is known about 3D changes during cancer progression to a chemotherapy-resistant state. We integrated chromatin conformation capture (Hi-C), RNA-seq, and whole-genome sequencing obtained from triple-negative breast cancer patient-derived xenograft primary tumors (UCD52) and carboplatin-resistant samples and found increased short-range (< 2Mb) interactions, chromatin looping, formation of topologically associating domains (TAD), chromatin state switching into a more active state, and amplification of ATP-binding cassette (ABC) transporters. Transcriptome changes suggested the role of long-noncoding RNAs in carboplatin resistance. Rewiring of the 3D genome was associated with TP53, TP63, BATF, FOS-JUN family of transcription factors and led to activation of aggressiveness-, metastasis- and other cancer-related pathways. Integrative analysis highlighted increased ribosome biogenesis and oxidative phosphorylation, suggesting the role of mitochondrial energy metabolism. Our results suggest that 3D genome remodeling may be a key mechanism underlying carboplatin resistance.

Disclosure(s):

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P1-14-01

Incidence, Clinicopathological Features and Treatment Outcomes Of Young Breast Cancer Patients: A Cohort Analysis From a High-Volume Tertiary Cancer Center in The United Arab Emirates

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Introduction

Breast cancer (BC) in women age 40 or younger represents approximately 7% of all BC cases. Studies have reported that BC in younger women is more likely to have adverse tumor characteristics and outcomes when compared to elder women. Despite the fact that BC in the Middle East seems to occur at a younger age, data on tumor characteristics in these patients are scarce, especially in the United Arab Emirates.

Objective

This study was conducted to investigate the incidence, clinicopathological characteristics, treatment modalities, and outcomes of young BC patients at a major cancer center in the UAE, Tawam Hospital. This will provide a better insight in local features and enables comparison of UAE data with other parts of the world.

Method

Data of 911 BC patients age ≤ 40 years treated at Tawam Hospital between 2000 and 2020 were analyzed. Information was obtained from the prospective Tawam Hospital Cancer Registry database and analyzed using (Python 3.9.7).

Result

A total of 911 patients were included in this study. Median follow up time 34 months (0.3 -1404). Patients ≤ 40 years of age comprised 24% (911/3782) of all BC cases diagnosed between 2000-2020. The clinical and pathological characteristics of these patients are provided in table 1. Of the total population, 625 (68.6%) patients were diagnosed based on palpable breast mass. 67 (7.3%) had pregnancy-related BC, and 346 (38%) had hereditary genetics testing conducted. Of those, 38 (11%) had pathogenic mutation (13 BRCA1, 16 BRCA2, 4 TP53, 2 PalbB2, 1 ATM, 1 APC, 1 NBN) and 59 (17%) had mutations with variants of unknown significance. Of patients with early-stage disease (N=764), 14 (2%) had excisional biopsy, 314 (41%) had a lumpectomy and 474 (62%) had a mastectomy, 257 (34%) had sentinel lymph node sampling, 439 (57%) had axillary lymph node dissection, 621(81%) had adjuvant radiation therapy, 727 (95%) had adjuvant/neoadjuvant systemic chemotherapy +/- anti-HER2/neu therapy. Of those who received neoadjuvant systemic therapy (N=341/727), 123 (36%) achieved pathologic complete remission. Of those with HR+ status early BC (N=487/764), 455 (93%) received adjuvant hormonal therapy (180 (40%) ovarian suppression, 391 (86%) tamoxifen, 39 (8.5%) aromatase inhibitor). Of all early BC patients, 180 (24%) developed recurrent disease (initial site: 45 (25%) locoregional recurrence, 83 (46%) visceral metastases, 66 (37%) bone metastases, 22 (12%) brain metastases, and 1 other sites). Kaplan Meier with log rank analysis and cox-proportional hazard models to be presented in the meeting.

Conclusion

The findings of this study are in accordance with previous studies on young BC patients. On initial presentation, patients had higher-grade tumors, a significant proportion with HER2/neu positive disease, larger tumor size, and nodal involvement. This study will help clinicians, researchers, and decision-makers better understand the unmet needs for young breast cancer patients in the UAE.

Table 1: Clinical and Pathological Characteristics of young BC patient ≤ 40 (N=911)

		N(%)			N(%)
Median age	36 (17-40)		Clinical T stage	Tis	47 (5.2)
Median BMI	26 (16-54)			T1	131 (14.4)
Gender	Female	909 (99.8)		T2	412 (45.2)
	Male	2 (0.2)		T3	151 (16.6)
Menarche (Median age)	13 (9-19)			T4	78 (8.6)
Any family history of BC	Yes	208 (22.8)	Clinical N stage	TX	92 (10.1)
	No	639 (70.1)		N0	347 (38.1)
	unknown	64 (7)		N1	279 (30.6)
History of OCH/HT use	Yes	138 (15.1)		N2	89 (9.8)
	No	559 (61.4)		N3	70 (7.7)
	Unknown	214 (23.5)	NX	126 (13.8)	
Smoking status	smoker	21 (2.3)	Grade	I	36 (3.9)
	Ex-smoker	19 (2)		II	320 (35.1)
	No	758 (83.2)		III	449 (49.3)
	Unknown	113 (12.4)		Unknown	106 (11.6)
Pregnancy related BC	Yes	65 (7.1)		Molecular subtype	HR+/HER2+
	No	756 (83)	HR+/HER2-		361 (39.6)
	Unknown	90 (9.9)	HR-/HER2+		109 (12.0)
stage	0	46 (5.0)	HR-/HER2-		147 (16.1)
	I	102 (11.2)	Unknown		70 (7.7)
	II	392 (43.0)	ER	Positive	584 (64.1)
	III	224 (24.6)		Negative	270 (29.6)
	IV	96 (10.5)		Unknown	57 (6.3)
	Unknown	51 (5.6)	PR	Positive	519 (57.0)
Histology	DCIS	30 (3.3)		Negative	332 (36.4)
	IDC	752 (82.5)		Unknown	60 (6.6)
	ILC	26 (2.9)	HER/neu	Positive	334 (36.7)
	LCIS	1 (0.1)		Negative	504 (55.3)
	Medullary	6 (0.7)		Unknown	73 (8.0)
	Metaplastic	9 (1.0)			
	Mixed	40 (4.4)			
	Mucinous	8 (0.9)			
	Papillary	4 (0.4)			
	Phyllodes	14 (1.5)			
	Sarcoma	1 (0.1)			
	Unknown	19 (2.1)			

Disclosure(s):

Aydah Al-Awadhi, MBBS: Astrazeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); BMS: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing).

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5:00 PM - 6:15 PM

P1-14-02

Breast cancer in pregnancy: A retrospective clinical study in a single large tertiary cancer center in the United Arab Emirates

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Breast cancer in pregnancy: A retrospective clinical study in a single large tertiary cancer center in the United Arab Emirates

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Introduction:

Pregnancy associated breast cancer (PABC) is defined as any breast cancer (BC) diagnosed during pregnancy or one year postpartum. BC considered the most common type of malignancy in pregnant women, occurring approximately once in every 3000 pregnancies. In view of the

fact that PABC is a relatively rare event surrounded by multiple variables, few studies address the best management and treatment options.

Objectives:

The aim of this study is to report the incidence, clinicopathological characteristics and treatment outcomes of PABC diagnosed over 20 years period treated in Tawam hospital. This will help clinician, researchers shed the light of the unmet needs for this entity of BC.

Method:

We reviewed all BC patients \leq 40 years of age diagnosed between 2000 -2020 in Tawam hospital and identified those with PABC as the definition above. Information was obtained from the Tawam Cancer Registry and analyzed. A retrospective data analysis was conducted. The data analyzed using the SPSS software. The study was approved by the hospital Research Ethics Board.

Results:

a total of 67 patients were identified in the study with pregnancy associated BC among all BC patients age \leq 40 years old which compromised 7.4% (67/911) from year 2000 till 2022. The clinical and the pathological characteristics of these patients are provided in table 1.

Around 22 (32.8%) of the patients were diagnosed at the second trimester. Only 6 (8.6%) patients found to have inflammatory breast cancer diagnosis. 31(42%) patients had hereditary genetic testing done of which 5 (16.1%) patients found to have pathogenic genetic mutations. Pathogenic mutations identified including 3 (9.7%) patients with BRCA2 mutation, 1 patient had BRCA1 mutation, and 1 patient had TP53 mutation.

Out of these 67 patients, 36 (65.5%) underwent modified radical mastectomy, 19 (34.5%) had lumpectomy, 37 (55.2%) had axillary lymph node dissection, 14 (20.8%) had sentinel lymph node biopsy, 13 (19.4%) had the surgery during the pregnancy and 45 (67.1%) had adjuvant radiation therapy post delivery. Regarding the chemotherapy, 29 (43.2%) patients received Neoadjuvant chemotherapy, 24 (35.8%) received Adjuvant chemotherapy, 11 (16.4%) were pregnant when they received chemotherapy. Only 7 (10.4%) patients had termination of their pregnancies, while 3 (4.4%) patients had spontaneous miscarriage. 47 (70.1%) patients delivered at our facility and 9 (13.4%) patients delivered at other facilities (unknown delivery details). In terms of delivery type, 24 (35.8%) patients had C-section surgery, and 23 (34.3%) patients had spontaneous vaginal delivery. All of the patients who had delivery in Tawam hospital, delivered healthy baby with no complications. Survival analysis and treatment outcome to be presented in the meeting.

Conclusion:

Our study showed that significant proportion of the patients with PABC diagnosed with HER2neu + disease, stage II-III disease, high grade tumors and nodal involvement on initial presentation. Patients were treated according to the standard of care with trend of favorable delivery outcomes. PABC is a unique entity of BC that requires careful planning and multidisciplinary approach with consideration of factors related to feral, pregnancy and maternal outcomes.

Table 1

		N (%)			N (%)
Age	25-30 years	17 (25.3%)	Molecular markers	HR +ve/HER-2 -ve	24 (35.8%)
	31-35 years	27 (40.2%)		HR -ve/HER-2 +ve	10 (14.9%)
	36-40 years	23 (34.3%)		Triple +	15 (22.3%)
Stage	I	6 (8.9%)	Triple -	13 (19.4%)	
	II	27 (40.3%)	Unknown	5 (7.4%)	
	III	21 (31.3%)	Total	16 (22%)	
	IV	11 (16.4%)	Bone alone	2 (13.3%)	
	Unknown	1 (1.5%)	Bone + Visceral	4 (26%)	
T, N, M Staging	T1	4 (5.9%)	iver	1 (6.6%)	
	T2	29 (43.2%)	Local	3 (20%)	
	T3	17 (25.4%)	Lymph node	1 (6.6%)	
	T4	11 (16.4%)	Visceral	4 (26%)	
	Tx	5 (7.4%)	TOC	53 (78.1%)	
Grade	N1	22 (32.8%)	Histology	ILC	2 (2.9%)
	N2	22 (32.8%)		DCIS	1 (1.5%)
	N3	9 (13.4%)		Intraductal	2 (2.9%)
	Nx	6 (11.9%)		Papillary	1 (1.5%)
	M0	54 (80.6%)		Phyllodes	2 (2.9%)
Grade	M1	11 (16.4%)	Mixed	2 (2.9%)	
	Mx	2 (2.9%)	Unknown	3 (4.4%)	
Family History	II	23 (34.3%)	Grade	II	35 (52.2%)
	Unknown	9 (13.4%)	Yes	13 (19.4%)	

Clinical and Pathological Characteristics of Pregnancy Associated Breast Cancer (N=67)

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5:00 PM - 6:15 PM

P1-14-03

Efficacy and safety of pyrotinib-based therapy in the treatment of HER2-positive breast cancer patients with brain metastases : a multi-center real-world study

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Background: An estimated 30-50% of patients with human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer (MBC) will develop brain metastases (BMs), and there are few effective treatment options. Pyrotinib has shown good efficacy in HER2-positive breast cancer patients with BMs in a single-arm phase II trial, but there is a lack of data from randomized controlled trial and real-world study. The purpose of this multi-center real-world study was to evaluate the efficacy and safety of pyrotinib-based therapy in HER2-positive breast cancer patients with BMs in real world. Methods: We reviewed the data of HER2-positive breast cancer patients with BMs who were treated with pyrotinib-based therapy from January 2018 to September 2021 at Shandong Cancer Hospital and Institute and other hospitals in Shandong Province in China. The initial dose of pyrotinib in most patients (n=92, 85.2%) was 400 mg once a day for every 21 days as a cycle. All patients were evaluated for tumor response every two cycles according to RECIST 1.1. The primary endpoint was progression free survival (PFS) and secondary endpoints were compounded objective response rate (ORR) and CNS-ORR (the ORR of central nervous system), compounded disease control rate (DCR) and CNS-DCR (the DCR of central nervous system) and overall survival (OS). The safety profile has also been assessed. The updated graded prognostic assessment for breast cancer patients with brain metastases (Breast GPA) includes age, Karnofsky performance status (KPS), extracranial metastases, number of brain metastases, and tumor subtype. It is divided into four subgroups (0-1.0, 1.5-2.0, 2.5-3.0 and 3.5-4.0) with different prognosis (the median survival: 6 months, 12.9 months, 23.5 months, and 36.3 months). Results: 101 patients were assessed for efficacy and toxicity. The median PFS is 10.0 months (95% CI, 6.9 to 13.1 months), and OS data were not available at the time of analysis. In overall patients, patients with GPA of 0-2.0 achieved shorter PFS (4.8 months vs 12.4 months, P=0.003). Trastuzumab (neo and adjuvant) (P=0.021), local therapy for BMs (P< 0.001) and pyrotinib treatment (P=0.022) had significant positive correlation with PFS. In patients with GPA of 0-2.0, the median PFS of different local treatment methods was significantly different (P< 0.001), stereotactic radiotherapy alone (13.6 months) was better than whole-brain radiotherapy alone (4.8 months) and combined local therapy (6.7 months); patients who received pyrotinib first in the BMs stage had longer PFS than those who did not (6.7 months vs 2.7 months, P=0.009) and radiotherapy for BMs (P=0.036) had correlation with longer PFS. Cox multivariate analysis indicated that GPA (0-2.0 vs 2.5-4.0) was independent predictor of PFS. For overall patients, the ORR was 42.6% and DCR was 88.1%. The CNS-ORR was 45.5% and CNS-DCR was 90.1%. Diarrhea (71.3%) was the most common adverse events (AEs), 47 patients (46.5%) reported grade 1-2 diarrhea, 25 patients (24.8%) reported grade 3 diarrhea. In addition, the more common AEs of grade 3 were loss of appetite (7.9%), hand-foot syndrome (6.9%), nausea (5.9%) and vomiting (5.0%). No grade 4 and 5 AEs occurred. Conclusions: Pyrotinib-based therapy is effective and tolerable in HER2-positive breast cancer patients with BMs. In the subgroup with Breast GPA 0-2.0, patients treated with radiotherapy had a better prognosis, and stereotactic radiosurgery alone was a viable option. Clinical trial information: ChiCTR2000037995.

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12/6/2022

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P1-14-04

A Phase 0 Clinical trial of Sacituzumab Govitecan in Patients with Breast Cancer Brain Metastases and Recurrent Glioblastoma

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Purpose: Sacituzumab govitecan has shown efficacy and acceptable tolerability in a multicenter phase I/II clinical trial (NCT01631552) in patients with advanced epithelial cancers. Our study was initiated to determine the bioavailability of Sacituzumab govitecan (SG) in breast brain metastasis and glioblastoma. The goals were to evaluate the extent by which SG can penetrate the blood brain barrier and access tumor tissues by testing free SN-38, SN-38G and total SN-38 concentrations in tumor tissue, serum, and CSF. Patients and methods: Patients diagnosed with brain metastatic breast cancer and recurrent glioblastoma were enrolled in a single-center clinical phase 0 study to receive a single intravenous dose of SG at 10 mg/kg one day before surgical resection. Tumor and corresponding serum were collected during surgery to measure their levels of SN-38 and its metabolites. Following recovery, patients resumed SG treatment at 10 mg/kg on days 1 and 8 of 21-day cycles and were assessed for responses by MRI every third cycle using response assessment in neuro-oncology (RANO) criteria. Total Sn-38 levels were quantified in tumor tissue and corresponding serum from the patients. Trop-2 and carbonic anhydrase IX (CAIX) expression was investigated by IHC. SG activity was tested in a breast cancer intracranial mouse model. Results: An average of 2365 ng/ml in serum and 132 ng/g in tissue of total SN-38 was quantified in our patient samples. Trop-2 expression was observed in 90% of patient tumors. 40% of the samples showed high expression of CAIX. SG significantly inhibited tumor growth in vivo and increased overall survival. 20% of patients in the breast cancer arm of the trial demonstrated a complete response by RANO criteria and the remaining 80% of patients demonstrated a partial response. Ultimately, 80% of the patients in the breast cancer metastasis arm survived. Conclusion: Sacituzumab govitecan is an effective drug that crosses the blood brain barrier to inhibit the growth of metastatic breast cancer to the brain after tumor resection surgery.

Disclosure(s):

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5:00 PM - 6:15 PM

P1-14-05

Pembrolizumab and Oral Metronomic Cyclophosphamide in Patients with Chest Wall Breast Cancer (PERICLES): an immune-biomarker analysis of tumor infiltrating lymphocytes (TILs) and programmed cell death ligand protein 1 (PD-L1)

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Background: Breast cancer (BC) with lymphangitic spread to the chest wall is a rare clinical entity affecting about 2% of pts, with poorer survival outcomes. A brisk immune infiltrate is typically reported, with up-regulation of inflammation and immune-tolerogenic genes. PERICLES clinical trial is testing the administration of pembrolizumab 200 mg Q3w plus cyclophosphamide 50 mg daily for BC with chest wall disease. In this exploratory biomarker analysis, we assessed the prevalence of the TILs score and the PD-L1 combined positive score (CPS) obtained from skin biopsies performed at screening.

Methods: PERICLES (NCT03971045) is a single-center, single-arm, interventional phase 2 trial. Main inclusion criteria: histologically confirmed, inoperable, locally recurrent and/or metastatic BC with lymphangitic spread to the chest wall (including and not limited to inflammatory BC); PD-L1 positive (CPS \geq 1; 22C3 pharmDx®) and/or TILs positive (\geq 1% of CD3 or CD20-positive cells) disease on skin biopsy obtained at screening; progression to at least one prior cytotoxic treatment; no prior immune checkpoint inhibitors. The primary endpoint is objective response rate as per immune-related RECIST criteria. 46 pts will be required for the study to power for the primary hypothesis. In this analysis, we describe the baseline immune-biomarker status, in the overall population enrolled based on hormone receptor status and HER2. Correlative analyses were provided (significance at p-value < 0.05).

Results: 37 pts were screened with skin biopsy of the chest wall disease (June 2020-June 2022). Biopsy and biomarker analysis were successful in 35 pts. Median age was 58 years (range: 35-79). Among the 35 pts included in the biomarker analysis, 25 (71%) pts had visceral disease and 20 (57%) had skin metastases at the diagnosis of metastatic disease; median number of previous lines of therapies was 4 (range: 1-12) and of chemotherapies was 4 (range: 1-10). 2 (6%) pts had HER2-positive disease, 13 (37%) HR-positive/HER2-negative disease, and 20 (20%) had triple-negative breast cancer (TNBC).

TILs and PD-L1 CPS were < 1 in 15 (43%) pts; 20 pts (57%) were eligible for CPS and/or TILs criteria: 16 (43%) were both PD-L1 positive and TILs positive, 4 only PD-L1 positive. Median PD-L1 CPS score was 5 (range: 0-80%) in the overall population and 17 (range: 2-80%) in eligible patients; 16/35 pts (43%) had CPS \geq 10. Median TILs score was 0% (range: 0-55%) in the overall population, 0% (range: 0-40%) in the HER2-negative (n=16), 0% (range 0-20%) in the HER2-low (n=18), and 37.5% (range 20-55%) in the HER2-positive (n=2).

No significant differences in baseline characteristics were found between positive and negative biopsies (Table). Considering only the TILs, a statistically significant correlation between HER2-positive status and TILs score was demonstrated (p < 0.001); no other correlations between receptor status (estrogen receptor, progesterone receptor, HER2) and PD-L1 CPS or TILs emerged.

Conclusions: 57% of patients with chest wall BC have skin metastases positive for PD-L1 CPS and/or TILs score \geq 1%. To our knowledge, these are the first prospective data on the prevalence of PD-L1 and TILs in metastatic BC with lymphangitic spread to the chest wall, highlighting potential actionability through therapeutic strategies with new immune-oncology

agents in this setting.

Characteristics of patients included in the biomarker analysis (n=35)

	Overall population (n=35)	PD-L1+ and/or TILs+ (n=20)	PD-L1- and TILs- (n=15)	p-value* (+ vs -)
Age - median (range)	58 (35-79)	49 (35-73)	60 (37-79)	0.33
Visceral disease - n. (%)	25 (71%)	15 (75%)	10 (67%)	0.71
Skin metastases at the diagnosis of metastatic disease - n. (%)	20 (57%)	12 (60%)	8 (53%)	0.74
Previous lines of therapies for metastatic disease - n. (range)	4 (1-12)	4 (1-10)	5 (1-12)	0.06
Previous lines of CT for metastatic disease - n. (range)	4 (1-10)	3,5 (1-10)	5 (1-7)	0.35
Subtype of BC				
TNBC - n. (%)	20 (57%)	11 (55%)	9 (60%)	1.00
HER2-positive - n. (%)	2 (6%)	2 (10%)	0 (0%)	0.49
HR+/HER2-negative - n. (%)	13 (37%)	7 (35%)	6 (40%)	1.00
HR+/HER2low - n. (%)	6 (17%)	4 (20%)	2 (13%)	0.68
HR+/HER2 0 - n. (%)	7 (20%)	3 (15%)	4 (27%)	0.43
Biomarker status				
PD-L1 CPS ≥ 1 - n. (%)	20 (57%)	20 (100%)	-	NA
PD-L1 CPS ≥ 10 - n. (%)	16 (43%)	16 (80%)	-	NA
TILs ≥ 1% - n. (%)	16 (43%)	16 (80%)	-	NA

*Calculated with T test or Fisher's exact test, as appropriate.

Keys: BC, breast cancer; CPS, combined positive score; CT, chemotherapy; HR; hormone receptor; n, number; NA; not available; PD-L1, Programmed cell death ligand protein 1; TILs, tumor infiltrating lymphocytes; TNBC, triple negative breast cancer.

Disclosure(s):

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Nicola Fusco, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Boehringer Ingelheim: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); GSK: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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12/6/2022

5:00 PM - 6:15 PM

P3-11-11

Impaired Succinate Metabolism Supports Endocrine Therapy Resistance in ER Positive Breast Cancers

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Estrogen receptor positive (ER+) breast cancer is the most common subtype among all breast cancers and is responsible for most breast cancer related deaths. Endocrine therapies, such as selective estrogen receptor modulators (SERM) and aromatase inhibitors (AI), often given in combination with cyclin-dependent kinase 4/6 (CDK4/6) inhibitors, are initially effective but the majority of advanced ER+ breast cancers eventually become refractory to endocrine therapies. Therefore, understanding the underlying molecular mechanisms that enable or promote resistance to endocrine therapies may lead to novel therapeutic targets. Cancer cells consume greater quantities of glucose to meet their energy and anabolic demands to support cell growth and proliferation. In this study, we used breast cancer cell models that are endocrine therapy sensitive and resistant and investigated the metabolites by growing the cells in the presence of the stable glucose isotope, UC13-Glucose. We measured the C13-labelled metabolites of glycolysis and the TCA cycle. Glucose consumption was higher in endocrine therapy resistant MCF7/LCC9 (LCC9) cells compared with parental MCF7 (MCF7) and estrogen independent, endocrine therapy sensitive MCF7/LCC1 (LCC1) cells. Notably, in LCC9 cells the m+4 and m+6 isotopomer of C-13 labelled citrate was absent with a concurrent high succinate:fumarate ratio. Furthermore, in LCC9 cells, most of the fumarate was unlabeled suggesting that fumarate was not generated from glucose. These results suggest that the TCA cycle is impaired in LCC9 cells and the conversion of succinate to fumarate is dysregulated. Succinate dehydrogenase (SDH) enzyme is responsible for reversible catalytic conversion of succinate to fumarate. SDH is a multimeric protein comprised of four different subunits and SDH assembly factor 2 (SDHAF2), which is a tumor suppressor gene. Comparable SDH enzyme activity was observed in LCC9 and LCC1 cells. Intriguingly, when SDH activity was inhibited using dimethylmalonate, the LCC9 cells were re-sensitized to both Fulvestrant and 4-hydroxytamoxifen. Succinate accumulation was accompanied with HIF 1-alpha stabilization and SDH inhibition led to lower levels of HIF1-alpha. This indicated that SDH may function in the conversion of fumarate to succinate in LCC9 cells. Our study further investigates the source of fumarate in LCC9 cells. Overall, this study suggests that targeting succinate metabolism may help to restore sensitivity to Fulvestrant and tamoxifen in endocrine therapy resistance in ER+ breast cancer cells.

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5:00 PM - 6:15 PM

Discussion 1 + Q&A: Disparities in Screening and Outcomes

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5:00 PM - 6:15 PM

Discussion 2 + Q&A: Biology, Race and Outcomes

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Disclosure(s):

Elena Martinez, Ph.D.: No financial relationships to disclose

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5:00 PM - 6:15 PM

Poster Spotlight Discussion 1: Racial Outcomes and Disparities

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12/6/2022

5:00 PM - 6:15 PM

PD1-01

PD1-01 The Impact of Structural Racism on Breast Cancer Stage at Presentation

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Background: Despite advances in diagnosis and treatment, racial and economic disparities in breast cancer-specific survival persist and this is exacerbated by later stage at presentation. It is essential to assess the factors that contribute to later stage at presentation to target racial and socioeconomic disparities in breast cancer mortality. The objective of this study was to analyze the effect of neighborhood socioeconomic status (SES) and race/ethnicity, as measured by the Index of Concentration at the Extremes (ICE), on breast cancer stage at presentation in a diverse metropolitan area that mirrors the projected demographics of many US regions.

Methods: Patients treated at our medical campus, comprised of a safety-net hospital and an academic cancer center, with stage I-IV breast cancer from 2005-2017 were identified from our tumor registry. Census tracts were used as neighborhood proxies. Using 5-year estimates from the American Community Survey, 5 ICE variables were computed: economic (high vs. low), race/ethnicity (non-Hispanic White (NHW) vs. non-Hispanic Black (NHB) and NHW vs. Hispanic) and racialized economic (low-income NHB vs high-income NHW and low-income Hispanics vs. high-income NHW) segregation. ICE uniquely captures spatial economic and racial/ethnic segregation by mapping social inequality not otherwise captured by evaluating a population of a specific socioeconomic level or belonging to a particular racial/ethnic group. We used five separate models based on each of the ICE variables to evaluate economic and racial/ethnic segregation. Model 1 captures economic segregation (high vs. low), Model 2 captures racial segregation (NHB vs. NHW), Model 3 evaluates racialized economic segregation (low-income NHB vs high-income NHW), Model 4 captures segregation by Hispanic ethnicity (Hispanic vs. Non-Hispanic), and Model 5 captures ethnic and economic segregation (low-income Hispanics vs. high-income NHW). Our main outcome was breast cancer stage at presentation categorized as early (Stage I and II) vs. late (Stage III and IV) disease. All models controlled for the following covariates: race/ethnicity, age, insurance status, tumor subtype, and comorbidities including hypertension, diabetes, coronary artery disease,

and hyperlipidemia.

Results:

The study population included 6,145 breast cancer patients. 52.6% were Hispanic, 26.3% were NHW, and 17.2% were NHB. Those living in the most economically marginalized neighborhoods (Quartiles 1 and 2) had significantly increased odds of presenting with later stage disease [ORQ1 1.36 (1.13-1.64), ORQ2 1.43 (1.18-1.75); $p < 0.05$]. Those living in the most racial/ethnic and economically marginalized neighborhoods (Quartile 1 of Models 3 and 5) had statistically significantly increased odds of presenting with later stage after controlling for all covariates compared to a NHW living in more economically advantaged neighborhoods [ORModel3 1.55 (1.21-1.99), ORMModel5 1.43 (1.11-1.85); $p < 0.05$].

Conclusions:

This study is the first to evaluate stage at presentation by ICE, which allows us to uniquely evaluate how residential racial and economic segregation may influence breast cancer disparities. Our study shows that patients in the most economically and racial/ethnically marginalized neighborhoods were more likely to present with later stage disease. This suggests that structural racism is influencing stage at presentation, and therefore effecting racial and economic disparities in breast cancer, even when accounting for demographics and tumor characteristics. To address these disparities, effective interventions are needed that account for the social and environmental contexts in which cancer patients live and can access care.

TABLE 1: Odds Ratios for Later Stage at Presentation with Breast Cancer by Different Types of Residential Segregation

TABLE 1: Odds Ratios for Later Stage at Presentation with Breast Cancer by Different Types of Residential Segregation

	Model 1	Model 2	Model 3	Model 4	Model 5
Economic (vs. Q4)					
q1	1.36 (1.13-1.64)*	-	-	-	-
q2	1.43 (1.18-1.75)*	-	-	-	-
q3	1.08 (0.88-1.31)	-	-	-	-
Black(vs. Q4)					
q1	-	1.34 (0.89-2.02)	-	-	-
q2	-	1.01 (0.67-1.52)	-	-	-
q3	-	1.08 (0.68-1.72)	-	-	-
NHB Economic(vs. Q4)					
q1	-	-	1.55 (1.21-1.99)*	-	-
q2	-	-	1.44 (1.14-1.82)*	-	-
q3	-	-	1.14 (0.87-1.49)	-	-
Hispanic(vs. Q4)					
q1	-	-	-	1.32 (1.09-1.60)*	-
q2	-	-	-	0.93 (0.75-1.15)	-
q3	-	-	-	1.02 (0.84-1.23)	-
Hispanic Economic(vs. Q4)					
q1	-	-	-	-	1.43 (1.11-1.85)*
q2	-	-	-	-	1.56 (1.17-2.08)*
q3	-	-	-	-	1.16 (0.86-1.56)

Model 1: Economic segregation (high-income vs low-income)

Model 2: NHB vs NHW segregation

Model 3: NHB and economic segregation (low-income NHB vs high-income NHW)

Model 4: Hispanic vs NHW segregation

Model 5 : Hispanic and economic segregation (low-income Hispanics vs. high-income NHW)

Q1: Most disadvantaged neighborhoods; Q4: Reference: most advantaged neighborhoods.

*p < 0.05

Model 1: Economic segregation (high-income vs low-income)

Model 2: NHB vs NHW segregation

Model 3: NHB and economic segregation (low-income NHB vs high-income NHW)

Model 4: Hispanic vs NHW segregation

Model 5: Hispanic and economic segregation (low-income Hispanics vs. high-income NHW)

Q1: Most disadvantaged neighborhoods; Q4: Reference: most advantaged neighborhoods.

*p < 0.05

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Alexandra Hernandez, MD, MPH: No financial relationships to disclose

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5:00 PM - 6:15 PM

PD1-02

PD1-02 Evaluating Racial and Ethnic Disparities in Diagnostic Breast Imaging: A Retrospective Cohort Study

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Purpose: The purpose of this study is to examine the association between race/ethnicity and diagnostic delays in patients with abnormal screening mammograms. **Methods:** HIPAA-compliant, institutional review board exempt retrospective cohort study was performed at a multi-location academic medical center located in the Midwest. Patients included women aged 40-74 years old undergoing screening mammography from 2013-2019 who received a Breast Imaging Reporting and Data System (BI-RADS) category 0 on their screening mammogram, derived from the electronic medical records. Primary outcome variables included timely follow up diagnostic imaging (< 30 days), days to diagnostic exam, timely recommended biopsy (< 60 days), and days to recommended biopsy. Primary exposure variables included race (American Indian/Alaska Native, Asian/Native Hawaiian/Other Pacific Islander, Black or African American, White) and ethnicity (Hispanic/Latino, and Not Hispanic/Latino). Binary outcomes (timely follow up diagnostic imaging, timely recommended biopsy) were analyzed using logistic regression and continuous outcomes (days to diagnostic exam, days to recommended biopsy) were

analyzed using Cox proportional hazards regression, adjusted for potential confounders (insurance, age, preferred language, having primary care doctor, married or domestic partnership, availability of on-site diagnostic imaging). Results: 13,269 unique patients received BI-RADS category 0 on screening mammogram (mean age 54.6). Adjusted for potential confounders, Black (OR 0.54, 95% CI 0.42 to 0.69, $p < 0.001$) and Asian (OR 0.62, 95% CI 0.45 to 0.85, $p = 0.004$) patients were less likely to have timely follow up diagnostic imaging compared to White patients. American Indian and Hispanic patients were comparably likely to have timely follow up diagnostic imaging ($p > 0.05$). Black (HR 0.76, 95% CI 0.69 to 0.84, $p < 0.001$), Asian patients (HR 0.78, 95% CI 0.70 to 0.87, $p < 0.001$), and Hispanic patients (HR 0.90, 95% CI 0.82 to 0.99, $p = 0.041$) experienced increased days to diagnostic examinations compared with White patients. American Indian patients experienced comparable times to diagnostic examinations ($p = 0.136$). 22.3% of patients received recommendations for biopsy (2,796/12,535). No statistically significant differences were found in timely follow up after recommended biopsy (< 60 days) comparing Black, Asian, American Indian, and Hispanic to White patients ($p > 0.05$). Black, American Indian, and Hispanic patients experienced comparable days to recommended biopsy ($p > 0.05$). Asian patients experienced increased days to recommended biopsy (HR 0.76, 95% CI 0.58 to 0.99, $p = 0.046$). Conclusions: Racial/ethnic minority patients are more likely to experience diagnostic delays after screening mammograms. Further research into culturally appropriate patient navigation services and improved accessibility of diagnostic imaging centers (operating hours, same day services, transportation, parking) to reduce disparities in diagnostic imaging delays is warranted.

Disclosure(s):

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5:00 PM - 6:15 PM

PD1-03

PD1-03 Neighborhood deprivation and breast cancer mortality among Black and White women

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Background: Neighborhood deprivation is hypothesized as a potential driver of racial disparities in breast cancer mortality. However, research shows that neighborhood deprivation is associated with increased breast cancer mortality among White women, but has little to no association among Black women. No study has previously considered the intersections of race, social cohesion, or urban/rural status in the association between neighborhood deprivation and breast cancer mortality. Methods: Neighborhood deprivation was examined in relation to breast cancer mortality among 31,358 non-Hispanic Black and non-Hispanic White women diagnosed with invasive breast cancer (stage I-IIIa) between 2010-2017, followed through 2019, and identified by the Georgia Cancer Registry. Two composite scores, the Area Deprivation Index (ADI) and neighborhood deprivation index (NDI), were used to characterize neighborhood deprivation. A third composite score, the Yost index, was assessed as a measure of neighborhood socioeconomic status (SES). Each composite score was composed of factors representing six domains: poverty, income, occupation, housing, employment, and education. Data on ADI were obtained from the Neighborhood Atlas and was assessed in deciles. American Community Survey data from 2011-2015 and principal components analysis were used to derive the NDI and Yost index. Both measures were assessed in quartiles. Each composite variable was measured at the block group level and linked to patient data. Cox proportional hazards regression was used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for the association between each composite variable and breast cancer mortality, overall and by race/ethnicity. Intersectionality will be examined by considering the joint effects of race/ethnicity, social cohesion, and urban/rural status. Results: During the 9-year follow-up period, 2,353 (1,347 non-Hispanic White, 1,006 non-Hispanic Black) women died from breast cancer. Regardless of which composite score was assessed, living in the most deprived or lowest SES neighborhoods was associated with an increased risk of breast cancer mortality in models adjusted for age and race (ADI decile 10 vs. 1: HR=1.57, 95% CI 1.26-1.96; NDI quartile 4 vs. 1: HR=1.43, 95% CI 1.26-1.63; Yost index quartile 1 vs 4: HR= 1.34, 95% CI 1.18-1.51). Stratification by race/ethnicity showed associations were slightly stronger among non-Hispanic White women but null among non-Hispanic Black women. Results from analyses examining the joint effects of race/ethnicity, social cohesion, and urban/rural status are

forthcoming and will be presented in December. Conclusions: Consistent with previous studies, our study found that living in a deprived neighborhood may increase breast cancer mortality among non-Hispanic White women, but not non-Hispanic Black women. Investigating the association with an intersectionality framework may help identify subgroups of women who are particularly susceptible to the adverse impact of neighborhood deprivation on breast cancer mortality.

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5:00 PM - 6:15 PM

PD1-04

PD1-04 Neighborhood Deprivation Index and Survival in Breast Cancer in the United States

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Introduction

Socioeconomic status (SES) of the individual and neighborhood plays an important role in patients' (pts) access to the health system and eventually in the outcomes of their disease. Owing to the inequalities in opportunities, education, income, and developmental infrastructures, the area with deprived individual and neighborhood SES may be associated with a poor prognosis of certain malignancies and worse outcomes. We analyzed the association between Neighborhood Deprivation Index (NDI) and survival of early-stage breast cancer (BC).

Methods

The NDI created by the National Cancer Institute includes variables from dimensions, such as, wealth and income, education, occupation, and housing conditions which have been used for our analysis. We analyzed the impact of NDI in quintiles (qn). We queried the SEER database from 2010-2016 for all early-stage BC pts and studied the overall survival (OS) and disease-specific survival (DSS) of BC in association with NDI. Cox multivariate regression modeling was performed to measure the association between NDI and OS/DSS. Kruskal-Wallis test was used for comparison for continuous and Chi-Square test was used for categorical variables. All analyses were adjusted for age, race, grade, insurance, surgery (SX), radiation (RN), and chemotherapy (CT). Statistics were performed using SAS.

Results

Out of the 88,572 early-stage BC pts, 27.4 % (n= 24,307) were in the most deprivation (MD) qn, 26.5% (n= 23,447) were in the average deprivation (AD) qn, 17% (n= 15,035) were in the

above average deprivation (AA) qn, 15.6% (n= 13,838) were in the least deprivation (LD) qn and 13.5% (n= 11,945) were in the below average deprivation (BA) qn. The median age of pts in the LD qn was 59 and MD qn was 61 yrs, p< 0.001. There was a predominance of racial minorities in the MD and AA qn with Blacks being 13-15% and Hispanics being 15% compared to only 8% Blacks and 6% Hispanics in the LD qn (p< 0.001). There was a higher percentage of uninsured pts in the MD qn compared to LD qn (2.2% vs 1.7%, p< 0.001). There were more rural areas in MD qn compared to LD qn (25.9% vs only 0.7%, p< 0.001). There were more pts with grade III disease in MD qn compared to LD qn (34% vs 31.9%, p< 0.001). 96.1% pts underwent SX in MD qn vs 97.1 % had SX in LD qn, p< 0.001. Similarly, 49.7% underwent RN in MD qn vs 56.5% had RN in the LD qn, p< 0.001. Greater percentage of pts received CT in MD qn compared to LD qn (44.6% vs 42.1%, p< 0.001). There was a higher percentage of more aggressive cancers such as triple-negative breast cancer (TNBC) and HER2 positive (HER2+) in MD qn compared to LD qn (14.5%, 17.7% vs 11.7%, 16.5% respectively, p< 0.001). In multivariate analysis, in the overall cohort, those who live in AA qn and MD qn have inferior OS and DSS when compared to those who live in LD qn (OS in AA: Hazard Ratio (HR) 1.3, 95% CI: 1.2-1.4; OS in MD: HR 1.2, 95% CI: 1.1-1.3; DSS in AA: HR 1.3, 95% CI: 1.2-1.5; DSS in MD: HR 1.2, 95% CI: 1.1-1.4, all p< 0.001). Similar results in OS and DSS were observed in hormone receptor-positive HER2 negative (HR+) and HER2+ subtypes, but not in TNBC (Table 1). The 5-year OS rates and DSS rates were also comparatively low in AA qn and MD qn compared to LD qn (OS: AA- 84%, MD- 85%, LD- 98%; DSS: AA- 91%, MD- 92%, LD- 95%, all p< 0.001).

Conclusion

Early-stage BC pts from areas with worse NDI have poor OS and DSS, after accounting for the demographic, clinicopathological, treatment-related factors. Investments in poor-resource neighborhoods and policies focusing on improving the SES of areas with high deprivation need to be implemented to reduce health care disparities and improve breast cancer outcomes.

Overall Survival and Disease Specific Survival

Subtype	NDI	OS		
		HR	95% CI	P-value
HR+	AA	1.3	1.2 - 1.5	<0.001
	MD	1.2	1.1 - 1.4	<0.001
HER2+	AA	1.2	1.1 - 1.5	0.02
	MD	1.2	0.99- 1.4	0.12
TNBC	AA	1.2	0.9 - 1.4	0.06
	MD	1.1	0.9 - 1.3	0.07
DSS				
HR+	AA	1.4	1.2 - 1.6	0.0002
	MD	1.3	1.1- 1.5	0.0007
HER2+	AA	1.5	1.2 - 2.0	0.001
	MD	1.3	1.0 - 1.6	0.03
TNBC	AA	1.2	0.97 - 1.4	0.08
	MD	1.2	0.96 - 1.4	0.10

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5:00 PM - 6:15 PM

PD1-05

PD1-05 Racial/Ethnic Segregation and Inequities in Metastatic Breast Cancer Treatment Initiation and Overall Survival

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Background While racial/ethnic segregation, a form of structural racism, has been linked to health inequities, there is limited information regarding segregation and its potential impact on breast cancer care and outcomes. Here we assessed whether and to what extent racial/ethnic segregation is associated with timeliness of care and real-world overall survival (rwOS) in patients diagnosed with metastatic breast cancer (mBC). Methods This retrospective study used the nationwide Flatiron Health electronic health record-derived de-identified database. The cohort included community oncology patients (≥ 18 years) diagnosed with mBC between January 2011 and April 2022. Census tract data from the American Community Survey (2015-2019) was used to characterize neighborhoods based on the most recent recorded patient address. Segregation was defined as predominant race/ethnicity (e.g., tracts whose population was $\geq 50\%$ non-Latinx Black were labeled as predominantly Black neighborhoods). Timeliness of care was defined as biomarker (estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2) testing within 30 days and systemic treatment initiation within 60 days of metastatic diagnosis (evaluated using X2 tests). We estimated Cox proportional hazard models adjusted for age and sex to examine rwOS (patients were followed from diagnosis to death or last recorded activity). Results Among 18,884 patients diagnosed with mBC (median age: 65 years), 71.0% lived in predominantly White neighborhoods, 7.5% in Black neighborhoods, and 8.7% in Latinx neighborhoods. Compared with patients residing in predominantly White neighborhoods, patients in Black and Latinx neighborhoods were more likely to be diagnosed with de novo mBC (30.7% vs. 34.8% and 33.5%, respectively) and have Medicaid (7.6% vs. 15.8% and 15.3%). Fewer patients in predominantly Black (74.4%) and Latinx (69.9%) neighborhoods received timely biomarker testing compared to patients in White

(77.7%) neighborhoods ($p < .01$). Similarly, fewer patients in predominantly Black (73.5%) and Latinx (72.6%) neighborhoods had timely treatment initiation compared to patients in White (79.6%) neighborhoods ($p < .01$). Patients in Black neighborhoods (HR 1.24, 95% CI 1.16-1.33) had worse rwOS than patients in White (ref.) and Latinx neighborhoods (HR 0.90, 95% CI 0.83-0.97). Conclusions Our results suggest that racial/ethnic segregation is associated with inequities in breast cancer care and outcomes, where patients in predominantly Black and Latinx neighborhoods are less likely to receive timely care than those in White neighborhoods. Living in predominantly Black neighborhoods was also associated with reduced survival. Therefore, efforts to reduce cancer inequities should target higher-order structural factors associated with worse cancer care and outcomes, including segregation and other forms of structural racism.

Disclosure(s):

Jenny S. Guadamuz, PhD, MSPH: Flatiron Health: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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Harlan Pittell, PhD: Flatiron Health: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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Amy E. Pierre, MSN, ANP-BC: BMS: CME Presentation (Terminated, November 12, 2021); Flatiron Health: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

Cleo A. Ryals, PhD: Flatiron Health: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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5:00 PM - 6:15 PM

PD1-06

PD1-06 Black patients with triple negative breast cancer (TNBC) have enriched stromal tumor infiltrating lymphocytes (sTILs) and receive preferential benefit from neoadjuvant immunotherapy

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Introduction TNBC is overrepresented in Black women, and Black patients with TNBC have worse clinical outcomes compared to non-Black patients. This disparity likely results from racial differences in clinical, biological, and demographic features of TNBC and social determinants of health. Neoadjuvant chemoimmunotherapy is current standard of care for high-risk TNBC. However, Black patients have been poorly represented in immunotherapy TNBC trials, making it difficult to assess comparative efficacy of immunotherapy in Black patients. Methods We utilized two TNBC neoadjuvant trials to assess racial differences in the tumor immune microenvironment composition and evaluate impact of race on response to chemotherapy vs

chemoimmunotherapy. NeoSTOP trial (NCT02413320) randomized 100 stage I-III TNBC patients to receive neoadjuvant carboplatin/paclitaxel + doxorubicin/cyclophosphamide (CbP+AC) or carboplatin/docetaxel (CbD). NeoPACT trial (NCT03639948) enrolled 120 patients with stage I-III TNBC who received neoadjuvant CbD + pembrolizumab (CbD+P). sTILs were centrally quantified, and RNA extracted from pretreatment tissue was subjected to next-generation sequencing. Relative leukocyte fractions were computed by CIBERSORTx. Factors were tested as predictors of pathologic complete response (pCR) using logistic regression analysis. Event-free survival (EFS) was estimated by the Kaplan-Meier method and compared between groups by log-rank test, followed by Cox regression analysis. Results The study population includes 197 patients with known race, sTILs, and gene expression data (84 patients from NeoSTOP, 113 from NeoPACT). 15/84 (18%) patients in NeoSTOP and 20/113 (18%) patients in NeoPACT self-reported Black race. There was no significant difference in age, T or N stage, or germline BRCA1/2 mutation status by race in either study. Black patients had significantly higher sTILs than non-Black patients (median 40% vs 15%, $P=0.048$) and were more likely to have $\geq 20\%$ sTILs than non-Black patients (66% vs 44%, $P=0.026$). There was no significant difference in pCR by race in NeoSTOP (OR=0.60, 95% CI 0.19-1.84, $P=0.37$; pCR 47% for Black vs 59% for non-Black). In contrast, in NeoPACT, Black patients had a significantly higher pCR compared to non-Black patients (OR=3.27, 95% CI 1.01-10.64, $P=0.049$; pCR 79% for Black vs 53% for non-Black). In NeoSTOP, EFS was similar for Black and non-Black patients (3-year EFS 92% and 94%, respectively, HR=0.88, 95% CI 0.11-7.28, $P=0.90$). In NeoPACT, EFS was numerically higher in Black vs non-Black patients (3-year EFS 93% and 81%, respectively, HR=0.43, 95% CI 0.05-3.36, $P=0.40$); NeoPACT survival follow-up is ongoing at the time of this report. On CIBERSORTx analysis, Black patients had relative depletion of immunosuppressive pro-tumorigenic M2 macrophages ($P=0.005$) and CD4+ memory resting T cells ($P=0.021$) compared to non-Black patients. Conclusions Compared to non-Black patients, Black patients with TNBC are more likely to have immune-enriched tumors with lower relative abundance of immunosuppressive leukocytes. These findings suggest potential for higher relative magnitude of benefit from checkpoint inhibitor therapy in Black compared to non-Black patients. Supporting this biological hypothesis, we noted that Black and non-Black patients had equivalent rates of pCR with neoadjuvant chemotherapy; however, pCR rate among Black patients was significantly higher than in non-Black patients when treated with neoadjuvant chemoimmunotherapy. These findings should be confirmed in other studies and can optimize utilization of neoadjuvant chemoimmunotherapy. Our findings also underscore the importance of efforts to address disparity in access and use of immunotherapy in Black patients.

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Roberto Salgado, MD, PhD: BMS: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing); Merck: Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Research support and lectures (Ongoing); Puma Biotechnology: research support (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing)

Joshua M. Staley, M.S.: No financial relationships to disclose

Anne O'Dea, M.D.: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Daichii Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Terminated,

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5:00 PM - 6:15 PM

PD1-07

PD1-07 Racial disparities in neoadjuvant chemosensitivity and survival in early breast cancer: A national database study.

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Background

Neoadjuvant chemotherapy (NAC) is the standard of care for locally advanced breast cancer (BC). Patients (pts) who attained pathological complete response (pCR) with NAC have a better prognosis when compared to those who have residual disease (RD). We analyzed the association of race with neoadjuvant chemosensitivity in early BC and the overall survival (OS) based on the chemosensitivity.

Methods

We queried the National Cancer Database for early BC pts who received NAC from 2010-2016. Preoperative chemosensitivity was defined as very sensitive (VS) (ypT0/TisN0), sensitive (S) (pathological TNM stage less than clinical, excluding ypT0N0), and refractory (R) (pathological greater than or equal to clinical). Demographic, clinical, treatment, and survival rates were summarized by race focusing on neoadjuvant chemosensitivity. All associations were compared using Kruskal-Wallis, Pearson's Chi-Squared, and Fisher's Exact Tests. Multivariate cox models were generated for the OS. All analyses were conducted in RStudio v4.0.2 at a significance level of 0.05.

Results

A total of 103,605 pts who received NAC were analyzed. 43.2% (n= 44,796) were R, 34.4% (n= 35,638) were S and 22.4% (n= 23,171) pts were VS. The 3-year (yr) OS rates for R, S, VS groups were 81%, 88%, 95% respectively (rsp) (p< 0.001). The 5-yr OS rates were 73%, 82%, 92% rsp (p < 0.001). In the hormone-receptor positive HER2 negative (HR+) subtype, only 8.9% (n= 3,837) were VS, while among triple negative breast cancer (TNBC) subtype, 28.4% (n= 9,224) pts were VS, among HER2 positive (HER2+) subtype, 36.7% (n=9,665) pts were VS and in both subtypes around 28-36% were R as opposed to 58.4% with R disease among HR+

subtype. Among HR+ group, pts had more R disease regardless of race (all races R: 54-57%, $p < 0.001$). Among HER2+ disease, Blacks had lower percentage of VS disease compared to other races (32% vs 37-40%, $p < 0.001$). Among TNBC, more R disease was seen among Blacks compared to other races (38% vs 30-35%, $p < 0.001$). In whole cohort, as expected, compared to pts with R disease, pts with S and VS disease had lower overall mortality risk (HR= 0.45, 95% CI= 0.43 – 0.46, $P < 0.001$, HR= 0.20, 95% CI = 0.19- 0.21, $p < 0.001$ rsp). In TNBC subgroup among pts with R disease, the median OS of Blacks was significantly lower compared to whites (71.9 vs 101.8 months, $p < 0.001$). Among BC subtypes, the 3-yr and 5-yr OS for R (65%, 56%) and S groups (83%, 76%) were significantly lower in TNBC when compared to other subtypes (HR+ R: 3-yr- 88%, 5-yr- 79% and S: 3-yr- 90%, 5-yr- 83%; HER2+ R: 3-yr- 85%, 5-yr- 77% and S: 3-yr- 92%, 5-yr- 86%, $p < 0.001$). In the whole cohort, Blacks with R, S, VS disease had significantly lower 3yr (73%, 85%, 94% rsp) and 5yr OS (63%, 78%, 91% rsp) compared to all other races and this was more prominent in the R and S groups (Table1).

Conclusion

Blacks diagnosed with TNBC were more resistant while other races were more sensitive to NAC. In all BC subtypes, Blacks had lower 3-yr and 5-yr OS regardless of chemosensitivity (including those who attained pCR), though this disparity was more predominant among those with residual disease after NAC (resistant and sensitive group). Since Blacks who do not attain pCR have worse survival compared to other races, it highlights the need to design more effective and personalized treatment strategies for Blacks to help them attain pCR, especially in the TNBC subtype.

Racial Disparities in Survival in Different Chemosensitivity Groups

Table 1:

Chemosensitivity	Survival Rates	Whites	Blacks	Hispanics	Asian	P-value
R	3-yr	82.8	72.8	83.6	88.2	<0.001
	5-yr	74	63.4	76.1	80.3	
S	3-yr	88.8	85	90	92.8	<0.001
	5-yr	82.2	78.7	85	89.4	
VS	3-yr	95.3	94.4	95.6	97.3	<0.001
	5-yr	92.1	91.4	93.4	95	

Racial Disparities in Survival in Different Chemosensitivity Groups

Disclosure(s):

Arya Mariam Roy, MD: No financial relationships to disclose

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12/6/2022

5:00 PM - 6:15 PM

PD1-08

PD1-08 PAM50 and 21-gene recurrence scores in younger and Black women with breast cancer

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Background: Black and younger women have poorer breast cancer outcomes. Using a diverse population-based study, we examined the role of biology as measured by genomic assays in outcome disparity among clinically HR+/HER2- women. Methods: Data and biospecimens from the Carolina Breast Cancer Study (CBCS, including 2,103 non-metastatic, invasive breast cancers) were used to perform RNA-based classification according to molecular subtype and research versions of known prognostic assays, the 21-gene Recurrence Score (RS) and the

PAM50-based Risk of Recurrence (ROR-PT) score. Prevalence odds ratios (PORs) and 95% confidence intervals (CIs) for subtype by race and age were estimated. Results: Black women had higher frequency of Luminal B [POR (95% CI): 2.08 (1.60, 2.71)], HER2-enriched [POR (95% CI): 2.01 (1.45, 2.79)], and Basal-like tumors [POR (95% CI): 3.51 (2.81, 4.40)] compared to non-Black women. Similarly, younger (< 50 years) women had higher frequency of Luminal B [POR (95% CI): 1.57 (1.21, 2.04)], HER2-enriched [POR (95% CI): 2.03 (1.46, 2.82)], and Basal-like tumors [POR (95% CI): 2.40 (1.92, 3.01)]. Additionally, within clinically-defined HR+/HER2- tumors, Black women had higher frequency of high ROR-PT among younger women [POR (95% CI): 2.88 (1.19, 6.97)], but this association was attenuated among older women [POR (95% CI): 1.99 (0.84, 4.71)]. Race was not significantly associated with the 21-gene RS among younger or older women. Conclusion: While Black and younger women with clinically-defined HR+/HER2- often have higher burden of non-Luminal/high genomic risk tumors, PAM50 and 21-gene assays show different demographic patterns and heterogeneity within age- and race-defined groups, underscoring the value of genomic testing in understanding outcome disparities.

Disclosure(s):

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(Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Royalty (Ongoing)

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12/6/2022

5:00 PM - 6:15 PM

PD1-09

PD1-09 Associations between the 21-gene Oncotype DX Recurrence Score (RS), Ki67, and Race in Early Breast Cancer (EBC) Using the National Cancer Database (NCDB)

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Background: The 21-gene RS (Oncotype DX) is a validated genomic signature that provides prognostic information for distant recurrence risk and is predictive of adjuvant chemotherapy benefit in patients with hormone receptor (HR)-positive, HER2-negative early breast cancer (EBC). Ki67 protein expression is a proliferation marker that is determined by immunohistochemistry (IHC) and is a prognostic biomarker in HR-positive EBC. Black race is associated with poorer prognosis in patients with EBC. RS, Ki67 and race have not been evaluated together and the impact of race on the association between Ki67 and RS is unknown. The goal of this study was to evaluate the association between the 21-gene RS and Ki67 based on race in patients with HR-positive EBC using the NCDB.

Methods: Women with HR-positive EBC with 0-3 involved lymph nodes, diagnosed between 2018 and 2019, who had available information on RS, IHC-measured Ki67, and race in the NCDB dataset were identified. Patients were stratified by RS of low (0-10), intermediate (11-25) and high (26-100) and categorized into Ki67 low ($\leq 30\%$) based on the International Ki67 Working Group prognostic classification (PMID: 33369635). Wilcoxon rank test was used to test for continuous variables and chi-square test was used for categorical variables. Agreement between Ki67 and RS was estimated using Fleiss Kappa statistic and corresponding p-value was reported.

Results:

43,898 eligible women were included. 17.43% were lymph node positive. 78% were Non-Hispanic White, 7.98% Non-Hispanic Black, 6.42% Hispanic, and 4.26% Asian American/Pacific Islander (AAPI). The table below describes the distribution of Ki67 and RS in the overall population and racial subgroups. The distribution of Ki67 scores was significantly different between races with a higher proportion of Black patients having high Ki67 scores, $p < 0.0001$. RS distribution varied as well with a greater percentage of high RS in the Black group, $p < 0.0001$. There was only slight agreement (Kappa 0.01-0.20) between Ki67 and RS in the overall population (Kappa=0.1929, $p < 0.0001$), low Ki67 subgroup (Kappa=0.069, $p < 0.0001$) and intermediate group (Kappa=0.066, $p < 0.0001$). However, there was fair agreement (Kappa

0.21-0.40) between high Ki67 and RS (Kappa=0.351, $p < 0.0001$). Based on race as a covariate, in the overall population, agreement between Ki67 and RS remained slight for White, Hispanic, and AAPI groups but was fair for Black patients (Kappa=0.2345, $p < 0.0001$). In the low Ki67 and intermediate Ki67 groups, agreement remained slight across all races, $p < 0.0001$. While there was fair agreement between high Ki67 and RS in all racial subgroups, agreement between high Ki67 and RS was highest in the Black subgroup (Kappa=0.392, $p < 0.0001$) followed by the AAPI (Kappa=0.363, $p < 0.0001$), White (Kappa=0.342, $p < 0.0001$) and Hispanic (Kappa=0.339, $p < 0.0001$) groups.

Conclusions:

In this large patient population from the NCDB, there was only slight agreement between Ki67 and RS in the overall, low Ki67, and intermediate Ki67 groups but fair agreement in the high Ki67 group. Agreement between high Ki67 and RS was greatest in the Black subgroup compared to other races. This may be attributed to the higher proportion of patients with high Ki67 and RS in the Black subgroup. Future analyses on overall survival will determine the impact of race on the prognostic value of Ki67 and RS.

Table 1. Distribution of Ki67 and RS by Racial/Ethnic Subgroup

	Overall	White	Black	Hispanic	AAPI	AIAN/Other/ Unknown
N (%)	43898 (100)	34275 (78.08)	3502 (7.98)	2819 (6.42)	1870 (4.26)	1432 (3.26)
Ki67						
Low (≤5%)	9580 (21.82)	7675 (22.39)	613 (17.50)	587 (20.82)	416 (22.25)	289 (20.18)
Intermediate (6-29%)	26075 (59.40)	20471 (59.73)	1994 (56.94)	1640 (58.18)	1101 (58.88)	869 (60.68)
High (≥30%)	8243 (18.78)	6129 (17.88)	895 (25.56)	592 (21.00)	353 (18.88)	274 (19.13)
Oncotype						
Low (0-10)	11422 (26.02)	9080 (26.49)	780 (22.27)	699 (24.80)	485 (25.94)	378 (26.40)
Intermediate (11-25)	26302 (59.92)	20643 (60.23)	1983 (56.62)	1706 (60.52)	1109 (59.30)	861 (60.13)
High (≥26)	6174 (14.06)	4552 (13.28)	739 (21.10)	414 (14.69)	276 (14.76)	193 (13.48)

AAPI: Asian American/Pacific Islander
AIAN: American Indian and Alaska Native

Disclosure(s):

Rima Patel, MD: No financial relationships to disclose

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Grace Van Hyfte, MS: No financial relationships to disclose

Joseph Sparano, MD, FACP: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing); BMS: Consulting Fees (e.g., advisory boards) (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); GE: Consulting Fees (e.g., advisory boards) (Ongoing); Genomic Health: Consulting Fees (e.g., advisory boards) (Ongoing); GHI: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing)

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12/6/2022

5:00 PM - 6:15 PM

PD1-10

PD1-10 Impact of Race on Clinical, Socioeconomic, and Genomic Characteristics, Clinical Trial Participation, and Receipt of Genotype-matched Therapy Among Patients with Metastatic Breast Cancer

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Background: Clinical outcomes in breast cancer differ across racial and ethnic populations. We have previously demonstrated that receipt of genotype-matched therapy targeted to an actionable mutation may potentially improve patient outcomes (Vidula, CCR, 2021). We evaluated the impact of race on clinical, socioeconomic, and genomic characteristics, clinical trial participation, and receipt of genotype-matched therapy among patients with metastatic breast cancer (MBC). **Methods:** We conducted a retrospective study of patients with MBC at an academic institution who underwent cell-free DNA testing (cfDNA, Guardant360, 74 gene panel) as part of routine clinical care from 11/29/2016-11/2/2020. Patient demographics (including self-reported race and ethnicity) and clinical trial enrollment (at same institution) were determined by retrospective data collection. Mutations identified in cfDNA were characterized as actionable based on the variant interpretation performed by Guardant360 using vetted genomic databases, and receipt of genotype-matched therapy targeted to an actionable mutation was determined as previously described (Vidula, CCR, 2021). Pearson's chi-squared and Wilcoxon rank-sum tests were used to compare categorical and continuous variables between groups, with $p < 0.05$ indicating statistical significance. **Results:** Four hundred and twenty-five patients with MBC and cfDNA results were identified, of which 369 were White (87%), 27 Black (6.4%), 15 Hispanic (3.5%), and 14 Asian (3.3%). There were no significant differences in median age at MBC diagnosis ($p=0.064$), disease subtype distribution ($p=0.74$), proportions of de-novo/recurrent MBC ($p=0.95$), presence of visceral metastases ($p=0.84$), Charleston comorbidity index ($p=0.93$), menopausal status ($p=0.3$), and level of education ($p=0.44$) across racial groups. Higher proportions of non-primary English speakers were seen in Hispanic (80%) and Asian (29%) races ($p < 0.001$). Median distance traveled to the institution also varied based on race, with White patients traveling further (White: 39.1 miles, Black: 21.8 miles, Hispanic 9.4 miles, Asian 9.1 miles, $p < 0.001$). In addition, type of insurance varied based on race, with White patients having the highest rates of commercial insurance and Medicare, Black patients having the highest rate of state-supported insurance, and Asian patients having the highest uninsured rates ($p < 0.001$). Clinical trial enrollment rates did not significantly differ by race (White: 44%, Black: 37%, Hispanic: 47%, and Asian 21%, $p=0.34$), but patients without insurance were significantly less likely to be enrolled on a trial than those with commercial insurance ($p=0.03$). The proportion of patients with ≥ 1 actionable mutation in cfDNA did not vary significantly by race (White: 78%, Black: 56%, Hispanic: 73%, Asian 86%, $p=0.18$) and the median number of actionable mutations found in cfDNA was similar across races ($p=0.31$). However, receipt of genotype-matched therapy targeted to an actionable mutation varied by race, with the highest rates of matched therapy in White patients (White: 28%, Black: 11%, Hispanic 13%, Asian 14%, $p < 0.001$). After multivariable logistic regression adjusting for subtype, commercial insurance versus other insurance types, and proximity to the center, White patients remained significantly more likely to receive matched therapy ($p=0.029$). **Conclusions:** We observed significant race-based differences in non-English speaking status, insurance type, and median distance traveled to the institution. Racial/ethnic minority patients were less likely to receive genotype-matched therapy than White patients. Further research is needed to identify barriers and reduce disparities in access to precision medicine.

Disclosure(s):

Rupali Sood, MD, MPH: No financial relationships to disclose

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12/6/2022

5:00 PM - 6:15 PM

Discussion 1 + Q&A: PD2-03, PD2-05, PD2-08, PD2-11 & PD2-04

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5:00 PM - 6:15 PM

Discussion 2 + Q&A: PD2-01, PD2-02, PD2-06, PD2-07, PD2-09 & PD2-10

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12/6/2022

5:00 PM - 6:15 PM

Poster Spotlight Discussion 2: Tumor Immunology and Novel Immune Therapy Strategies

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12/6/2022

5:00 PM - 6:15 PM

PD2-01

PD2-01 Local and lymphoid immune surveillance mechanisms in “exceptional survivors” of stage 4 cancers following standard of care chemo- and targeted therapies

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Breast cancer patients with advanced metastatic disease can exhibit rapid disease progression, disease stabilisation or partial responses of varying duration. However, for reasons that are not fully elucidated, a small fraction of patients will elicit an exceptional durable response to standard anticancer treatments or survive significantly longer than patients with clinically comparable tumours. Here, we investigate the drivers of immune surveillance mechanisms across breast cancer subtypes in stage IV exceptional survivors (n=13) with matched control cohorts of stage IV typical responders (n=6), early breast cancer patients (n=5) and healthy volunteers (n=17). Peripheral blood mononuclear cells (PBMCs) from patients were stained with 8 panels providing 241 non-redundant immune parameters for flow cytometry analysis. Principle Component Analysis (PCA) showed distinct segregation of the exceptional survivors from the other control groups with an immune signature in exceptional survivors constituting of activated NK, CD8 T cells and gamma delta (gd) T cells pointing towards higher innate immunogenicity in these individuals. Specifically, although these metastatic exceptional responder patients possessed comparable NK cell frequencies, the proportion of NKG2D+CD56dimCD16+ NK cells were significantly enriched compared to the typical responders. Additionally, proportions of CD8+ central memory (CD45RA- CD27+) and effector memory (CD45RA- CD27-) gd T cells, were also seen to be significantly increased. Functional in vitro validation of these findings along with scRNA sequencing of lymph node and tumour tissue is currently underway. To our knowledge, this work is the first to explore in depth the immune signatures in the peripheral blood of exceptional survivors with metastatic breast cancer. Elucidating the immunological reasons for favourable atypical responses alongside functional tumour microenvironment analysis offers unique insights for predictive biomarker identification and discovery of axes that could be exploited therapeutically to benefit those with

less favourable responses. Written informed consent was obtained from all individuals in accordance with the Declaration of Helsinki under the following research ethics committee; London-Chelsea approved study (REC ID 13/LO/1248).

Disclosure(s):

Helen Kakkassery, MRes: No financial relationships to disclose

Thanussuyah Alaguthurai, MSc: No financial relationships to disclose

Rosalind Graham, PhD: No financial relationships to disclose

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Sheeba Irshad, MD PhD: No financial relationships to disclose

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5:00 PM - 6:15 PM

PD2-02

PD2-02 Longitudinal local and peripheral immunologic changes associated with checkpoint inhibition response in murine models of breast cancer

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Immune checkpoint inhibitors (ICI) have significantly enhanced patient survival in some cancer types but yield limited success in breast cancer. ICIs activate anti-tumor immunity by overriding the inhibition of tumor infiltrating lymphocytes (TILs). Clinical trials in triple negative breast cancer (TNBC) patients, who are more likely to harbor TILs within tumor stroma, have demonstrated increased progression-free survival (IMpassion130) and pathologic complete response (KEYNOTE-522) to ICI. Consequently, combinations of ICI and chemotherapy have been FDA-approved for metastatic TNBC. However, the therapeutic benefit of ICIs is highly heterogeneous among breast cancer patients; as such, we sought to model ICI response in vivo to evaluate therapeutic resistance and response heterogeneity, as well as ascertain predictive biomarkers for favorable outcomes to ICI in breast cancer. We used an immunocompetent EMT6 orthotopic mammary tumor model to investigate the efficacy of ICI (anti-PD-L1). Analysis of the primary tumor immune landscape was performed by flow cytometry and single-cell RNA sequencing. Matched longitudinal samples of the tumor microenvironment (collected by fine-needle aspiration) and peripheral blood (PBMC) from mice were profiled by bulk RNA and T-cell receptor (TCR) sequencing to identify systemic genomic alterations and T-cell expansion, respectively. Single-agent ICI robustly suppressed primary tumor growth ($p = 0.0046$) and extended survival ($p < 0.0001$) beyond the control group in the EMT6 model. The addition of chemotherapy (paclitaxel and/or doxorubicin) demonstrated moderate therapeutic efficacy but failed to enhance ICI benefit. Phenotypic profiling of the tumor microenvironment (TME) revealed increased T cells, dendritic cells, and NK cells in anti-PD-L1 only and chemotherapy combination groups. Despite using a genetically identical tumor model and murine host, we found that PD-L1 blockade induced heterogeneous responses, similar to clinical outcomes in breast cancer patients, ranging from complete response to intrinsic resistance. Analysis of the primary tumor microenvironment showed upregulated signatures of cytotoxic T cell response and activation, specifically inflammatory interferon signaling (both prior to and post ICI administration) that corresponded to favorable response to anti-PD-L1 in individual mice. Longitudinal analysis of the peripheral blood identified modest changes among mice at baseline that progressively deviated by response type (non responders-vs-responder mice). Moreover, mice harbored enriched myeloid signatures and

clonal T cell expansion during therapy corresponding to ICI resistance and response, respectively. Further investigations of matched peripheral blood and the primary tumor microenvironment signatures may identify systemic biomarkers and tumor antigen-specific T cell clones to accurately predict ICI response in patients and uncover mechanisms for sensitizing tumors refractory to ICI. In conclusion, we identify a heterogeneously ICI-responsive in vivo model that emulates TNBC patient response to combinatorial ICI approaches. We describe host-specific signatures, specifically myeloid cell responses, that correlate with differential responses to immunotherapy, which may serve as a basis for tracking immunotherapy response in peripheral blood from breast cancer patients.

Disclosure(s):

Ann Hanna, Ph.D.: No financial relationships to disclose

Xiaopeng Sun, B.S.: No financial relationships to disclose

Quanhui Sheng, Ph.D.: No financial relationships to disclose

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Justin Balko, PhD, PharmD: Genentech: Contracted Research (Ongoing); Incyte: Contracted Research (Ongoing)

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5:00 PM - 6:15 PM

PD2-03

PD2-03 Targeting TGF- β and over-expressing GM-CSF in the Tumor Microenvironment (TME) with AMUN-003 Inhibits Tumor Growth and Metastases and Augments Immune Checkpoint Inhibitor (ICI) Response in Triple Negative Breast Cancer (TNBC)

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Introduction: Despite several therapeutic advancements, metastatic TNBC remains incurable for nearly all patients and is a frequent cause of cancer-related deaths worldwide. We tested the hypothesis that inhibiting suppressive signals sustained by TGF- β and concurrently stimulating recruitment of inflammatory cells with GM-CSF within the TME would result in improved anti-tumor responses. We report here pre-clinical single agent and ICI combination data for a newly developed oncolytic adenovirus rAd.sT.GM (AMUN-003) that expresses both sTGF β RIIFc (a TGF- β protein decoy), and GM-CSF tested in an immunocompetent mouse model. **Methods:** In addition to manufacturing Amun-003 which is a replication competent adenovirus encoding both sTGF β RIIFc and GM-CSF transgenes, we generated multiple replication competent control viruses coding for sTGF β RIIFc alone, GM-CSF alone or no transgene. We implanted 4T1 cells in the flanks of BALB/c mice, a syngeneic tumor model that is immune competent. On day 7 and day 10 post tumor cell inoculation, we performed saline or single agent virus injections into the tumor. We monitored the health of the animals, performed periodic tumor caliper measurements and collected sera for analysis of cytokines and markers of tissue injury. Animals were sacrificed on Day 25 and tissues collected. Similarly, with the same animal model and using reduced dose Amun-003, we tested combinations with systemic anti-CTLA-4, anti-PD-1 monoclonal antibodies, or both. Animals were sacrificed on Day 25 with specimens collected as above but also to report the metastatic burden in distant tissues. **Results:** In single agent experiments, all adenovirus constructs were similarly tolerated by the animals with no notable differences in animal weights. General safety as assessed by serum LDH and IL-6 demonstrated no difference between animal groups treated with the different virus constructs. All adenovirus resulted in delay of cancer growth and on day 25, excised tumors from sacrificed animals weighed less than tumors from animals treated with buffer. However, a single dose of Amun-003 was the most effective at delaying tumor progression than

any other tested constructs (Day 21 and Day 25: $P < 0.0001$ vs the buffer group by two-way ANOVA analysis). Next, we conducted experiments evaluating a single dose of Amun-003 alone or in combination with anti-CTLA4, anti-PD1 or both ICI. Combinations of Amun-003 with ICI delayed progression better than ICI treatments alone or Amun-003 alone. Moreover, the combination with both ICI and Amun-003 was most effective at delay of tumor progression (Day 22 and Day 25: $P < 0.0001$ vs the buffer group; D25: $P=0.0119$ vs dual ICI therapy). Lung surface metastatic nodule counts and lung tissue luciferase assay for 4T1-luc2 cells both showed treatment consisted of Amun003 and both ICI was most potent in inhibiting lung metastasis (Lung nodules: $P < 0.0001$ vs the buffer group; Relative luminescence: $P=0.0036$ vs the buffer group, both by one-way ANOVA analysis). Finally, the metastatic burden in the lung was least in animals treated with Amun-003 and both ICI (42% metastases free) ($P = 0.0373$ vs the buffer group by fisher's exact test). Conclusions: In syngeneic immune competent animals harboring an aggressive TNBC tumor, single agent Amun-003 appeared safe and was more effective at controlling tumor progression following an intratumoral injection when compared to other tested adenovirus constructs. In the same model, combinations of ICI with Amun-003 resulted in delayed tumor growth and control of metastatic spread. These results with Amun-003 support advancement to human clinical testing.

Disclosure(s):

Sooncheon Shin, PhD: AmunBio: Salary (Ongoing)

Benjamin Filimon, n/a: No financial relationships to disclose

Yuefeng Yang, n/a: No financial relationships to disclose

Zebin Hu, n/a: No financial relationships to disclose

Prem Seth, n/a: AmunBio: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing)

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5:00 PM - 6:15 PM

PD2-04

PD2-04 Preclinical development of CodaLytic™, a codon-modified influenza virus, as a novel virotherapeutic agent for breast cancer immunotherapy

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Multiple species of oncolytic viruses (OVs) have been shown to modulate the tumor microenvironment (TME) by increasing immune cell infiltration and activating stimulatory immune responses, leading to the induction of a tumor-specific immune response. Many engineered OVs achieve tumor specificity by either gene deletion or mutations and are then armed with immunomodulatory transgenes to promote anti-tumor immune responses. In an alternative approach, OVs derived from Codagenix's codon/codon pair modification platform aim to leverage the natural immunostimulatory capacity of selected viral species for efficacy and take advantage of defects in innate immune sensing and apoptosis mechanisms in cancer cells as well as receptor overexpression for tumor selectivity. CodaLytic is a novel virotherapeutic derived from influenza virus strain A/California/07/2009, that is synthetically engineered to contain over 600 silent mutations in hemagglutinin and neuraminidase genes and is being developed as a novel immunotherapeutic for breast cancer. In the orthotopic EMT6 triple-negative breast cancer model, known for its moderate sensitivity to immunotherapies, intratumoral injection of 108 PFU three times a week for up to 4 weeks as a monotherapy led to significant tumor growth inhibition by 76% ($p < 0.001$ vs vehicle control), translating into a significant survival benefit with a 66% cure rate. Intravenous rechallenge of EMT6 long-term survivors led to a 27-fold reduction in lung nodule formation and a tumor-specific interferon- γ memory response was observed *ex vivo* in their splenocytes. Anti-tumor efficacy after CodaLytic treatment was accompanied by a change in the composition of the tumor immune infiltrate with significant increases in T, B and NK cells and increased gene expression of pathways and genes related to T cell effector function, dendritic cell activation, antigen presentation and chemoattraction. In immunotherapy-resistant orthotopic 4T1 tumors, combination of CodaLytic with a CTLA-4 inhibitory antibody, but not anti-PD-1 blockade – a combination that had demonstrated combination benefit in several other preclinical models – led to reduction in tumor growth by 75% ($p < 0.0001$ vs vehicle control and PD-1 combination group). Median overall survival improved from 22 to 30 days with addition of CTLA-4 blockade. Triple combination including PD-1 inhibition led to improved long-term survival beyond 50 days with 30% complete regressions. In summary, these preclinical data demonstrate CodaLytic's ability to induce broad innate and adaptive changes in the breast cancer TME, resulting in anti-tumor efficacy and prolonged survival. Characterization of the tumor immune infiltrate after CTLA-4 combination and pharmacodynamic changes achieved after CodaLytic/checkpoint combination treatment in human breast cancer tumoroids will further support identification of correlates of efficacy with translational implications. Together with preclinical toxicology data and demonstrated clinical safety of this attenuated influenza virus after intranasal administration in healthy individuals, CodaLytic emerges as a promising novel viroimmunotherapeutic agent and is planned to enter a phase 1 clinical trial in early 2023.

Disclosure(s):

Marcin Stawowczyk, PhD: Codagenix Inc.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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5:00 PM - 6:15 PM

PD2-05

PD2-05 CSF-1R antibody targeting therapy with combined metronomic chemotherapy enhances a B and T cell response for the treatment of metastatic triple negative breast cancer.

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Background: Increased macrophage infiltration is associated with the poorest outcome following neo-adjuvant chemotherapy in patients with triple negative breast cancer (TNBC). We have extensively characterized three different preclinical syngeneic claudin-low Trp53^{-/-} tumor models (T11, T12 and 2151R), that have high Tumor Associated Macrophage (TAM) infiltration. These “claudin low” models closely phenocopy the EMT/TAM subtype observed in patients. Treatment using conventional chemotherapy, Cyclophosphamide (CTX) in combination with Pexidartinib (PXB, PLX3397) an anti CSF-1R small molecule inhibitor yielded a durable response in two of the models, T12 and 2151R (Singh et al. Cancer Res. 2022). However, due to potential liver toxicity and dual targeting of c-kit and FLT-3, PXB is not moving forward into the clinic for TNBC. Accordingly, we asked if SNDX-ms6352 a specific, high affinity monoclonal antibody targeting CSF-1R in combination with CTX might provide an alternative approach for treating primary TNBC as well as established lung metastases. Methods: Tumor chunks were transplanted into the mammary fat pad to generate primary tumors. Single cells from primary T12 mammary tumors were introduced via tail vein (TV) injection to obtain lung metastases. After fifteen days for primary tumors and twelve days following TV injection, respectively, the mice were randomized into treatment groups and administered four weekly treatments of IgG, CTX, SNDX-ms6352 or CTX+SNDX-ms6352. Primary tumors, lungs and mammary glands were harvested and fixed overnight in 4% paraformaldehyde then placed in 70% EtOH for paraffin embedding and stained for H&E, immunohistochemistry (IHC), immunofluorescence (IF) and imaging mass cytometry (IMC). Results: Following, four weekly treatments of CTX+SNDX-ms6453 we observed a significantly decreased primary tumor volume as compared to IgG, CTX and SNDX-ms6352 alone. Mice that fully responded to the treatment were re-challenged with tumor cells in the contralateral mammary gland to determine if there was a long-term immune memory response. We observed a fifty percent tumor re-challenge rejection in both T12 and 2151R. Increased expression of CD20 B and CD8 T cells was observed within the mammary gland of the complete responders, this was accompanied by macrophage depletion in the SNDX-ms6352 and combination treated mice. SNDX-ms6352 induced macrophage apoptosis as evidenced by the activation of cleaved caspase 3. For lung

metastases TV injected mice were administered BrdU to identify micro-metastatic lesions. Following four weekly combination treatments of CTX+/-SNDX-ms6352 we observed a decreased lung metastatic burden and increased overall survival as compared to IgG, CTX and SNDX-ms6352 alone. Interestingly we also observed increased CD8 T-cell infiltration, but only in the combination treated mice following 28 and 56 days post treatment. Conclusion: These results suggest that targeting macrophages enhances the immunostimulatory effect of low dose cyclophosphamide in treating not only primary tumors, but also established lung metastasis via the activation of the tumor immune microenvironment. Supported by CA148761 and T32 CA203690 grants.

Disclosure(s):

Diego Pedroza, Ph.D.: No financial relationships to disclose

Weiguo Wu, M.D., Ph.D.: No financial relationships to disclose

Paul Porter, Ph.D.: No financial relationships to disclose

Xiang Zhang, Ph.D.: No financial relationships to disclose

Jeffrey Rosen, PhD: No financial relationships to disclose

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5:00 PM - 6:15 PM

PD2-06

PD2-06 Implications of Heterogeneity in Breast Tumor Cell MHC-I Expression on Immunity and Therapeutic Resistance

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Background Immune checkpoint inhibitors (ICIs) targeting the PD-1/L1 axis are approved in early-stage treatment for triple-negative breast cancer (TNBC), but only a fraction of patients benefit. Tumor expressed antigens bound to major histocompatibility complex-I (MHC-I) are required for CD8-mediated tumoricidal activity, and thus, response to anti-PD-1/L1 targeted ICI. However, many breast tumors downregulate, or heterogeneously express, MHC-I, making them less susceptible to ICIs. Tumor cells downregulating MHC-I may be effectively targeted by natural killer (NK) cells due to 'missing self' signals. However, this heterogeneity in MHC-I expression is poorly modeled in most preclinical studies, limiting our understanding of how to overcome ICI resistance in the context of heterogeneous MHC-I expression, as is often observed clinically. Objective We aimed to 1) quantitatively delineate how intratumoral heterogeneity in MHC class I expression affects immune responses and immunotherapy outcomes in mouse models and 2) determine whether targeting inhibitory signals on NK cells can overcome ICI resistance in MHC-I heterogenous TNBC. Methods We performed quantitative immunofluorescence for MHC-I, CD8, CD56, and pan-cytokeratin on breast cancer tumors from diverse subtypes (n=314) to obtain single-cell-resolution MHC-I expression and spatial information of tumor and immune cells. Fluorescence intensity and spatial analysis were processed to output individual tumor/stromal cell MHC-I expression and the composition of the local tumor microenvironment. To determine the functional effect of MHC-I heterogeneity in vivo, we generated a CRISPR-guided B2m knockout (B2m-null) in a murine orthotopic model (EMT6). We then combined MHC-I-proficient and MHC-I-deficient isogenic lines at various ratios to model how populations of MHC-I loss affected the immune microenvironment. We also assessed a second, intrinsically heterogenous (MHC-I expression) TNBC model E0771. To evaluate changes in the microenvironment, we used flow cytometry and an immune NanoString panel to evaluate gene expression patterns in tumor cells and infiltrating immune cells. Results TNBC patients had the highest MHC-I expression level across tumor cells, but also the highest variability and probability of demonstrating bimodal MHC-I expression (consisting of high and low/absent cells within a single tumor). ER+ tumors were unimodally low. Using spatial analysis, we identified that heterogenous MHC-I tumors had significantly higher levels of infiltrating NK cells (Paired T-Test: p=0.03). In murine models, even 10% or less of MHC-I-null

(B2m-null) EMT6 cells in the tumor injection resulted in acquisition of ICI resistance. Interestingly, heterogeneity in expression of MHC-I resulted in a substantial infiltration by NKG2A+ NK cells compared to MHC-I high or -low tumors (Student T-Test: $p=.002$). Activation of these infiltrating NK cells via anti-NKG2A and anti-PD-L1 combination treatment restored complete responses in heterogeneous EMT6 tumors, and significantly extended survival in both E0771 (Mantel-Cox: $p < 0.0001$) and EMT6 models (Mantel-Cox: < 0.0001). Additionally, anti-NKG2A and anti-PDL1 combination treatment improved complete response in the heterogeneous MHC-I EMT6 model to 30% and in the parental EMT-6 tumors to 70%. Conclusion Combined therapy with anti-NKG2A (targeting NK cells) and anti-PD-L1 (targeting CD8+ T cells) can restore immunotherapy responses and overcome resistance due to lack of MHC-I expression in tumor cell subpopulations.

Disclosure(s):

Brandie C. Taylor, MS: No financial relationships to disclose

Xiaopeng Sun, B.S.: No financial relationships to disclose

Justin Balko, PhD, PharmD: Genentech: Contracted Research (Ongoing); Incyte: Contracted Research (Ongoing)

Paula Gonzalez-Ericsson, MD: No financial relationships to disclose

Melinda Sanders, M.D.: No financial relationships to disclose

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5:00 PM - 6:15 PM

PD2-07

PD2-07 Tumor CD73 regulates zoledronate induced TIL accumulation into triple negative breast cancer.

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Keywords: CD73, bisphosphonates, zoledronate, B cells, tumor growth, TNBC Background: CD73 is a membrane-bound protein that by extracellular adenosine production, regulates immune cell function. Low CD73 expression is associated with better prognosis among triple-negative breast cancer (TNBC) patients. Adjuvant bisphosphonates (BPs, such as zoledronate) improve survival among post-menopausal breast cancer patients, but the mechanism for this is unknown. Since BPs also affect immune cells, we studied 1) whether zoledronate-treatment has an effect on tumor infiltrating lymphocytes (TILs) and 2) whether tumor CD73 expression affects these responses in TNBC tumors. Methods: 4T1 mouse mammary cells, stably expressing non-targeting shRNA (sh-NT, control cells) or sh-CD73 were inoculated into the mammary fat pads of Balb/c mice. The mice were treated with i.p. vehicle or zoledronate (ZOL) each 4th day for total of six times. Additionally, to deplete B-cells, the mice were treated with an anti-CD20 or control IgG antibody. Tumor sizes were assessed with a caliper, TILs were studied with immunostainings. Blood lymphocytes were analyzed with Flow cytometry. Results: Sh-CD73 cells formed significantly smaller tumors, than sh-NT cells. ZOL significantly inhibited the growth of both sh-CD73 and sh-NT tumors, but at sacrifice, this effect of ZOL was more significant against sh-CD73 tumors. ZOL increased the % of CD19+/CD21+ and CD19+/23+ in blood of both mice groups, and this effect was inhibited by anti-CD20 antibody. Although neither treatment alone had an effect, the % of CD3+/CD8+ cells in blood were increased in both mice groups by the combination of ZOL and anti-CD20-antibody. ZOL induced

accumulation of B220+, CD4+ and CD8+ TILs into both tumor groups. These TIL effects were reduced with anti-CD20 antibody treatment. Anti-CD20 antibody alone inhibited significantly sh-CD73 tumor growth. Anti-CD20 antibody did not interfere with ZOL inhibition of tumor growth in either group. Conclusions: ZOL has inflammatory effects on blood lymphocytes and TILs, which may be affected by tumor expression of immune system regulating proteins, such as CD73. B cell depletion may further prevent tumor growth, in the context of CD73 inhibition. Further studies are needed to investigate whether B-cell inhibition affects ZOL-induced tumor growth inhibition.

Disclosure(s):

Nataliia Petruk, MSc: No financial relationships to disclose

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5:00 PM - 6:15 PM

PD2-08

PD2-08 Targeting of eIF4A1 along with anti-PD-L1 therapy limits lung metastases efficaciously in triple-negative breast cancer

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Title: Targeting of eIF4A1 along with anti-PD-L1 therapy limits lung metastases efficaciously in triple-negative breast cancer Dharmindra Dulal, Andrew Boring, and Dayanidhi Raman
Department of Cell and Cancer Biology, College of Medicine and Life Sciences, The University of Toledo-Health Science Campus, Toledo, OH Background: Triple-negative breast cancer (TNBC) is the most aggressive subtype of metastatic breast cancer with poor clinical prognosis. Currently used neoadjuvant chemotherapy for TNBC, such as taxanes, and/or anthracyclines demonstrate an initial treatment response but is often followed by drug resistance, tumor relapse, and high proclivity to develop metastases. There is an unmet need to develop effective combination therapies against metastatic TNBC (mTNBC). eIF4A1 is an mRNA helicase that help translate many oncogenic mRNAs including PD-L1 (through STAT1 translational regulation) that are involved in tumor growth, chemoresistance and metastases. Our prior studies pointed out that eIF4A1 is intricately linked to cancer stemness and drug resistance in TNBC. Emerging evidence has revealed that the tumor immune microenvironment (TIME) of TNBC do consist of mononuclear cells and lymphocytes. Combining chemotherapy with immune checkpoint inhibition had demonstrated a significant benefit for high-risk TNBC patients. In this study, we examine the efficacy of targeting eIF4A1 along with anti-PD-L1 therapy as an effective therapeutic strategy to limit cancer stemness, primary tumor progression and metastasis in an immunocompetent murine model of TNBC. Approach: Initially, we examined the human TNBC biospecimens and found that eIF4A1 protein level is upregulated in drug-resistant cases. STAT1 is an upstream regulator of PD-L1 and a downstream effector of eIF4A1. The protein level of STAT1 was significantly elevated as assessed by immunoblotting of human tumor lysates. In human TNBC cells, when eIF4A1 is pharmacologically or genetically targeted, PD-L1 was downregulated at the protein level. Based on this premise, we targeted eIF4A1 with the small molecule inhibitor, Rocaglamide A (RocA), along with anti-PD-L1 immunotherapy in orthotopically implanted 4T1 mouse TNBC tumors in BALB/c mice. The treatment arms were 1) Control (vehicle for RocA + control IgG) 2) RocA 3) RocA + anti-PD-L1 antibodies 4) Control IgG only 5) Anti-PD-L1 antibodies only with 10 mice in each group. Results: The combination treatment comprising of RocA and anti-PD-L1 antibodies worked out efficaciously as the primary tumor volume, wet tumor weight, bioluminescent tumor imaging and quantitation were significantly lower than the combination vehicle control.

Furthermore, metastasis to the lungs were significantly impaired (1 out of 10 mice only had metastasis and that too it was small). On the contrary, 'RocA single arm' group had 6 out of 10 mice with lung metastasis. The lung metastases were observed in 4 out of 10 mice in the PD-L1 single arm and 6 out of 10 mice in control IgG single arm group. The RocA was tolerated well at 0.6 mg/kg with no significant change in the body weight and the liver and kidney function test values were within the normal range. Importantly, the combination treatment with RocA and PD-L1 was also tolerated well. Conclusions: The combination therapy involving RocA and PD-L1 had the significant impact in reducing lung metastases and may pave the way for phase I/II clinical trials.

Disclosure(s):

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PD2-09

PD2-09 Characterization of the lymphovascular invasion microenvironment reveals immune response dichotomy

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Background: Metastasis is the leading cause of cancer related deaths in breast cancer patients. Lymphovascular invasion represents one of the earliest stages of metastasis wherein the cells are introduced to a very different and distinct microenvironment. Methods: We leveraged spatial techniques developed for limited specimens in archival tissue to study patient matched cross-sectional tumor samples from different stages of breast neoplasia including normal breast, ductal carcinoma in situ (DCIS), primary invasive carcinoma (IBC), lymphovascular invasion (LVI) and regional lymph node metastasis. We selected a set of 21 patients with ER+ breast cancer to generate cross-sectional samples of each of these stages, for a total of 331 samples. The areas of LVI were identified by a combination of H&E review and immunohistochemistry for podoplanin. We performed smart-3SEQ for gene expression profiling and light pass whole genome sequencing for DNA copy number alterations. Results: We profiled the spectrum of

neoplasia for transcriptome-wide gene expression. Principal component analysis of all 252 DCIS, LVI, IBC, or metastasis samples using the top 500 genes with the highest variance demonstrated that clustering was roughly based on the diagnostic stage (i.e. DCIS, LVI, IBC, or metastasis). Differential gene expression profiling identified thousands of genes increased or decreased in expression across the transitional stages with the largest change in gene expression being the transition from normal breast to DCIS, dominated by gene expression down regulation. We next performed NMF clustering on 62 samples of LVI from 18 cases and identified two patterns of gene expression which define two subgroups. Gene ontology analysis revealed that one cluster was associated with increased proliferation and metabolism, whereas the second cluster was dominated by an immune response. When we analyzed the immune and proliferative LVI subgroups separately, we found that the immune profiles in the patient matched IBC and LVI samples from the LVI Immune cluster were similar, whereas the immune profiles in the patient matched IBC and LVI samples from the Proliferative cluster were significantly different. At the LVI stage, all immune cell populations estimated by CibersortX were decreased in the Proliferative LVI cluster. These changes were validated using immunofluorescence for proliferation (Ki67), T cells (CD3) and macrophages (CD68) on the same samples. Using the LVI centroids, we built a model that could predict the same clusters in the METABRIC IBC. Kaplan-Meier analysis showed a significant difference between groups, with the Proliferative-like IBC group having a worse prognosis than the Immune-like IBC group. Conclusions: We observed a dichotomy at the LVI stage with a more proliferative cluster that may escape the immune response and an immune cluster which has a microenvironment with a similar pattern to its primary IBC. The recognition of two groups of LVI, differing in immune association and proliferation, raises the possibility that the risk of metastasis could be different in these two groups, leading to different biological pathways of progression.

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5:00 PM - 6:15 PM

PD2-10

PD2-10 MiR-150 expression in breast cancer cells attract infiltration of lymphocytes to tumor microenvironment and is associated with better survival of the patients

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MicroRNA (miRNA) are known as a key player in tumor biology and is shown to epigenetically regulate a large number of protein-coding genes, including tumor-related genes. MiR-150, a hematopoietic cell-specific miRNA, has been suggested to have various effects on cell proliferation, differentiation, apoptosis, migration, and invasion. However, there has been no study that investigated the role of miR-150 in the tumor microenvironment (TME) of breast cancer patients. We hypothesized that miR-150 expressed in breast cancer cells attract infiltration of lymphocytes to tumor microenvironment and is associated with better survival of the patients. In silico analyses of 1961 breast cancer patients were performed using multiple independent large cohorts, and in vitro studies by overexpressing miR-150 using its mimic in triple negative breast cancer (TNBC) cell lines were conducted. We found that miR-150 expression in patient breast tumors were strongly correlated with immune-related gene set scores, Allograft rejection, IL6/JAK/STAT3 signaling, Interferon- γ response, Inflammatory response, IL2/STAT5 signaling, and complement, in Hallmark collection of gene set variation analyses consistently in both METABRIC and TCGA cohorts (all spearman's rank correlation coefficient (r) > 0.50, all p < 0.01). MiR-150 expression was also strongly correlated with

cytolytic activity (CYT) score in both cohorts ($r = 0.824$ and 0.786 , respectively, both $p < 0.01$). Furthermore, miR-150 expression was significantly correlated with infiltrating fraction of CD8+ T cells ($r = 0.799$ and 0.525 , respectively), CD4+ memory T cells ($r = 0.759$ and 0.656 , respectively), dendritic cells ($r = 0.735$ and 0.696 , respectively), and B cells ($r = 0.759$ and 0.576 , respectively), as well as mRNA expression of major immune checkpoint molecules, including PD-1, CTLA4, IDO1, TIGIT, BTLA, and LAG3, in both cohorts (all $r > 0.50$, and all $p < 0.01$). MiR-150 expression in triple negative breast cancer (TNBC) was the highest among the subtypes (both $p < 0.001$). MiR-150 expression level was significantly correlated with Nottingham histologic grade (both $p < 0.001$). MiR-150 high tumor enriched not only immune-related gene sets but also apoptosis, KRAS signaling up, MTORC1, and p53 pathway by gene set enrichment analysis in both cohorts. High miR-150 expression patients were significantly associated with better overall survival (OS) in both cohorts ($p < 0.001$ and $p = 0.030$, respectively). Subgroup analysis revealed that a high miR-150 was associated with better OS in ER-positive/HER2-negative breast cancer in both cohorts ($p = 0.002$ and 0.044 , respectively), and in TNBC in the METABRIC cohort ($p = 0.006$). Unexpectedly, overexpression of miR-150 by its mimic shown no significant effect on cell proliferation, migration, nor invasion consistently in two TNBC cell lines. On the other hand, overexpression of miR-150 by its mimic significantly attracted Jurkat immortalized lymphocytes consistently in two cell lines, which effect was abolished by addition of miR-150 inhibitor. Finally, we found that mimic overexpression of miR-150 significantly expressed multiple cytokines and multiple inflammatory signaling pathways which at least partially explained the increased attraction of T cells in patient samples and in vitro condition. In conclusion, miR-150 expression in breast cancer cells may be associated with better patient survival outcomes by attracting and activating immune cells in breast cancer TME.

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5:00 PM - 6:15 PM

PD2-11

PD2-11 Human Cytomegalovirus Reactivation in Immunosuppressive Th2 Tumor Microenvironment Facilitates Brain Metastatic Outgrowth

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Background Brain metastases is a fatal consequence of advanced breast cancer with a poor prognosis. Both tumor intrinsic molecular underpinning of the primary tumor and microenvironmental brain niche factors have been reported to allow invading cancer cells to colonize and outgrow into the brain. A systemic investigation of these tumor intrinsic and microenvironmental factors using same patient paired primary breast and brain metastatic tumor samples are warranted. Methods Nine pairs of primary breast and brain metastatic tumor samples were collected for RNA sequencing. Pairwise differential gene expression analysis and gene set enrichment analysis (GSEA) were conducted. TCGA-BRCA (n=1222) dataset and a combined breast cancer cohort (n=2,765) were used for clinical and immune-infiltration correlation analysis. GSE12276 (n=204) dataset was used for brain-metastasis free survival correlation. Immunohistochemistry staining of HCMV was conducted on a total of 16 primary breast and brain metastatic tumor sections including 2 pairs. Two patient-derived xenograft (PDX) models were used for antiviral treatment and mechanism investigation. Results 371 up-regulated and 2,153 down-regulated genes in the 9 paired brain metastatic tumors vs. breast tumors ($P < 0.05$; $\log_2 FC > 1$ or < -1) were identified from the RNAseq data. Reactome Human cytomegalovirus (HCMV) early and late events was the top enriched pathway for the 371 brain metastasis up-regulated genes, and Reactome IL4 and IL5 signaling was the top enriched pathway for the 2,153 primary breast tumor up-regulated genes. Among the 371 brain metastasis up-regulated genes, 287 genes are also up-regulated in primary breast cancer vs. normal breast in the TCGA 1222 cohort ($P < 0.05$). High expression of 23 out of the 287 genes

are significantly associated with shorter distant metastasis-free survival (DMFS) in a combined breast cancer cohort of 2,765 patients (Logrank $P < 0.05$), and 19 of the 23 genes are associated with poor brain metastasis-free survival (BMFS) in the GEO dataset GSE12276 ($n=204$)(Logrank $P < 0.05$). We further identified that elevated expression of 12 out of the 19 genes are consistently associated with Th2 cell activation and NK cell deactivation in the TCGA 1222 cohort, for which the immunosuppressive Th2 cells are defined by secretion of IL4 and IL5 signature cytokines. Immunoreactive HCMV immediate early proteins indicating virus infection were examined in all the 16 patient tumor tissues, and strong positive signals were seen in both the paired breast tumor and brain metastatic specimens. Preventive treatment of anti-HCMV drug ganciclovir by suppressing viral DNA replication inhibited tumor colonization in the mouse brain in the two HCMV-positive PDX models. Conclusions Our systemic analysis of paired primary breast and brain metastatic tumor tissues identified a causal relationship between HCMV infection and reactivation, immunosuppressive Th2 cell activation and NK cell deactivation, and brain metastatic outgrowth. Since HCMV reactivation frequently induce encephalopathy during chemotherapy or radiation therapy, anti-HCMV agents may represent an effective strategy in preventing and controlling brain metastases.

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Discussion 1 + Q&A: PD3-01

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Discussion 2 + Q&A: PD3-03, PD3-04, PD3-05 & PD3-06

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Poster Spotlight Discussion 3: New Radiation Techniques

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5:00 PM - 6:15 PM

PD3-01

PD3-01 Neoadjuvant pembrolizumab + chemotherapy vs placebo + chemotherapy followed by adjuvant pembrolizumab vs placebo for early TNBC: Post hoc analysis of adjuvant radiation therapy in the phase 3 KEYNOTE-522 study

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Background: The phase 3 KEYNOTE-522 study (NCT03036488) showed that pembrolizumab (pembro) administered in combination with neoadjuvant chemotherapy (chemo) and then continued as adjuvant monotherapy resulted in statistically significant and clinically meaningful improvements in pathological complete response (pCR) and event-free survival (EFS) in patients with early triple-negative breast cancer (TNBC). In this post hoc analysis, we assessed outcomes by patterns of adjuvant radiation therapy (RT) administration.

Methods: Patients with previously untreated, nonmetastatic, stage T1c/N1-2 or T2-4/N0-2 TNBC were randomized 2:1 to pembro 200 mg Q3W or placebo, both given with 4 cycles of paclitaxel + carboplatin, then 4 cycles of doxorubicin or epirubicin + cyclophosphamide (neoadjuvant phase). After definitive surgery, patients received pembro or placebo for 9 cycles or until recurrence or unacceptable toxicity (adjuvant phase). Dual primary endpoints are pCR, defined as ypT0/Tis ypN0, and EFS. EFS and adverse events (AEs) that occurred during the adjuvant phase were examined in patient subgroups defined by receipt of adjuvant RT (yes or no) and the pattern of adjuvant RT and pembro administration, either concurrent (the last adjuvant RT exposure was after the first dose of adjuvant pembro or placebo) or sequential (the last adjuvant RT exposure was before the first dose of adjuvant pembro or placebo).

Results: Among 1174 randomized patients, 715 (60.9%) received adjuvant RT (n=454 pembro; n=261 placebo) and 459 (39.1%) did not (n=330 pembro; n=129 placebo). At data cutoff (March 23, 2021), median follow-up was similar (~38 months) in both subgroups. EFS was longer in the pembro arm compared to the placebo arm in patients who received adjuvant RT (either concurrently or sequentially) and those who did not (Table). Grade 3-5 treatment-related AE rates for pembro vs placebo were 5.9% vs 2.7% with adjuvant RT (4.9% vs 2.2% with concurrent RT; 6.8% vs 3.1% with sequential RT) and 7.5% vs 2.9% without adjuvant RT. Treatment-related AEs led to death in 2 patients (0.4%); both occurred in the pembro arm in patients who received adjuvant RT. Immune-mediated AE rates were 10.6% vs 5.0% with

adjuvant RT (9.7% vs 4.4% with concurrent RT; 11.8% vs 5.7% with sequential RT) and 9.0% vs 10.0% without adjuvant RT in the two treatment arms, respectively.

Conclusion: In this post hoc analysis, the addition of pembro to neoadjuvant chemo followed by adjuvant pembro provided a clinically meaningful EFS benefit, independent of adjuvant RT administration. An EFS benefit was observed in patients who received pembro with either concurrent or sequential adjuvant RT. The addition of pembro to adjuvant RT was generally well tolerated. Similar rates of treatment-related AEs and immune-mediated AEs were seen in patients who received adjuvant RT and pembro either concurrently or sequentially, although the sample sizes are modest. These results are consistent with the therapeutic benefit seen with neoadjuvant pembro plus chemo followed by adjuvant pembro in the intention-to-treat population of patients with early TNBC randomized in KEYNOTE-522.

Table. EFS by Adjuvant RT in KEYNOTE-522

Population	Pembro	Placebo	HR
	No. events/No. patients (%)	No. events/No. patients (%)	(95% CI)*
With Adjuvant RT [†]	55/454 (12.1)	52/261 (19.9)	0.58 (0.40 – 0.85)
Concurrent [‡]	16/144 (11.1)	14/91 (15.4)	0.70 (0.34 – 1.44)
Sequential [§]	28/280 (10.0)	35/159 (22.0)	0.42 (0.26 – 0.69)
Without Adjuvant RT	68/330 (20.6)	41/129 (31.8)	0.60 (0.41 – 0.89)

*Based on a Cox regression model with Efron's method of tie handling with treatment as a covariate. [†]Refers to the post-surgery adjuvant RT prior to the date of all treatment discontinuation or completion. [‡]Last adjuvant RT exposure was after the first dose of adjuvant pembro or placebo. [§]Last adjuvant RT exposure was before the first dose of adjuvant pembro or placebo.

Disclosure(s):

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PD3-03

PD3-03 Preoperative robotic radiosurgery for early breast cancer: results of the phase II ROCK trial (NCT03520894)

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Introduction. Breast-conserving surgery (BCS) followed by postoperative radiotherapy (RT) still represents the standard of care for early breast cancer (BC) patients. Hypofractionated schedules in maximum 15 fractions are currently accepted as the gold standard for external beam whole and partial breast irradiation (PBI). PBI for selected early BC patients allowed a shorter overall treatment duration and an improved patient compliance as compared to old-fashioned RT schedules. Preoperative PBI, due to the advantage of treating a well-defined volume, has been gaining attention in this multidisciplinary scenario. It avoids local treatment delay and might allow tumour downstaging with increased rates of BCS and improved cosmetic outcomes. Since local recurrence might be driven by biological mechanisms of radioresistance rather than geographical miss, higher dose per fraction may overcome repair mechanisms allowing tumoral cells to escape from conventional RT damage. We report the results of the phase II ROCK trial (NCT03520894), enrolling early BC patients treated with preoperative robotic radiosurgery (prRS), in terms of acute and early late toxicity, disease control, and cosmesis.

Material and methods. The study recruited between August 2018 and September 2021 at the Radiation Oncology Unit of the University of Florence (Florence, Italy). Eligible patients were women aged 50+ years, with histologically proven invasive early BC, HR+/HER2-disease, without lymph vascular invasion, tumour size up to 25 mm suitable for BCS. Exclusion criteria were clinical node positive disease, multiple foci tumours, and patients with breast lesion limiting within 5 mm from the skin surface. The study aimed to prospectively assess the safety and feasibility of a single Cyberknife® (Accuray Incorporated, Sunnyvale, CA, USA) 21Gy-fraction prRS in preoperative setting, and to identify predictive factors for outcomes based on biologic and clinical features. The primary endpoint was the acute skin toxicity (from the end of prRS to surgery) according to the RTOG and the EORTC scales. Secondary endpoints were the rate of early late skin and non-skin toxicity as measured 90 days from the end of prRS, the rate of pathological complete response (pCR) according to Chevalier score. Cosmetic outcomes were prospectively scored every 6-month using the BCCT.core software.

Results. From August 2018 to September 2021, a total of 70 patients were recruited and enrolled. Of those, 41 were excluded due to tumour biology exclusion criteria and 7 due to multiple foci breast disease evidenced at basal MRI. Therefore, 22 patients were successfully treated with prRS. Median age at diagnosis was 68 years (range 50-86), median tumour size was 14 mm (range 7.5-25). Required target dosimetric parameters were met in all patients, as well as normal tissue constraints. Patients received surgery after a median time of 29 days from biopsy, without any delay or postoperative complication. Overall, three G1 adverse events (13.6%) were recorded within 7 days from prRS (1 erythema, 2 breast pain). Three events (13.6%) were recorded between 7 and 30 days from prRS, one G2 breast oedema and two G1 breast pain. No acute toxicity greater than G2 was recorded. Five patients experienced early late G1 toxicity (1 breast pain, 4 breast induration). One patient reported G2 breast induration. No early late toxicity greater than G2 was observed. At a median follow up of 18 months (range 6-29.8), cosmetic results were scored excellent/good and fair in 14 and 5 patients, respectively, while 3 patients experienced a poor cosmetic outcome. Overall, pCR after surgery was reported in 2 patients (9%). Two patients received postoperative whole breast irradiation, according to histopathological results.

Conclusions. ROCK trial showed that a single 21 Gy dose prRS represents a feasible technique for selected patients affected by early BC, showing a good safety profile and a promising effectiveness.

Disclosure(s):

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12/6/2022

5:00 PM - 6:15 PM

PD3-04

PD3-04 Locoregional Stereotactic Body Radiotherapy in Breast Cancer Patients Unsuited for Surgical Resection

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Purpose: Breast cancer (BC) patients (pts) who are not surgical candidates or decline surgical resection are usually managed with palliative systemic therapy alone or palliative radiotherapy if clinically appropriate. Stereotactic body radiotherapy (SBRT) has shown excellent results for different primary malignancies, and we hypothesized it could improve outcomes in this context with acceptable toxicity. This study aims to assess the local control (LC) and toxicity rates of breast SBRT in pts unsuitable for surgical resection. Methods and Materials: We performed a retrospective analysis using an institutional registry of all BC pts unsuitable for resection who underwent breast and/or regional lymph node (LN) SBRT to a dose of 35-40 Gy in 5 fractions from 2014 to 2021. Patients were deemed unsuitable for resection if they were medically inoperable, declined surgery, had unresectable tumors, or where surgery was not appropriate, such as due to metastatic disease. The primary endpoint was LC (defined as no evidence of

progression of the treated lesion as per RECIST 1.1 criteria) and toxicity grade ≥ 3 (as per CTCAE v5.0). Secondary endpoints included radiological response (RR) of the target tumor at the last follow-up, progression-free survival (PFS), and overall survival (OS). All endpoints were assessed per course of treatment, with death as a competing factor for LC. Results: This study included 61 treatment courses in 57 pts. The median age was 81 years (range 38-99), 74% being older than 70 years of age. Eighteen percent had stage I-II, 44% stage III, and 38% stage IV disease. Unresectable tumor (10%), patient refusal (18%), medically inoperability (34%), and metastatic disease (38%) were the main causes of not having surgery. The molecular subtypes were HER-2 in 3%, basal-like 23%, and luminal disease 74%. Previous systemic treatment consisted of endocrine therapy (ET) alone (49%), chemotherapy (CT) or target therapy (TT) alone (11%), both ET and CT/TT (18%), or none (21%). Seventy-two percent of tumors were progressing on ET (44%) or CT/TT (28%) at the time of SBRT. The median interval from cancer diagnosis to SBRT was 14.6 (range 0.5-180) months (mos). Fifty-four percent had breast SBRT, 15% LN SBRT, and 31% both. For LN treatment, axillary, internal mammary, and supraclavicular nodes were the target in 43%, 3%, and 2% of treatments, respectively. The median clinical and radiological follow-up was 16.8 (range 0.2-87) and 13.4 mos (range 1-81), respectively. The worst acute and late grade ≥ 3 toxicity was 16% and 4%, respectively, and all cases consisted of radiation dermatitis. No patient was unable to complete treatment due to acute toxicity. There was one case of grade 4 skin necrosis 6.3 mos after 35 Gy in 5 fractions to an axillary LN. The LC rate at 1 year was 100% and 2 years 88.6% (95% CI = 79-99%). The median time to local progression among those who progressed was 18.2 mos (95% CI = 12-not reached). At last FU, the RR of treated tumors was: complete response = 8%, partial response = 46%, stable disease = 38%, and progressive disease = 8%. The PFS and OS rates at 1 year was 69.8 % (95% CI = 58-82) and 74.6% (95% IC = 63-86), 2 years 39.1% (95% CI = 26—52) and 50.6% (95% IC = 36-65), 3 years 26.7 % (95% CI = 14-39) and 38.7% (95% IC = 24-54), and 4 years 18.5 % (95% CI = 8-29) and 29.2% (95% CI = 14-44), respectively. The median PFS was 21.7 mos (95% CI = 17-28) and OS 31.1 mos (95% CI = 21- 38). Ongoing analysis intends to identify clinical and pathological predictors of LC, PFS, and OS. Conclusion: Our initial data suggest that breast SBRT safely provides excellent LC rates in non-operable BC pts. This approach may be a treatment option in pts who are not good surgical candidates, particularly in elderly pts with multiple comorbidities, which comprised 74% of our cohort. A clinical trial is underway to determine the optimal dose and side effect profile for primary breast SBRT with curative intent in pts not undergoing definitive surgery.

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12/6/2022

5:00 PM - 6:15 PM

PD3-05

PD3-05 Early results of the French multicenter, randomized SHARE trial comparing whole breast irradiation versus accelerated partial breast irradiation in postmenopausal women with early-stage breast cancer.

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Purpose: The aim of current analyses is to report toxicity and cosmetic outcomes at 3 and up to 9 years of follow-up of post-menopausal patients randomized to receive either standard external beam whole breast radiotherapy (WBI), including hypofractionated options, versus accelerated partial breast irradiation (APBI). Methods and materials: From December 2010 to July 2015, 1006 patients were enrolled in 34 French centers (503 in each arm). Among the whole population, 28 patients who did not meet the final selection criteria or withdrew consent were excluded leading to a modified intention to treat analysis dataset of 978 patients (WBI: n=488; APBI: n=490). Median age (65y) and tumor stage pT1 (99%) rates were similar in both arms. Patients had conservative surgery with clip placement in the tumor bed. Clear margins (> 2mm) were observed in 99% of the patients. In both arms, 96-97% of the patients had negative sentinel lymph node biopsy (SLNB; median number: 4 in WBI arm and 5 in APBI), luminal BC. Ductal histology was observed 82%. Only 2% and 1% of patients had grade III and pN(i+) disease. The median time interval between surgery and radiotherapy was 57d in WBI vs 62d in APBI. WBI schedules consisted of: 50Gy in 25fr + 16Gy boost (n=212) or 40Gy in 15fr (n=156) or 42.5Gy in 16fr (n=120), while APBI arm consisted of 38.5Gy or 40Gy in 10fr. Overall, 94 patients from the APBI arm finally received standard WBI. For statistical considerations, SHARE trial, sponsored by UNICANCER (NCT01247233) is a non-inferiority randomized controlled trial comparing APBI versus WBI in terms of local control as primary objective. Secondary endpoints were severe toxicity (NCI-CTCAE v4 grade ≥ 2), and cosmetic results, evaluated by doctors and by patients, over the entire follow-up. For both outcomes, we estimated the cumulative incidences (CI) using Kalbfleish and Prentice method, considering

disease relapse, secondary cancer or death as competing events. Treatment effect (APBI vs WBI) was estimated by cause-specific Hazard Ratios (cs-HR) from Cox models adjusted on stratification factors. Results: Median follow-up was 5.8y (range, 0.13-9.5). The number of deaths was 27, and the number of local relapses was 8. Among the 978 patients, 582 and 396 had finally WBI and APBI, respectively. The rates of post-operative hematoma, edema and infection were low: 8-9%, 2%, 3-2%, respectively. When considering any type of severe toxicity, we observed a significant reduction rate in APBI compared to WBI: cs-HR=0.73 (95% confidence interval: 0.61-0.88); p=0.001, and 3-year cumulative incidence (CI) of severe toxicity at 45% (41-49) in WBI vs 36% (32-40) in APBI arm. The difference was also in favor of APBI when considering breast skin toxicity alone: cs-HR=0.55 (0.44-0.70), p< 0.001 and 3-year CI at 36% (32-40) in WBI vs 21% (18-25) in APBI arm. Conversely, for breast other toxicities, WBI was found less toxic than APBI: cs-HR= 2.10 (1.51-2.91), p< 0.001, and 3-year CI at 8% (5-10) vs 15% (12-19), respectively. When considering cosmetic results according to the investigator, we observed no significant difference between the two arms: cs-HR=1.04 (0.81-1.33), p=0.26 and 3-year probability of remaining with good to excellent cosmetic results at 77% (73-81) in WBI arm and 78% (74-81) in APBI arm. Findings were similar when considering results according to the patient: cs-HR=1.07 (0.85-1.37), p=0.23, and 3-year probability at 74% (70-78) and 75% (70-79), respectively. Conclusions Historically SHARE is the first APBI trial that included hypofractionated schedules in the standard arm. We reported increased risk of severe toxicity and skin breast toxicity in standard arm as compared with APBI arm without any difference in terms of cosmetic results. Longer follow-up is needed.

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12/6/2022

5:00 PM - 6:15 PM

PD3-06

PD3-06 Robotic Stereotactic APBI for Early-Stage Breast Cancer: 2-year Outcomes of a Prospective Multi-Institutional Trial

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Purpose: Outcomes following adjuvant accelerated partial breast irradiation (APBI) in select women with early-stage breast cancer are comparable to whole breast irradiation. Robotic stereotactic accelerated partial breast irradiation (RSAPBI) with fiducial tracking is an attractive treatment option, but limited outcomes data are available for this approach. We report 2-year outcomes for a prospective multi-institutional trial treating select women with RSAPBI. Materials and Methods: Post-menopausal women with DCIS and Stage IA breast cancer were treated over a five-year period extending from November 2015 to November 2020 and were followed for a minimum of 18 months. Treatments were delivered with a robotic radiosurgery system. Four gold fiducials were implanted around the lumpectomy cavity prior to the start of treatment for tumor bed delineation and target tracking. The CTV was defined as the lumpectomy cavity with a uniform 5-15 mm expansion confined to the breast tissue and the PTV was defined as the CTV with a 0-5 mm uniform expansion. The PTV was prescribed 30 Gy in 5 fractions. Disease status assessments were completed at 4 weeks, 3 months, 6 months, 12 months, 18 months, 24 months and yearly intervals thereafter for five years. Results: Eighty-one patients (median age 68 years) with hormone receptor-positive tumors were treated over a median 9 days (range, 5-15). Sixty-eight women had invasive ductal carcinoma (84%) and thirteen had DCIS (16%). The median treated PTV was 108 cm³ (IQR 66-156) and the median prescription isodose line was 81% (IQR 79-83). The median CTV expansion was 10 mm (range 5-10) and the median PTV expansion was 3 mm (range 0-5). At a median follow up of 2 years there was one new ipsilateral breast tumor diagnosed. There were no local, regional, or distant treatment failures. Conclusions: Two-year results suggest that RSAPBI with fiducial tracking is an effective technique for the adjuvant treatment of post-menopausal women with hormone receptor-positive early-stage breast cancer. Additional follow-up is planned to confirm this preliminary finding.

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

P2-01-01

Interim analysis (n=200) from ELEANOR: a multi-national, prospective, non-interventional study among patients with HER2+ and HR+ early breast cancer treated with extended adjuvant neratinib in the clinical routine

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Background Recent advances in the treatment of human epidermal growth factor receptor positive (HER2+) early breast cancer (eBC) have led to a reduction in recurrence risk; still a relevant percentage of patients relapses over time, predominantly presenting with distant recurrence. Neratinib is registered in Europe as extended adjuvant treatment for adult patients with HER2+, hormone receptor positive (HR+) eBC, who completed adjuvant trastuzumab-based therapy within one year prior to start of neratinib. In the ExteNET study, neratinib improved the absolute 5-year invasive disease-free survival (iDFS) rate by 5.1% versus placebo in this population (90.8% vs. 85.7%; HR 0.58 [95% CI 0.41-0.82]), mainly by reducing the rate of distant metastases. According to explorative analyses from ExteNET, the effect may be even more pronounced in patients with non-pCR after neoadjuvant trastuzumab treatment and/or in patients completing the full duration of neratinib therapy (i.e. ≥ 11 months of neratinib treatment). Diarrhea, the most common grade 3 adverse event (neratinib: 39% without primary diarrhea prophylaxis, median cumulative duration 5 days; placebo: 1%; no grade 4 events) can generally be managed through adequate prophylaxis and treatment management. ELEANOR is the first non-interventional study (NIS) of real-world use of neratinib and its management in eBC patients in Germany, Austria and Switzerland. Methods Enrollment of 300 adult female patients with HER2+/HR+ eBC is planned in accordance with the SmPC specifications. Primary endpoint is the rate of patients adherent to neratinib treatment (i.e. neratinib use for $\geq 75\%$ of treatment days). Secondary objectives include characterization of patients scheduled to receive neratinib, details on neratinib treatment, recurrences, safety / tolerability, and health-related quality of life (HRQoL). CANKADO, an eHealth application developed to support patient/physician communication, is an integral part of the NIS. Here, we report results of the preplanned interim analysis based on 200 enrolled patients. Results At data cut-off (May 2022), 202 patients had been observed for 3 months; patient enrollment is ongoing. Median age was 53.0 years and 66.3% of patients were at increased risk of disease recurrence (defined as non-pCR or AJCC stage > I). Most patients had received prior neoadjuvant treatment (79.7%). Post-neoadjuvant treatment included dual HER2 blockade with trastuzumab and pertuzumab (38.8% / 23.9% of pCR / non-pCR patients) and trastuzumab-emtansine (T-DM1, 53.5% of non-pCR patients). Neratinib treatment had been documented for 187 patients, treatment was ongoing for 46.0% of patients. Diarrhea was the most common adverse event (78.6% any grade, 19.3% grade 3, 2 patients grade 4), but was markedly lower when indirectly compared to ExteNET (39% grade 3). The neratinib dose escalation schedule was chosen for 36.4% of patients and

led to a decreased incidence of severe diarrhea (16.2% grade 3, no grade 4 events). 93.9% (95% CI: 87.9-97.5%) of 115 evaluable patients adhered to neratinib treatment. Conclusion The results of this preplanned interim analysis reflect the current treatment landscape in Germany, Austria and Switzerland. These results confirm, in line with the observed adherence data, that extended adjuvant neratinib use is feasible in typical clinical practice settings. Furthermore, treatment management strategies such as diarrhea prophylaxis or neratinib dose escalation are routinely used and can increase treatment tolerability markedly. The study is funded by Pierre Fabre Pharma GmbH (Freiburg, Germany), Pierre Fabre Pharma Austria (Wels, Austria) and Pierre Fabre Pharma AG (Allschwil, Switzerland).

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Clinicopathological characteristics, treatment patterns and disease outcomes of germline BRCA1/2 carriers with early stage HER2-negative breast cancer and potential eligibility for adjuvant Olaparib

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Title: Clinicopathological characteristics, treatment patterns and disease outcomes of germline gBRCA1/2 carriers with early stage HER2-negative breast cancer and potential eligibility for adjuvant Olaparib

Background: Approximately 5-10% of early breast cancers (eBC) occur in patients (pts) carrying a germline BRCA1/2 (gBRCA1/2) pathogenic (P) or likely P (LP) variant. In the OlympiA trial, 1-year (yr) adjuvant (adj) olaparib (OLA) improved both invasive disease-free survival (iDFS) and overall survival (OS) in gBRCA carriers with high-risk HER2- eBC. Whether benefit of adj OLA might extend beyond the high-risk population defined by the OlympiA criteria remains to be defined.

Methods: Consecutive pts who underwent surgery for a first diagnosis of eBC at Dana-Farber Brigham Cancer Center between 1/2016 and 8/2021 were identified. Genetic data were retrieved from an institutional dataset to identify gBRCA1/2 P/LP carriers tested through Dana-Farber. Clinicopathological variables, treatment and outcomes were characterized. Eligibility for adj OLA was based on the OlympiA study criteria, as follows: triple-negative BC (TNBC) with \geq pT2 or \geq pN1 prior to adj chemotherapy (ACT) or non-pCR after neo-adj CT (NACT); hormone receptor (HR)+ eBC with \geq 4 positive nodes prior to ACT or non-pCR and CPS+EG score \geq 3 after NACT.

Results: We identified 188 gBRCA (105 BRCA1, 83 BRCA2) carriers with newly diagnosed HER2- eBC. Median age was 42.5 years and 119 (63%) were premenopausal. Tumor stage, grade and subtype are reported in Table 1. Recurrence Score (RS) was performed on 46 pts, with a median value of 25 (2% 0-10 RS, 52% 11-25 RS, 46% \geq 26 RS). 97 pts (52%) received NACT, 55 (29%) ACT only and 36 (19%) did not receive CT. Most pts received both anthracyclines and taxanes, either as NACT (68%) or ACT (53%). 19 (20%) and 8 (8%)

received platinum as NACT or ACT, respectively. 4 pts received adj OLA. 43 (44%) pts had a pCR after NACT. The pCR rate was higher in BRCA1 than BRCA2 carriers (52 vs 25%, odds ratio (OR) 3.27, p=0.015) and in pts with TNBC than HR+ eBC (50 vs 32%, OR 2.10, p=0.101). After a median follow up for survival of 37 months, 16 iDFS events were recorded, including 4 second primary tumors (3 ovarian and 1 pancreatic cancer). 3-yr iDFS was 89% (95% CI, 84-95) in the overall cohort, with no significant difference according to BRCA status (BRCA2 vs BRCA1: 85% vs 93%, hazard ratio [HR] 2.65 (95% CI, 0.92-7.63), p=0.071) or tumor subtype (HR+ vs TNBC: 87 vs 93%, HR 1.72 (95% CI, 0.60-4.94), p=0.316). 3-yr relapse-free survival (RFS) was 92% (95% CI, 87-97).

54 (29%) pts were potentially eligible for adj OLA. Eligible pts more frequently had TNBC (67 vs 36%, p< 0.001), higher stage (stage I 9 vs 55%, stage II 63 vs 37%, stage III 28 vs 9%), and grade 3 disease (85 vs 69%, p=0.045), were less likely to have ODX performed (2 vs 34%, p< 0.001), and more likely to have received NACT (83 vs 39%, p< 0.001) and radiation therapy (78 vs 33%, p< 0.001). 3-yr iDFS was 87% and 90% for pts eligible vs not eligible (HR 1.36 (95% CI, 0.49-3.74), p=0.555). 10/16 iDFS events occurred among not eligible pts. 3-yr RFS was lower in eligible pts (87 vs 94%; HR 2.23 (95% CI, 0.72-6.92), p=0.165).

Conclusions: In our cohort, approximately 30% of pts were eligible for adj OLA. 3-yr iDFS was similar between pts eligible and not eligible for adj OLA according to OlympiA criteria. Our findings raise a concern regarding proper selection of all gBRCA carriers who may benefit from adj OLA. Further research is needed to identify additional groups of pts who may benefit from adding OLA to CT in higher risk disease or potentially replacing CT in lower risk settings.

Characteristics and outcomes of gBRCA1 vs gBRCA2

	gBRCA1 carriers (n=105)	gBRCA2 carriers (n=83)
Clinical stage – n (%)		
I	44 (42)	43 (52)
II	54 (51)	30 (36)
III	7 (7)	10 (12)
Tumor subtype - n (%)		
TNBC	68 (65)	16 (19)
HR+	37 (35)	67 (81)
HR-low	8 (8)	3 (4)
HER2-low	47 (45)	48 (58)
Tumor grade – n (%)		
I	3 (3)	4 (5)
II	14 (13)	27 (33)
III	88 (84)	50 (60)
pCR rate (%)	52	25
3-year iDFS (%)	93	85
3-year RFS (%)	94	89
Pts eligible for adj OLA – n (%)	34 (32)	20 (24)
HR+	6 (18)	12 (60)
TNBC	28 (82)	8 (40)

Table 1

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Real-world clinical outcomes of patients with stage I HER2-positive breast cancer treated with adjuvant paclitaxel and trastuzumab

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Background: One year of adjuvant trastuzumab with 12 cycles of weekly paclitaxel represents the standard of care for patients with pathological tumor size ≤ 2 cm, node-negative, HER2-positive early breast cancer. Data supporting this indication derive from a single-arm, phase II trial that enrolled 410 patients in the United States only, where the 3 years invasive disease-free survival (DFS) rate was 98.7% (95% CI 97.6-99.8). Therefore, real-world data regarding the clinical outcomes of these patients are needed to confirm the efficacy and safety of this adjuvant anthracycline-free regimen in this population. Methods: We conducted a retrospective, observational, multicentric study to investigate survival outcomes of patients with stage I HER2-positive early breast cancer treated with adjuvant paclitaxel and trastuzumab in seven selected sites in two countries (Belgium and Italy). Eligible patients were men and women with early breast cancer of pathological tumor size between 5 and 20 mm, node-negative (N0 or N1mic), and treated with weekly adjuvant paclitaxel for 12 weeks and trastuzumab (6 mg/kg every 3 weeks administration for 1 year). Patients with a history of previous cancers were not included. The primary endpoint was disease-free survival (DFS) at 3 years from diagnosis. Thus, an optimal follow-up of 3 years from surgery was required. Baseline clinico-pathological characteristics, treatment data, disease recurrences and survival status were extracted from medical records. Survival analysis was performed using log-rank regression test. Results: Overall, 240 patients who received their adjuvant treatment between January 2014 and December 2018 were included in the analysis. The median age was 59.5 years (IQR 50.0-66.9), and 69.6% of patients were post-menopausal at the time of diagnosis. Seventy (31.8%) patients had hypertension and 20 (8.3%) had other cardiac comorbidities. Ductal carcinoma was the most represented histological type (86.3%). The median tumor size was 12mm (IQR 9-15), only seven (2.9%) patients had N1mic, and the majority of tumors (85.0%) were ER-positive. Breast-conserving surgery was performed in 80.8% of patients and 78.2% of patients had adjuvant radiotherapy. The median number of administered cycles of weekly paclitaxel was 12 (range 1-12) and for trastuzumab 18 (range 1-19). Only one patient stopped trastuzumab prematurely because of safety reason. Aromatase inhibitors were the most frequently administered endocrine therapy (75.7% of patients with ER-positive disease). With a median follow-up of 4.7 (IQR 3.6-5.6) years, we observed a 3-year DFS rate of 98.8% (95% CI 96.2-99.6), with only three disease recurrences (one local and two distant) and four deaths (none of which was breast cancer related) during the duration of the follow-up. Conclusions: In this real-world clinical outcome of patients with stage I HER2-positive breast cancer treated with adjuvant trastuzumab and paclitaxel appeared excellent, with a 1.2% rate of recurrence at 3 years. Our data support the efficacy of an anthracycline-free regimen in this population. A longer follow-up will provide more mature data on overall survival and late relapses, especially in the ER-positive subgroup of patients.

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12/7/2022

7:00 AM - 8:15 AM

P2-01-05

MBQ-167 chemosensitizes triple-negative breast cancer cells to current chemotherapies and reduces paclitaxel-induced metastasis

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Triple-negative breast cancer (TNBC) is an aggressive and recurrent type of breast cancer that accounts for over 15% of new diagnoses yearly. Patients with TNBC have limited response to hormonal or targeted therapies due to the lack of ER, PR, and HER2. Therefore, the standard treatment for TNBC is anthracycline/taxane-based chemotherapies, paclitaxel (PXL), and doxorubicin (DOX), for which patients often develop chemoresistance. PXL, particularly, induces metastasis in TNBC patients by activating the Toll-Like Receptor 4 (TLR4)/NF κ B signaling pathway. Since there are few targeted therapies for TNBC, there is an urgent need to identify new “druggable” molecular targets. The oncogenic GTPases Rac and Cdc42, and their downstream effector, p-21 Activated Kinase (PAK), play critical roles in TNBC development and metastatic cancer progression. Therefore, we developed MBQ-167 as a potent Rac/Cdc42 inhibitor that decreases tumor cell growth and metastasis in TNBC mouse models with no apparent toxicity. To test the hypothesis that inhibiting Rac/Cdc42 with MBQ-167 will chemosensitize TNBC cells to PXL and DOX, we treated TNBC human cell lines MDA-MB-231 and MDA-MB-468 with different concentrations of MBQ-167 (250 nM-500 nM), PXL (5 nM-10 nM), DOX (250 nM-500 nM), and their combinations. The efficacy of single and combined treatments was determined on cell proliferation with the MTT assay, apoptosis with the Caspase-Glo 3/7 assay, and cell migration with the wound healing assay. In addition, we evaluated the effect of single or combined MBQ-167 (per oral 50 mg/kg, 5X a week) and PXL (IP 10mg/kg, 1X a week) on tumor growth and metastasis in an orthotopic Luciferase tagged-MDA-MB-468 TNBC mouse model. Our in vitro results demonstrate that treatments with MBQ-

167, PXL, DOX, and their respective combinations, decreased TNBC cell viability and increased apoptosis compared to vehicle controls. Both combination treatments reduced cell viability and increased apoptosis compared to PXL or DOX alone. Moreover, MBQ-167 was more effective than PXL at reducing MDA-MB-231 cell migration. DOX treatment did not affect cell migration, while combination treatment of DOX with MBQ-167 decreased migration. Moreover, in the mouse model, MBQ-167 significantly reduced MDA-MB-468 mammary tumor growth by 85% compared to vehicle treatments. This decrease in tumor growth was comparable to PXL treatment alone and in combination with MBQ-167. As expected, PXL treatment increased metastasis to the lungs and liver, while MBQ-167 prevented lung and liver metastases and reduced PXL-induced metastasis. Therefore, inhibiting Rac/Cdc42 with MBQ-167 improves the responses to current TNBC chemotherapies, PXL and Dox, and reduces PXL-induced metastasis, making MBQ-167 a potential adjuvant treatment against TNBC. This conclusion will be tested since we recently obtained IND approval from the US FDA for MBQ-167 and plan to conduct clinical trials in TNBC patients.

Disclosure(s):

Nilmary Grafals-Ruiz, Ph.D.: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-01-06

Real-world outcome and cost analysis of the addition of pertuzumab to neoadjuvant therapy in localized HER2 positive breast cancer: a single center experience

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BACKGROUND: Breast cancer is the most common cancer in woman and can be classified based on the expression of hormonal receptor as well as the human epidermal growth factor receptor 2 (HER2). HER2 amplification is associated with an aggressive clinical course and higher recurrence rates following curative intend surgery. For non-metastatic T2 or node-positive HER2-positive disease neoadjuvant treatment is favored. The National Comprehensive Cancer Network (NCCN) guidelines have endorsed the use of dual HER2 blockage with trastuzumab and pertuzumab combined with chemotherapy in the neoadjuvant setting. However, pertuzumab isn't frequently reimbursed in public health care systems for this indication. Patients who don't achieve a pathological complete response (pCR) at surgery are eligible for adjuvant T-DM1, adding significant side effects on patients and cost on the healthcare system.

METHODS: We conducted a retrospective analysis of patients receiving anti-HER2 therapy in the neoadjuvant setting at the Jewish General hospital between 2015 and 2021. After 2019, pertuzumab was routinely added to standard neoadjuvant therapy enabling us to compare patients treated with or without dual-HER2 blockade. Our primary endpoint is the percentage of pCR at surgery. Secondary objectives are to estimate and compare the cost of anti-HER2 targeted therapy in the perioperative setting and side effect burden on patients. Statistical analyses were done using fisher exact test with statistical significance defined p value < 0.05 in a one-sided test. Drug cost was calculated using publicly available resources.

RESULTS: We identified 83 patient who underwent neoadjuvant chemotherapy for HER2 amplified breast cancer. 44 patients received only trastuzumab has anti-HER2 therapy and 39 patients were treated with dual HER2 blockade containing pertuzumab. The addition of pertuzumab was associated with improved the pCR rate (67% vs. 27%; $p = 0.0016$). The increased pCR rate was observed in hormone-receptor positive and negative tumors. We also described a non-statistically significant trend in reduction in the requirement for axillary dissection with the use of pertuzumab (28% vs. 39%; $P=0.2208$). The increased in pCR rate with pertuzumab reduced the number of patients eligible for adjuvant T-DM1. If all patients with residual disease had received adjuvant T-DM1, the cost of neoadjuvant pertuzumab would be neutral, with a mean anti-HER2 drug cost of 65 150 CA\$ in the pertuzumab-trastuzumab group and 66 116 CA\$ in the trastuzumab group.

CONCLUSION: Our real-world analysis confirmed that neoadjuvant chemotherapy with dual HER2-blockade was well tolerated and associated with increased the pCR rate compared to regimens containing trastuzumab only. This measure is neutral on drug cost by reducing the amount of patients eligible for adjuvant T-DM1. Further research is warranted to estimate the overall health-care utilization costs of neoadjuvant pertuzumab-trastuzumab in settings where adjuvant T-DM1 is available.

Table 3: Pathologic complete response (pCR) and type of surgery in patients who received dual HER2 blockade with neoadjuvant pertuzumab-trastuzumab plus chemotherapy and in patients receiving trastuzumab only with chemotherapy at Jewish General Hospital between 2015 and 2021 . ** $p < 0,01$, ns non-statistically significant

Variable	N (%)			P value
	Overall population N = 83	Trastuzumab with pertuzumab N = 39	Trastuzumab N = 44	
Pathology at surgery				
Pathological complete response (pCR)	36 (43%)	24 (62%)	12 (27%)	0.0016 **
pCR in ER or PR positive	14 (29%)	8 (40%)	6 (21%)	0.13 ns
pCR in ER and PR negative ($\leq 10\%$)	22 (65%)	16 (84%)	6 (40%)	0.0098 **
Type of surgery				
Axillary dissection	28 (34%)	11 (28%)	17 (39%)	0.2208 ns
Mastectomy	40 (48%)	23 (59%)	17 (39%)	0.0802 ns

Disclosure(s):

Francois Panet, M.D. M.Sc.: No financial relationships to disclose

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Stephanie Wong, M.D. M.Sc.: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-01-07

Combination of pyrotinib with trastuzumab, taxanes and platinum as neoadjuvant therapy in patients with HER2-positive early or locally advanced breast cancer: a multicenter phase II trial

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Background: Pyrotinib (an irreversible pan-ErbB inhibitor) plus capecitabine have shown clinically and statistically meaningful progression-free survival and overall survival benefits with acceptable tolerability in patients with HER2-positive metastatic breast cancer in phase 3 trials. In this study, we assessed the efficacy and safety of neoadjuvant pyrotinib plus trastuzumab, taxanes and platinum in women with HER2-positive early or locally advanced breast cancer. Methods: In this multicenter, single-arm, phase II trial (ChiCTR2000039286), treatment-naive patients with early or locally advanced (T2-3, N0-3, M0) breast cancer received pyrotinib 400 mg once daily, plus trastuzumab (8 mg/kg loading dose and 6 mg/kg maintenance dose), docetaxel (75 mg/m²) or nab-paclitaxel (125 mg/m²), and carboplatin (AUC=5-7) on day 1 of each 21-day cycle for 6 cycles before surgery. All patients also received 1-year adjuvant pyrotinib combined with trastuzumab after surgery. The primary endpoint of the study was total pathological complete response (tpCR, ypT0/is ypN0) rate. The secondary endpoints were breast pathological complete response (bpCR) rate, objective response rate, adverse events (AEs) and invasive disease-free survival. Results: Between October 2020 and March 2022, a total of 35 patients were enrolled from 7 sites. By the data cut-off date on June 29, 2022, two patients withdrew from the study, and one received other anti-tumor therapies. Thirty-two patients received neoadjuvant therapy and surgery (modified intention-to-treat [mITT] population), and 30 of whom completed the 6-cycle neoadjuvant therapy (per-protocol [PP] population). The local pathologist-assessed tpCR rate was 59.4% (19/32) and 60.0% (18/30) in the mITT and PP populations, and bpCR rate was 65.6% (21/32) and 66.7% (20/30) in the mITT and PP populations, respectively. The tpCR rate was 68.8% (11/16) among patients with hormone receptor-negative disease and 50.0% (8/16) among those with hormone receptor-positive disease in the mITT population. Of 30 patients with preoperative imaging assessments, 26 (86.7%) achieved an objective response. Treatment-related AEs (TRAEs) were reported in 34 (97.1%) of 35 patients, with the most common being diarrhea (82.9%) and platelet decreased (48.6%). The most common grade ≥ 3 TRAEs were diarrhea (25.7%), platelet decreased (8.6%), neutropenia (8.6%), vomiting (5.7%), and alanine aminotransferase increased (5.7%). No grade 4 or 5 diarrhea events occurred. Conclusions: This study showed similar efficacy with previous reports, neoadjuvant pyrotinib plus trastuzumab-based chemotherapy exhibits promising efficacy and manageable toxicity in patients with HER2-positive early or locally advanced breast cancer.

Disclosure(s):

Hao Zhou, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-01-08

The Efficacy of Anlotinib Combined with TEC in Neo-adjuvant Treatment for Triple-Negative Breast Cancer and The Value of Multi-point Core Needle Biopsy in Prediction of Pathologic Complete Remission: A Retrospective analysis

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background While neo-adjuvant anthracycline and taxane-based chemotherapy remains the standard of care for locally advanced TNBC, the optimal chemotherapy regimen is debatable. Anlotinib, a novel multi-target tyrosine kinase inhibitor that effectively inhibits VEGFR, FGFR, c-KIT, c-MET, and RET, monotherapy has been proven effective in HER-2 negative metastatic breast cancer. This study aims to evaluate the efficacy and safety of anlotinib combined with TEC in neo-adjuvant treatment for locally advanced TNBC, and to evaluate the value of predicting pathological response by multi-point core needle biopsy during neo-adjuvant therapy. method This study retrospectively analyzed 18 patients (Pts) with locally advanced triple-negative breast cancer who received anlotinib combined with TEC neo-adjuvant therapy and surgical treatment from August 2020 to January 2022 in the Breast Diagnosis and Treatment Center of Anhui Cancer Hospital. Pts with clinical stage IIb/III TNBC were to be treated with 6 cycles of anlotinib (12mg, d1-14, q3w) plus 6 cycles of docetaxel (75 mg/m², d1, q3w), Epirubicin (90 mg/m², d1, q3w) and cyclophosphamide (600 mg/m², d1, q3w) followed by surgery. Before the fifth cycle of treatment, ultrasound-guided multi-point Core needle biopsy was performed to evaluate the efficacy of neo-adjuvant therapy and predict the pathological complete response, as well as to guide the selection of surgical methods. The primary endpoint was pathological complete response (pCR, ypT0/is). Result Eighteen pts, the median age was 48 years (range, 23-60), were included in the statistical analysis. All patients completed 6

cycles of anlotinib combined with TEC neo-adjuvant therapy followed by radical mastectomy for breast cancer. Regarding pathological response, there were 4 (22.2%), 2 (11.1%), and 12 (66.7%) patients realizing Miller-Payne grade G3, G4, and G5, respectively. Besides, 12 (66.7%) patients achieved pCR. Additionally, the accuracy of multi-point core needle biopsy in predicting pCR was 94.4% in the interval between neo-adjuvant therapy. The grade 3 or 4 AEs were neutropenia and thrombocytopenia in 3 cases each, anemia, arrhythmia, and ALT increased in cases 1 case each. One patient dropped out of the group due to tumor rupture and bleeding. conclusion Anlotinib combined with TEC as neo-adjuvant therapy showed manageable toxicity and promising antitumor activity for locally advanced TNBC. It is safe, reliable, feasible and accurate to evaluate the efficacy of neo-adjuvant therapy and to predict pathological complete response by multi-point core needle biopsy. It means that the clinical evaluation of neo-adjuvant therapy can transition from imaging evaluation to pathological evaluation, which is helpful for the choice of surgical methods.

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12/7/2022

7:00 AM - 8:15 AM

P2-02-01

Benefit of adjuvant bisphosphonates in early breast cancer treated with contemporary systemic therapy: A meta-analysis of randomized control trials

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Introduction

Based on trials performed over a 25-year period, the Early Breast Cancer Trialists Collaborative Group (EBCTCG) identified a small but significant benefit of adjuvant bisphosphonates (BP) in reducing bone recurrence with a subsequent modest improvement in breast cancer-specific survival in post-menopausal women. Multiple studies show that contemporary event rates in early-stage breast cancer are much lower than those observed over a decade ago. This observation likely reflects the impact of modern adjuvant systemic therapy such as anthracycline and taxane chemotherapy and aromatase inhibitors. Therefore, re-evaluating the benefit of adjuvant bisphosphonate in the modern era is warranted.

Methods:

We reviewed reports of randomized trials of adjuvant BP that accrued patients exclusively beyond 2000 and extracted 5-year disease free survival (DFS) and overall survival (OS) in BP and control group arm along with hazard ratios (HR) when reported. The mean 5-year DFS and OS weighted by study sample size was calculated for each group. HR for DFS and OS were pooled in a meta-analysis using generic inverse variance and random effects modelling. Trial level absolute differences in DFS and OS between BP and control arms were calculated. Meta-regression comprising linear regression weighted by sample size (mixed effects) was then performed to explore association between disease and treatment related factors and absolute differences in benefit from BP. Quantitative significance was explored using methods described by Burnand et al. Analyses were performed using SPSS version 28 (IBM Corp, Armonk NY) and Review manager v5.4.

Results

Twelve trials comprising 24109 patients were included in the analysis. Weighted mean DFS and OS in patients receiving BP were 85.8% and 91.7% respectively. For control group patients, these estimates respectively were 83.4% and 91.0%. For DFS, pooled HR across

trials was 0.89 (0.81-0.97) with a 2.9% weighted mean difference favoring BP over control. Among patients receiving anthracycline and taxane based chemotherapy (n=3007), relative benefits were smaller; (HR DFS 0.94, 0.85-1.05). There was no significant OS benefit with BP (HR 0.92, 0.82-1.03) and this finding was observed irrespective of type of chemotherapy. The impact of BP on OS was smaller in both relative and absolute terms in studies with recruitment occurring more recently. Meta-regression results are shown in Table. There was lesser benefit in higher risk patients (node+, larger tumor size, ER-, grade 3 or those receiving chemotherapy). Overall, 1.13% patients experienced osteonecrosis related to BP therapy.

Conclusions

Compared to EBCTCG data, relative and absolute benefit from BP is similar or modestly lower among more recent trials. Benefit from adjuvant BP appears smaller in patients treated with more contemporary adjuvant systemic therapy especially anthracycline and taxane containing chemotherapy. It is uncertain if the impact of BP on OS (rather than breast-cancer specific survival) is of a clinically meaningful magnitude. Despite de-escalated dosing compared to metastatic disease, osteonecrosis was observed in >1% of patients. It is possible that the benefits of BP are driven by patients with clinically low-risk disease rather than those with at high-risk. The balance between benefits and risks of adjuvant BP should be considered in individual patients.

Metaregression Results

Delta DFS				Delta OS		
Variable	Beta coefficient	p-value	N studies	Beta coefficient	p-value	N studies
Final year of accrual	0.2	0.58	10	-0.12	0.75	8
Duration of BP	-0.21	0.57	10	-0.12	0.75	8
Median age	-0.010	0.98	7	0.43	0.34	6
Post-menopausal	0.031	0.98	10	0.48	0.19	8
pN+	-0.87	0.005	8	0.54	0.21	6
>=pT3	-0.98	<0.001	6	0.57	0.23	6
HR negative	-0.52	0.19	8	0.74	0.06	6
Grade 2	-0.25	0.62	8	-0.1	0.85	5
Grade 3	-0.63	0.1	8	0.52	0.23	6
Received NACT/ACT	-0.77	0.02	9	0.73	0.03	8
Taxane%	-0.22	0.68	6	0.10	0.85	5
Anthracycline%	-0.89	0.02	6	0.57	0.24	5
DFS HR				OS HR		
Final year of accrual	-0.34	0.96	9	0.75	0.03	7
Duration of BP	0.42	0.27	9	-0.08	0.85	7
Median age	0.20	0.71	6	0.55	0.25	5
Post-menopausal	-0.13	0.75	8	0.51	0.20	6
pN+	-0.06	0.9	8	0.49	0.26	5
>=pT3	0.13	0.83	5	0.03	0.97	5
HR negative	-0.17	0.69	8	0.54	0.21	6
Grade 2	-0.69	0.2	5	0.99	0.002	4
Grade 3	-0.47	0.29	7	0.38	0.45	5
Received NACT/ACT	-0.14	0.75	8	0.60	0.12	7
Taxane%	-0.85	0.03	6	0.65	0.16	5
%Anthracycline	-0.26	0.62	6	0.15	0.78	5

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

P2-02-02

Phase I trial of the safety and immunogenicity of a tri-antigen vaccine targeting HER2, IGFBP-2, and IGF-IR in patients with non-metastatic breast cancer

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Background: HER2, IGFBP-2, and IGF-IR are proteins that are overexpressed in breast cancer. These three proteins, when used as immunogens, provide broad antigenic coverage to all molecular breast cancer subtypes. The proteins are also up-regulated in pre-invasive and high-risk breast lesions which are associated with progression to invasive cancer. Therefore, generating protective immunity against these antigens could have the result of preventing cancer development in high risk patients. We identified epitopes derived from these proteins, termed Th1 selective epitopes, that specifically stimulated T-helper 1 immune responses in humans and mice. The tri-antigen vaccine was effective in preventing the development of breast cancer in a transgenic mouse model of neu-expressing mammary cancer. We conducted a dose finding study of a plasmid-based vaccine encoding three extended Th1 selective epitopes derived from these antigens in breast cancer patients. Methods: Patients with non-metastatic, node positive, HER2 negative breast cancer that are in remission and defined as no evidence of disease were enrolled sequentially to one of 3 dose arms: 150, 300, and 600 mcg of the tri-antigen vaccine plasmid with 10 evaluable patients per arm (NCT02780401). Vaccines were given monthly intradermally for three total doses with rhu-GM-CSF (100mcg) as an adjuvant. The primary endpoint was safety through the 6-month follow-up visit and the secondary endpoints were immunogenicity, persistence of the immune response after vaccination, and assessment of potential stimulation of T-regulatory (T-reg) cells or myeloid derived suppressor cells to the overexpressed non-mutated antigens as well as determining the recommended Phase II dose. Results: Thirty-two patients were enrolled and 97% received all three vaccinations. The mean age at enrollment was 51.9 years with 61% of patients being pre-menopausal and 39% post-menopausal. The majority of patients were Stage II/III. Eighty-eight percent of patients had hormone receptor positive tumors and twelve percent were triple negative disease. The majority of adverse events (AE) (>95%) were grade 1 or 2. The most common AE were injection site reactions, flu like symptoms, fatigue, chills, myalgia, and nausea. All doses were immunogenic with the greatest magnitude antigen specific Type I immune responses seen in the low and intermediate doses. Eighty percent of patients at the 300mcg dose retained high levels of antigen specific immunity at 1 and 6 months after immunization as compared to 57% and 50% at the 100 and 600mcg doses respectively. No antigen specific Th2 cells, MDSC or T-reg were generated with vaccination. Immunizations did not upregulate PD-1 on CD4 or CD8 T-cells. Conclusions: A plasmid-based vaccine encoding extended Th1 selective epitopes derived from HER2, IGFBP-2, and IGF-IR could be administered safely and generate high levels of antigen specific interferon gamma secreting T-cells (Th1). The 300mcg dose elicited significant immune responses in the majority of patients which persisted at least 6 months after the end of immunization. A Phase II study of the vaccine given in the neoadjuvant setting to patients with HER2 positive breast cancer is ongoing (NCT04329065).

Disclosure(s):

Sasha E. Stanton, MD PhD: IMV Inc: Contracted Research (Ongoing); Stanford Burnham Prebys: Consulting Fees (e.g., advisory boards) (Ongoing)

Kari B. Wisinski, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Context: Contracted Research (Ongoing), Contracted Research (Ongoing); DSI: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Genentech/Roche: Contracted Research (Ongoing), Contracted Research (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Relay Therapeutics: Contracted Research (Ongoing), Contracted Research (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Seagen: Contracted Research (Ongoing), Contracted Research (Ongoing)

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12/7/2022

7:00 AM - 8:15 AM

P2-02-03

Efficacy and Safety of the Addition of Internal Mammary Irradiation to Standard Adjuvant Radiation in Early-Stage Breast Cancer: A Systematic Review and Meta-analysis

Presenting Author(s) and Co-Author(s):

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Background: Adjuvant regional nodal irradiation together with whole breast or chest wall irradiation is considered standard of care in most node positive early breast cancer. Existing data on adding internal mammary irradiation (IMNI) to the regional nodal fields are inconsistent. The objective of this study was to conduct a meta-analysis to explore the efficacy and safety of adding IMNI to adjuvant radiotherapy in early-stage, high risk breast cancer. Methods: A search of PubMed and EMBASE identified randomized trials that investigated the addition of IMNI to standard adjuvant radiation in early-stage breast cancer. Hazard ratios (HRs) and 95% confidence intervals (CI) were extracted for overall survival (OS), breast cancer specific survival (BCSS), disease-free survival (DFS) and distant-metastasis free survival (DMFS). The odds ratios (ORs) for regional and loco-regional recurrence, non-breast cancer mortality, secondary non-breast cancer, contralateral breast cancer and cardiovascular morbidity and mortality were also extracted. These data were pooled in a meta-analysis using RevMan 5.4. Results: Analysis included 5 trials comprising 10,994 patients. Compared to the control group, IMNI was associated with a small, but statistically significant improvement in OS (HR=0.91, 95% 0.85-0.97, p=0.004), BCSS (HR=0.84, 95% 0.77-0.92, p< 0.001), DFS (HR=0.89, 95% CI 0.82-0.98, p= 0.01) and DMFS (HR=0.89, 95% 0.81-0.98, p=0.02). IMNI was also associated with reduced odds for regional (OR=0.58, 95% 0.44-0.75, p< 0.001) and loco-regional recurrence (OR=0.85, 95% CI 0.72-1.00, p=0.04). Subgroup analyses for OS by tumor location (medial/central vs. lateral) and by nodal burden showed similar benefit in all subgroups. The odds for cardiotoxicity were higher, but did not reach statistical significance (OR=1.23, 95% 0.99-1.53, p=0.07). There was no association with cardiovascular mortality (OR=1.00, 95% 0.69-1.46, p=1.00). There were also comparable odds for non-breast cancer mortality (OR=1.05, 95% 0.79-1.41, p=0.74), secondary cancer (OR=0.95, 95% 0.82-1.10, p=0.51) and contra-lateral breast cancer (OR=1.07, 95% 0.77-1.51, p=0.68). Conclusions: Compared to the control group the addition of IMNI in high-risk patients is associated with a statistically significant improvement in survival, albeit with a magnitude of questionable clinical meaningfulness. Non-significant association with increased cardiovascular toxicity requires further study in longer-term studies.

Disclosure(s):

Yasmin Korzets, Dr: No financial relationships to disclose

Dina Levitas, Dr: No financial relationships to disclose

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Hadar Goldvaser, Dr: Eli-Lilly: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 20, 2022); Gilead: Consulting Fees (e.g., advisory boards) (Terminated, May 17, 2022); MSD: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, May 15, 2021); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, February 28, 2022); Rhenium Oncotest: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Roche: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

12/7/2022

7:00 AM - 8:15 AM

P2-02-04

De-escalation of bone-targeted treatment: Does the number of 6-monthly adjuvant zoledronate infusions received affect treatment efficacy for early breast cancer? A sub-study of ABCSG-12

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Background: The results of the Early Breast Cancer Trialist Group (EBCTCG) meta-analysis (Lancet 2015) led to the widespread adoption of bisphosphonates as adjuvant therapy for postmenopausal early-stage breast cancer (EBC). Despite evaluating multiple bisphosphonate agents and regimens, there was no signal of varying efficacy with different agents, routes of administration or dose / dose intensity. We evaluated the question of treatment de-escalation using long-term outcome data from the prospective randomized ABCSG-12 trial.

Patients and methods: Between 1999 and 2006, ABCSG-12 accrued 1803 patients with hormone-receptor positive EBC on ovarian function suppression for three years that were randomized to receive 4 mg zoledronic acid 6-monthly or not (and tamoxifen or anastrozole, in a 2:2 factorial design). In the current retrospective study, we evaluated whether the number of zoledronate infusions actually received had an impact on breast cancer-specific and fragility fracture outcomes. Based on the results of the EBCTCG meta-analysis, we hypothesized that amongst patients who receive less infusions than the planned seven zoledronate infusion in this trial, the number of infusions has no differential effect on these outcomes. Time to event endpoints were analyzed with Cox models and Kaplan Meier curves starting from a 3-year landmark. BMD subset analyses were restricted to patients who participated in the BMD sub-study with available BMD data.

Results: 725 patients who received at least one zoledronate infusion were included in the time-to-event-analysis. There was no statistically significant difference in disease-free survival (adjusted HR 0.83, 95% CI 0.48–1.44, p=0.51) or overall survival (HR 0.97, 95% 0.30-3.11, p=0.96) in patients who received ≤6 zoledronate infusions (n=170) compared to those who received ≥7 zoledronate infusions (n=555) (adjusted HR 0.83, 95% CI 0.48 – 1.44, p=0.51). Both subgroups show stable lumbar spine and total hip BMD measurements across the five years.

Conclusions: Comparable to the metastatic bone disease and fragility fracture settings, there was no evidence observed to indicate that a reduced number of zoledronate infusions is associated with reduced adjuvant efficacy. Further studies to define optimal regimens of adjuvant bone-targeted therapies (prospective evaluation of “how-low-can-you-go”) are required.

Table 1: Multivariate Cox Regression: DFS and OS

Table 1: Multivariate Cox Regression: DFS and OS

Covariate		Outcome=DFS		Outcome=OS	
		HR (95% CI)	P-value	HR (95% CI)	P-value
Number of ZOL infusions	≤6 infusions vs. ≥7 infusions	0.83 (0.48, 1.44)	0.51	0.97 (0.30, 3.11)	0.96
Endocrine Therapy	Tamoxifen vs. Anastrozole	0.77 (0.49, 1.21)	0.26	0.85 (0.31, 2.37)	0.76
pT-Stage	pT2/pT3 vs. pT1	2.36 (1.47, 3.78)	<0.001	4.36 (1.54, 12.30)	0.006
pN-Stage	Positive vs. Negative	1.34 (0.84, 2.13)	0.22	0.80 (0.27, 2.42)	0.70

Table 2: BMD and percent change from baseline at the total hip and lumbar spine (L1-L4) over 60 months

Table 2: BMD and percent change from baseline at the total hip and lumbar spine (L1-L4) over 60 months¶

Timepoint [¶]		Zoledronic acid <= 6 infusions¶ N= 218 [¶]			Zoledronic acid >= 7 infusions¶ N= 562 [¶]		
		¶	Hip [¶]		¶	L1-L4 [¶]	
		n [¶]	Mean, 95% CI [¶]	Mean, 95% CI [¶]	n [¶]	Mean, 95% CI [¶]	Mean, 95% CI [¶]
Baseline [¶]	BMD [¶]	39 [¶]	1.02 (0.98, 1.05) [¶]	0.72 (0.68, 0.76) [¶]	128 [¶]	1.01 (0.99, 1.03) [¶]	0.71 (0.69, 0.73) [¶]
6 months [¶]	BMD [¶]	36 [¶]	1.03 (0.99, 1.07) [¶]	0.73 (0.69, 0.76) [¶]	118 [¶]	1.02 (1.00, 1.04) [¶]	0.72 (0.69, 0.74) [¶]
6 months [¶]	% Change [¶]	35 [¶]	1.19 (0.31, 2.07) [¶]	1.33 (0.24, 2.43) [¶]	116 [¶]	0.99 (0.51, 1.48) [¶]	0.70 (0.17, 1.22) [¶]
12 months [¶]	BMD [¶]	30 [¶]	1.04 (1.00, 1.09) [¶]	0.74 (0.70, 0.78) [¶]	121 [¶]	1.02 (1.00, 1.04) [¶]	0.71 (0.69, 0.73) [¶]
12 months [¶]	% change [¶]	30 [¶]	1.46 (0.52, 2.40) [¶]	0.97 (0.57, 2.51) [¶]	120 [¶]	1.13 (0.56, 1.71) [¶]	0.85 (0.21, 1.49) [¶]
36 months [¶]	BMD [¶]	17 [¶]	1.00 (0.93, 1.07) [¶]	0.74 (0.70, 0.79) [¶]	112 [¶]	1.03 (1.00, 1.05) [¶]	0.72 (0.70, 0.74) [¶]
36 months [¶]	% change [¶]	17 [¶]	-1.67 (-4.36, 1.02) [¶]	2.32 (1.28, 3.36) [¶]	110 [¶]	1.30 (0.29, 2.32) [¶]	1.02 (0.18, 1.86) [¶]
60 months [¶]	BMD [¶]	18 [¶]	1.06 (1.01, 1.12) [¶]	0.77 (0.71, 0.83) [¶]	92 [¶]	1.07 (1.04, 1.10) [¶]	0.74 (0.72, 0.77) [¶]
60 months [¶]	% change [¶]	18 [¶]	2.11 (-1.63, 5.86) [¶]	1.58 (-0.86, 4.02) [¶]	90 [¶]	5.78 (4.03, 7.53) [¶]	3.08 (1.64, 4.51) [¶]

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Richard Greil, n/a: Abbvie: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Travel / Accomodation / Expenses (Ongoing); Amgen: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Travel / Accomodation / Expenses (Ongoing); BMS: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Travel / Accomodation / Expenses (Ongoing); Celgene: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Travel / Accomodation / Expenses (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Travel / Accomodation / Expenses (Ongoing); Janssen C: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Travel / Accomodation / Expenses (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from

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12/7/2022

7:00 AM - 8:15 AM

P2-02-05

Patterns of adjuvant bone modifying agent use in patients with early-stage breast cancer in the United States

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Background: The bone modifying agents (BMAs), bisphosphonates, reduce risk of cancer recurrence after diagnosis of early-stage breast cancer (EBC), particularly in postmenopausal women, while another BMA, denosumab, has not been shown to improve EBC outcomes. The 2017 American Society of Clinical Oncology (ASCO) and Cancer Care Ontario (CCO) clinical guidelines recommended consideration of adjuvant bisphosphonates for postmenopausal women with EBC who are candidates for adjuvant systemic therapy. Despite this, small survey-based studies suggest that their prescribing is variable. The goal of this study was to evaluate prescribing of adjuvant BMAs in the United States before and after publication of the 2017 ASCO/CCO guidelines (ACGD).

Methods: This retrospective cohort study used the nationwide Flatiron Health electronic health record (EHR)-derived de-identified database and included 11,740 patients diagnosed with stage I-III breast cancer from 2012 to 2019. We analyzed data on use of BMAs (bisphosphonates or denosumab) in the adjuvant setting, defined as receiving first dose of BMA within 24 months of breast cancer diagnosis and before diagnosis of metastatic disease. Any episodes of BMA use after a metastatic recurrence were excluded. We used Chi-squared test to compare the proportion of patients receiving adjuvant BMAs pre- and post-ACGD. We used univariable and multivariable logistic regression analyses with list-wise missing value deletions to identify predictors of adjuvant BMA prescribing.

Results: Of 11,740 patients, 7,391 were diagnosed pre-ACGD and 4,349 post-ACGD. Of the pre-ACGD patients, 545 (7.4%) patients received adjuvant BMAs, and of the post-ACGD patients, 390 (9.0%) patients received adjuvant BMAs. Patients diagnosed post-ACGD were more likely to receive adjuvant BMAs compared with patients diagnosed pre-ACGD (OR 1.23; 95% confidence interval (CI) 1.08-1.42; p=0.002). Of patients age \geq 50 (n=9,654), 522 of 6,027

(8.7%) and 360 of 3,627 (9.9%) received adjuvant BMAs pre- and post-ACGD, respectively (OR 1.146; 95% CI 0.996-1.319; p=0.0572). In multivariable analysis, age \geq 50 years at diagnosis, post-menopausal status, having T2 or higher stage at diagnosis, adjuvant endocrine therapy, and coexisting bone loss diagnosis were significantly associated with receipt of adjuvant BMAs (Table 1). Of the 935 patients who received adjuvant BMAs, 615 (65.8%) had denosumab only, 305 (32.6%) had a bisphosphonate only, and 13 (1.4%) received both a bisphosphonate and denosumab during the course of adjuvant treatment. Two patients received an adjuvant BMA as part of a clinical trial.

Conclusions: Adjuvant BMA prescribing in our cohort was overall low; there was a modest increase in uptake in patients with EBC diagnosed after the publication of the 2017 ACGD. Older age, higher T stage, endocrine therapy, and coexisting bone loss diagnoses were significantly associated with receipt of adjuvant BMAs. Despite the recommendations for bisphosphonates in the adjuvant setting in EBC, the majority of patients received denosumab only. Considering these findings, further research is required to determine barriers to BMA prescribing and factors that influence physician and patient decisions. There continues to be a need for improved implementation and dissemination of recent guidelines, including the updated 2021 ASCO/CCO recommendations which continue to endorse bisphosphonate use in the adjuvant setting.

Univariable and multivariable logistic regression analyses to identify predictors of receiving adjuvant BMAs

Table 1. Univariable and multivariable logistic regression analyses to identify predictors of receiving adjuvant BMAs

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age at Diagnosis (\geq 50 versus <50 years)	3.86 (2.91-5.11)	<0.001*	1.61 (1.03-2.52)	0.038*
Post-menopausal Status	4.38 (3.34-5.74)	<0.001*	2.89 (1.94-4.32)	<0.001*
Practice Type (Community versus Academic)	1.61 (1.24-2.09)	<0.001*	1.31 (0.93-1.84)	0.117
T stage (T1 versus T2 or higher)	1.09 (0.95-1.26)	0.229	1.48 (1.17-1.87)	0.001*
Node Positive Status	1.00 (0.86-1.17)	0.991	1.14 (0.92-1.42)	0.241
Stage at Diagnosis (I versus II or higher)	0.91 (0.79-1.04)	0.165	0.83 (0.64-1.08)	0.164
ER Positive Status	3.24 (2.45-4.29)	<0.001*	1.11 (0.65-1.89)	0.701
PR Positive Status	1.50 (1.26-1.78)	<0.001*	0.90 (0.71-1.14)	0.381
HER2 Positive Status	0.88 (0.72-1.08)	0.224	1.04 (0.80-1.35)	0.778
Adjuvant Chemotherapy	0.78 (0.68-0.89)	<0.001*	1.08 (0.90-1.31)	0.401
Adjuvant Endocrine Therapy	4.06 (2.95-5.61)	<0.001*	4.11 (2.38-7.09)	<0.001*
Coexisting Bone Loss Diagnosis	6.19 (4.43-8.65)	<0.001*	5.03 (3.24-7.80)	<0.001*

Abbreviations: BMA: bone-modifying agent (bisphosphonates or denosumab); ER: estrogen receptor; PR: progesterone receptor; HER2: human epidermal growth factor receptor 2

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12/7/2022

7:00 AM - 8:15 AM

P2-02-06

Adjuvant Denosumab treatment in early breast cancer: a systematic review and meta-analysis of randomized controlled clinical trials.

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Background. Adjuvant denosumab treatment improved bone-health related outcomes in early breast cancer (BC) patients with discordant survival results. We undertook a systematic review and meta-analysis of randomized controlled trials (RCTs) to assess efficacy and safety of adjuvant denosumab in addition to standard anticancer therapy. **Methods.** PubMed, CENTRAL, Scopus, Embase, clinicaltrials.gov and key oncological meetings websites were screened to identify potentially eligible RCTs based on the PICO model: P) Participant: pre and postmenopausal early BC patients; I) Intervention: adjuvant denosumab; C) Comparator: placebo; O) Outcomes: Disease-free survival (DFS), Bone Metastasis-free survival (BMFS), Overall Survival (OS), fracture incidence and time to first fracture were adopted as survival endpoints, and Adverse Events, Serious Adverse Events, Osteonecrosis of the Jaw (ONJ) and Atypical Femur Fractures (AFF) as safety endpoints; S) Study design: phase III RCTs. Risk of bias was assessed with Cochrane Collaboration Risk of Bias Tool. Pooled hazard ratios (HR), risk ratios (RR), risk differences (RD) and respective confidence intervals (CI) were computed using both a fixed and a random effect model. Subgroup analyses based on menopausal status, hormone receptor and HER2 status and immunophenotype were performed. **Results.** Two phase III RCTs were included (ABCSG-18, D-CARE), for an overall population of 7929 early BC patients receiving denosumab or placebo. Denosumab addition to standard of care anticancer treatment showed no difference in DFS (HR 0.93; 95% CI 0.75-1.16, p=0.53), BMFS (HR 0.90; 95% CI 0.75-1.07, p=0.23) and OS (HR 0.92; 95% CI 0.72-1.17, p=0.49). In hormone receptor-positive/HER2 negative patients, denosumab significantly prolonged both DFS (HR 0.88; 95% CI 0.78-0.99, p=0.04) and BMFS (HR 0.83; 95% CI 0.71-0.97, p=0.02). No interaction was found between denosumab addition and menopausal status. Fracture incidence (RR 0.79; 95% CI 0.70-0.89, p< 0.01) and time to first fracture (HR 0.76; 95% CI 0.66-0.87, p< 0.01) were also improved with denosumab. No association between denosumab addition and overall toxicity was seen and no difference was observed in terms of ONJ and AFF between the 60mg every 6 months schedule and placebo (RD 0.001, 95% CI from -0.001 to 0.002, p=0.48) **Conclusions.** Findings from this meta-analysis validate the role of denosumab as a highly effective anti-resorptive agent. We provide robust evidence that its addition to standard anticancer treatment significantly improves survival outcomes in hormone receptor-positive/HER2 negative early BC patients, suggesting that the implementation of denosumab use in combination with endocrine therapy in this patient population should be reconsidered. Systematic Review Registration: <https://www.crd.york.ac.uk/prospero>, identifier CRD42022332787.

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12/7/2022

7:00 AM - 8:15 AM

P2-02-07

Patients' selection of daily timing of oral intake of adjuvant hormonotherapy (HT) and everolimus (EVE) for high risk early breast cancer in the UCBG-UNIRAD phase III trial.

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Background :

Everolimus (EVE) addition to adjuvant hormonotherapy (HT) for high-risk early breast cancer (BC) did not improve 3-year disease-free survival (DFS) compared with ET alone in the randomized UNIRAD trial (NCT01805271) (1). Most patients (pts) withdrew from EVE for adverse events nearly midway before the expected treatment duration of 2 years. The main EVE target involves m-TOR-induced S6 protein phosphorylation, which is controlled by the molecular circadian clock in mice and cells. Toward the analysis of possible circadian time-dependencies in EVE toxicities and efficacy, we first determine the actual distribution of the daily times chosen by the patients for both oral EVE and HT intakes.

Patients and methods:

The registered pts were asked to record the clock hours they chose for both HT and EVE or placebo (PLAC) intakes within four possible daily 6-h slots, i.e. from 06:00 to 11:59 (morning), 12:00 to 17:59 (midtime), 18:00 to 23:59 (evening), or 24:00 to 05:59, (night) in a daily diary throughout their participation in the trial. Modifications in times of drugs intake were reported. Comparisons between groups involved Kruskal-Wallis sum test and Pearson's Chi-squared and Fisher's exact tests.

Results:

Out of 1,278 randomized patients, 1063 (83,1 %) recorded the times of EVE or PLAC intakes, 852 recorded those for HT intakes. Only 10 pts reported night EVE/PLAC intakes and were not considered here. Of the 1053 evaluated pts; 549 pts took EVE/PLAC in the morning, 82 pts at midtime and 422 in the evening. As compared with evening intakes, morning or midtime intakes of EVE or PLAC were significantly associated with an older age, and post-menopausal status, whilst younger and premenopausal women preferentially chose evening intakes ($p < 0.001$ for both). Consistently, HT with aromatase inhibitors (AI) were mostly taken in the morning or at midtime, whereas tamoxifene (TAM) was mostly taken the evening ($p = 0.001$). Tumor size, lymph nodes involvement, histological grade, hormonal receptors status, and EVE initial dose

were similarly distributed among the three time slots (Table 1). A similar distribution of oral intake times as in the whole timing study population was found according to age, menopausal status and HT type in the EVE arm (N=508 pts), and in the HT population (+/- EVE or PLAC) (N=852 pts). Initial oral timing intake was modified for EVE by 50 of 508 pts (10%) and for HT by 10 of 852 pts (1%).

Conclusion:

To the best of our knowledge, it is the first time that the patients' spontaneous selection of daily times for oral intakes of a targeted agent (EVE) and HT is reported in a large series of early breast cancer pts. Age and menopausal status were important determinants of patient-selected daily timing intakes of both EVE and HT, as well as HT types. These findings will be carefully considered in the analyses of possible EVE and HT timing effects on adverse events and efficacy of the current adjuvant regimens.

1) Bachelot T et al, J Clin Oncol. 2022 May 23

Variable	Overall ¹ N = 1053 ¹	Morning N = 549 ¹	Midtime N = 82 ¹	Evening N = 422 ¹	p-value ²
Age at BC diagnosis	53 (48, 62)	55 (49, 63)	60 (50, 67)	51 (46, 59)	<0.001
ECOG					0.4
	0 941 (90%)	491 (90%)	70 (85%)	380 (90%)	
	1 109 (10%)	57 (10%)	12 (15%)	40 (9.5%)	
Menopausal status					<0.001
Postmenopausal	698 (68%)	390 (73%)	64 (79%)	244 (58%)	
Premenopausal	335 (32%)	144 (27%)	17 (21%)	174 (42%)	
(Missing)	20	15	1	4	
Pathological T stage (TNM)					
pT0 or pTis	12 (1.1%)	5 (0.9%)	0 (0%)	7 (1.7%)	
pT1	288 (27%)	132 (24%)	25 (31%)	131 (31%)	
pT2	524 (50%)	291 (53%)	36 (44%)	197 (47%)	
pT3	203 (19%)	106 (19%)	17 (21%)	80 (19%)	
pT4	22 (2.1%)	12 (2.2%)	3 (3.7%)	7 (1.7%)	
(Missing)	4	3	1	0	
Pathological N stage (TNM)					
0	7 (0.7%)	5 (0.9%)	2 (2.4%)	0 (0%)	
[1-3]	478 (46%)	241 (44%)	33 (40%)	204 (49%)	
[4-9]	393 (38%)	207 (38%)	31 (38%)	155 (37%)	
10 and more	168 (16%)	91 (17%)	16 (20%)	61 (15%)	
(Missing)	7	5	0	2	
SBR Grade					>0.9
Grade I	83 (8.1%)	42 (8.0%)	7 (8.5%)	34 (8.2%)	
Grade II	622 (61%)	315 (60%)	52 (63%)	255 (61%)	
Grade III	319 (31%)	170 (32%)	23 (28%)	126 (30%)	
(Missing)	29	22	0	7	
PR status					0.5
Negative	160 (15%)	78 (14%)	16 (20%)	66 (16%)	
Positive	886 (85%)	464 (86%)	66 (80%)	356 (84%)	
(Missing)	7	7	0	0	
Class HT					<0.001
Aromatase inhibitors	642 (61%)	357 (65%)	62 (76%)	223 (53%)	
Tamoxifen	411 (39%)	192 (35%)	20 (24%)	199 (47%)	
Arm					0.007
Everolimus	508 (48%)	248 (45%)	52 (63%)	208 (49%)	
Placebo	545 (52%)	301 (55%)	30 (37%)	214 (51%)	
Initial dose					0.14
5	660 (63%)	358 (65%)	53 (65%)	249 (59%)	
10	392 (37%)	191 (35%)	29 (35%)	172 (41%)	
(Missing)	1	0	0	1	

¹ Median (IQR); n (%)

² Kruskal-Wallis rank sum test; Pearson's Chi-squared test; Fisher's exact test

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7:00 AM - 8:15 AM

P2-03-01

Sarcopenia on baseline imaging is associated with toxicity-related discontinuation of endocrine therapy in women with early-stage hormone-positive breast cancer

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Background Adjuvant endocrine therapy (ET) is standard of care in women with hormone receptor-positive (HR+) breast cancer (BC) with the goal to reduce recurrence. However, early discontinuation of ET occurs in 30-40% of women, largely attributable to toxicity, and leads to increased recurrence risk. There is considerable overlap in risk factors that predict toxicity from ET and chemotherapy, including age, co-morbidities, and geriatric conditions. Baseline low skeletal muscle area (SMA) on chest computed tomography (CT) is a surrogate marker for sarcopenia and predicts for significant toxicity and intolerance to chemotherapy in women with BC. No study has assessed the association of sarcopenia with toxicity-related discontinuation of ET in women with early-stage HR+ BC. Methods This single center retrospective cohort study included consecutive women with Stage 0-II HR+ BC who received ET and adjuvant radiotherapy (RT) from 01/2011-12/2017. Inclusion required a minimum of 5-year clinical follow-up after diagnosis. We used a validated deep learning pipeline to quantify SMA (cm²) at the tenth thoracic (T10) vertebral body on existing RT planning CT. The skeletal muscle index (SMI [cm²/m²] = SMA / (patient height (m))²) was calculated to adjust for patient height. Sarcopenia was defined as SMI < 32.3 cm²/m², based on a previously validated independent cohort of young healthy women. The primary endpoint was toxicity-related discontinuation of ET less than 60 months after initiation of ET. Secondary endpoints included any NCI CTCAE v5.0 Grade 3-5 toxicity from ET and ipsilateral breast tumor recurrence. We assessed associations

between ET discontinuation and SMI (continuous), as well as thoracic sarcopenia (dichotomous), using logistic regression adjusting for baseline characteristics. We used cox proportional hazards regression to assess disease-free survival (DFS), defined as ipsilateral breast tumor recurrence, locoregional recurrence, or distant metastasis adjusting for baseline and treatment characteristics. Results A total of 265 women (median age 67 years) met inclusion criteria. The majority of women had a comorbidity index of 0-1 (89%) and were Caucasian (89%). The median follow-up was 82 months, 5-year overall survival was 96% and 5-year DFS was 94%. Diagnoses included DCIS (12%), IDC (76%), or ILC (12%); most were T1 (69%) or T2 (18%) and N0 (85%), ER-positive (100%), PR-positive (85%), or HER2-negative (9%). Most common ET type was anastrozole (63%), letrozole (16%), and tamoxifen (17%). SMI (continuous) was not associated with older age, Charlson Comorbidity Index (CCI), race, or tumor stage. A total of 64 (24%) women experienced toxicity-related early discontinuation of ET. On multivariate analysis (MVA), lower SMI was associated with increased toxicity-related early discontinuation of ET (Odds Ratio [OR] 0.89 per 1 cm²/m² SMI, p=0.001) independent of age, CCI, ET type, or receipt of adjuvant chemotherapy. Lower SMI was associated with higher risk of grade 3-5 toxicity from ET (OR 0.89 per 1 unit SMI, p=0.001) independent of age, CCI, ET type, or receipt of adjuvant chemotherapy. On MVA, sarcopenia was associated with higher risk of toxicity-related early discontinuation of ET (OR 2.43, p=0.019). DFS was associated with toxicity-related early discontinuation of ET (HR 8.06, p=0.005), grade 3 histology (HR 1.42, p=0.042), and multifocal disease (HR 2.55, p=0.040), but not age, histology, stage, or lymphovascular invasion (p>.05 for all). Conclusion Low baseline thoracic skeletal muscle is associated with toxicity-related early ET discontinuation in women with early-stage HR+ BC. Further studies should attempt to generalize this association to all HR+ BC who are candidates for ET. High-risk patients may be candidates for aggressive symptom management or alternative adjuvant therapies.

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7:00 AM - 8:15 AM

P2-03-02

Prospective assessment of the decision-making impact of the Breast Cancer Index in the BCI Registry Study

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Background: The Breast Cancer Index (BCI) is a validated gene expression assay that provides a quantitative individualized risk of late recurrence and predicts the likelihood of benefit from extended endocrine therapy (EET) in HR+ early-stage breast cancer. The objective of this analysis was to assess the impact of BCI on clinical decision-making regarding EET in the BCI Registry Study. Methods: The BCI Registry Study is an ongoing, prospective, large-scale study to investigate the long-term clinical outcome, decision impact, and medication adherence in

HR+ early-stage breast cancer patients receiving BCI testing as part of routine clinical care. Per protocol, physicians and patients completed pre- and post-BCI test questionnaires to assess the following: physician decision-making regarding EET; physician confidence with decision-making; patient preferences for EET; patient concerns about the cost, side effects, drug safety and benefit of EET; and patient satisfaction regarding treatment recommendation. Pre- and post-BCI responses were compared using McNemar's test and Wilcoxon signed rank test. Results: Pre- and post-BCI test physician and patient questionnaires were completed for 843 and 823 patients, respectively. For the patients included in this analysis, mean age at enrollment was 65y and 88.4% of patients were postmenopausal. 74.7% of tumors were T1, 53.4% were G2, 75.3% N0, and 13.8% HER2-positive. Following BCI testing, physicians changed treatment recommendations for EET in 40.1% (338/843) of patients ($p < 0.0001$). In cases in which physicians recommended EET prior to BCI testing, 44.7% (214/479) changed their recommendation not to extend endocrine therapy. Of these cases, 98.1% (210/214) were BCI Prognostic low risk and/or BCI (H/I) Predictive low likelihood of benefit from EET. In cases in which physicians did not recommend EET prior to BCI testing, 34.6% (124/358) changed their recommendation in favor of EET. In such cases, 87.1% (108/124) of cases were BCI Prognostic high risk and/or BCI (H/I) Predictive high likelihood of benefit from EET. Further, following BCI testing, 38.8% (327/843) of physicians felt more confident in their recommendation ($p < 0.0001$). The percentage of physicians having high confidence levels (confident or strongly confident) increased from 58.1% (490/843) before BCI testing to 80.5% (679/843) after BCI testing. The percentage of physicians having low confidence levels (not at all confident, not confident, or ambivalent) decreased from 39.1% (330/843) before BCI testing to 18.7% (158/843) after BCI testing. In addition, 40.5% (341/843) of patients felt more comfortable with their EET decision ($p < 0.0001$) following BCI testing. Notably, changes in patient preferences for EET correlated with BCI test results. In BCI (H/I)-Low patients, 46.9% (241/514) showed a decreased preference for EET ($p < 0.0001$) while in BCI (H/I)-High patients, 28.2% (87/309) showed an increased preference for EET ($p < 0.0001$). Compared with baseline, after BCI testing, significantly more patients were less concerned about cost (20.9%, $p < 0.0001$), drug safety (25.4%, $p = 0.0014$), and the benefits of EET (29.3%, $p = 0.0002$). No significant change in concern regarding side-effects was observed ($p = 0.1486$). Conclusions: This first analysis in a large patient cohort of the BCI Registry confirms previous findings on the significant clinical decision-making impact of BCI for extending adjuvant endocrine therapy. Incorporating BCI into clinical practice resulted in changes in physician recommendations for EET in over 40% of cases, while at the same time increasing physician confidence in their recommendations. Knowledge of the BCI result also improved patient satisfaction and reduced patient concerns regarding cost, drug safety and benefit of EET.

Disclosure(s):

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7:00 AM - 8:15 AM

P2-03-03

Neutrophil-to-Lymphocyte Ratio (NLR) as a Potential Prognostic Marker in Patients with Hormone Receptor-Positive/HER2-Negative Advanced-Stage Breast Cancer Treated with CDK4/6 Inhibitors: A Focus on Ribociclib

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Background: Cyclin-dependent kinase (CDK) 4/6 inhibitors combined with endocrine therapies (ET) have become the mainstay treatment for patients with hormone receptor (HR)-positive, HER2-negative advanced-stage breast cancer. However, there is no established prognostic markers to predict its efficacy to better guide its utilization. Neutrophil-to-lymphocyte ratio (NLR), an indicator of the host systemic inflammatory/immune response, is widely studied marker in various settings in different cancer sites with variable but promising results. In this study, we evaluate the impact of NLR, as a prognostic biomarker, at baseline and prior to the third and fourth cycles of ET/ribociclib in patient with advanced-stage breast cancer. Methods: Data on consecutive patients with HR-positive/HER2-negative advanced-stage disease treated with ribociclib and an aromatase inhibitor or fulvestrant, were retrospectively reviewed from our institutional cancer registry and patients' electronic medical records. NLR was calculated from blood counts performed at base line prior to commencing the first cycle of ribociclib, then prior to the third and fourth cycles, too, and was considered high if ≥ 2 . Ribociclib was given at the usual dose and schedule; 600 mg daily for 3 weeks on and one week off. Progression-free survival (PFS) was defined as the time from the initiation of CDK4/6 inhibitor to the date of radiological or clinical progression or death. Multivariate analysis for PFS was performed using Cox's proportional hazards regression model, covariates included age at diagnosis, ECOG performance status (≥ 1 vs. 0), body mass index (BMI) (≥ 25 vs. < 25), ribociclib beyond first line vs. first line, type of ET (aromatase inhibitors vs. fulvestrant), visceral metastasis, postmenopausal vs. premenopausal, smoking status and de novo metastasis vs. recurrent disease and histopathology. Results: Between June 2017 and May 2020, a total of 257 patients were included, median age was 48 (22-87) years. Majority (n=163, 63.3%) received ribociclib as a first-line, 211 (82.4%) had invasive ductal carcinoma, 137 (53.3%) patients had de novo metastasis and 122 (47.7%) were premenopausal. Progression-free survival was significantly lower among patients with high NLR (n=143, 55.6%) at baseline; 17.8 vs. 22.9 months, P=

0.028. A similar trend for lower PFS was also noted for high NLR measured prior to the third (20.6 vs. 18.6 months) and the fourth cycles (21.6 vs. 18.2 months), however both were not statistically significant; $P=0.154$ and 0.09 , respectively. Multivariate analysis confirmed an independent association between high NLR and lower PFS (adjusted HR 1.46, 95% CI 1.03-2.06, $P=0.032$). Visceral metastasis (aHR 1.57, 95% CI 1.11-2.23, $P=0.012$) and receiving ribociclib beyond the first line (aHR 1.96, 95% CI 1.38-2.77, $P<0.001$), were also independent factors predicting inferior PFS. Conclusions: To the best of our knowledge this is the largest study to show a significant association between high NLR at baseline and lower PFS in patients with HR+ advanced-stage breast cancer treated with ribociclib and ET. If confirmed, NLR at base line may provide reliable, accessible, and widely available prognostic marker that can be used easily in routine clinical practice.

Disclosure(s):

Baha' sharaf, MD: No financial relationships to disclose

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Faris Tamimi, MD: No financial relationships to disclose

Hala Abu-Fares, MD: No financial relationships to disclose

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Hikmat Abdel-Razeq, MD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-03-04

Long-Term Benefit from Adjuvant Tamoxifen in Luminal A and Luminal B Breast Cancer Patients

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Background:

The risk for patients with estrogen receptor (ER)-positive breast cancer remains stable decades after primary diagnosis, with a large proportion of distant metastatic events occurring late. Thus, long-term follow-up studies are essential to understand true treatment benefit. Tamoxifen (TAM) therapy is a fundamental endocrine treatment for ER-positive breast cancer. We have

previously shown a long-term tamoxifen therapy benefit for patients with less aggressive tumor characteristics in ER-positive/HER2-negative patients. However, ER-positive breast cancer is highly heterogeneous and can be separated into different molecular subpopulations that behave differently during extended follow-up. The long-term tamoxifen benefit by molecular subtype is largely unexplored. We therefore aimed to investigate the long-term benefit from tamoxifen by clinically used tumor characteristics in Luminal A vs Luminal B patients in the Stockholm tamoxifen (STO)-trials with complete 20-years follow-up.

Methods:

Secondary analysis of ER-positive/HER2-negative patients with Luminal A or B molecular subtype (n=952) from the STO-trials (1976-1997) randomized to TAM (40 mg) vs no endocrine therapy (control). Gene expression data was generated using custom designed Agilent arrays from FFPE breast cancer tumor tissue and was used to define PAM50 molecular subtypes. The clinically used markers were reannotated in 2014 and 2020. Complete 20-year follow-up was obtained from Swedish high-quality registries. The long-term distant recurrence-free interval (DRFI) was assessed by Kaplan-Meier, multivariable Cox proportional hazard regression and time-varying analysis, using flexible parametric modelling.

Results:

Multivariable analysis showed significantly improved long-term DRFI from TAM vs control for both Luminal A (HR=0.59; 95% CI, 0.44-0.81) and Luminal B (HR=0.67; 95% CI, 0.46-0.99) patients. Time-varying analysis showed that patients with Luminal A subtype significantly benefitted from TAM for 15 years (HR=0.60, 95% CI, 0.39-0.94 at year 15), whereas patients with Luminal B subtype had a significant TAM benefit for 5 years (HR=0.64, 95% CI, 0.42-0.98 at year 5), see Table.

Furthermore, a significant long-term TAM benefit for patients with large tumor size (pT>20mm: HR=0.46; 95% CI, 0.25-0.84), tumor grade 1-2 (HR=0.55; 95% CI, 0.40-0.77), lymph node-negative (HR=0.51, 95% CI, 0.34-0.78), PR-positive (HR=0.57, 95% CI, 0.40-0.81) and Ki-67-low tumors (HR=0.55, 95% CI, 0.39-0.77) was seen for Luminal A patients.

In Luminal B patients, significantly improved long-term DRFI from TAM vs control was seen for small tumor size (pT≤20mm: HR=0.44; 95% CI, 0.24-0.80), tumor grade 1-2 (HR=0.51; 95% CI, 0.29-0.90), lymph node-negative (HR=0.40, 95% CI, 0.19-0.83), PR-positive (HR=0.59, 95% CI, 0.38-0.93) and Ki-67-low tumors (HR=0.45, 95% CI, 0.25-0.84).

Conclusions:

This study suggests a 15 years tamoxifen benefit for patients with Luminal A subtype tumors, whereas the benefit for patients with Luminal B tumors is up to five years after diagnosis. Furthermore, our study suggests a long-term tamoxifen benefit for patients with less aggressive tumor characteristics regardless of tumor subtype, except for tumor size in Luminal A patients. ER-positive breast cancer is a heterogeneous disease and long-term follow-up studies in molecular subtypes are essential to understand differences in treatment benefit.

Table. Time-varying analysis of long-term tamoxifen therapy benefit by PAM50 molecular subtype.

ER-positive/HER2-negative patients		Years since randomization	Risk of distant recurrence HR (95% CI)
Luminal A (n=651)	Tamoxifen vs. Control	5	0.55 (0.40-0.77)*
		10	0.58 (0.41-0.83)*
		15	0.60 (0.39-0.94)*
		20	0.62 (0.37-1.03)
Luminal B (n=254)	Tamoxifen vs. Control	5	0.64 (0.42-0.98)*
		10	0.60 (0.33-1.07)
		15	0.57 (0.29-1.15)
		20	0.56 (0.26-1.20)

Time-varying analysis of distant recurrence-free interval (DRFI) to assess how tamoxifen benefit varied over the 20 year of follow-up using flexible parametric survival modelling. Patients included in analyses with no missing values. Estimated hazard ratios (HR) at year 5, 10, 15 and 20 for patients with Luminal A or Luminal B molecular subtype tumors randomized to tamoxifen therapy, as compared with patients randomized to no endocrine therapy (control). Adjusted for age, period of primary breast cancer diagnosis, tumor size, tumor grade, lymph node status, PR status, Ki-67 status, chemotherapy, radiotherapy, type of surgery, and menopausal status. *indicates significant findings P<0.05

Disclosure(s):

Huma Dar, MSc: No financial relationships to disclose

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P2-03-05

HOXB13/IL17RB-low breast cancers are predicted to respond to PIK3CA inhibitors independent of PIK3CA mutational status

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Background: The Breast Cancer Index is a gene expression-based signature comprising two functional biomarker panels, the Molecular Grade Index (MGI) and the two-gene ratio, HOXB13/IL17BR (H/I). MGI measures tumor proliferation, while H/I measures estrogen signaling. Integration of MGI and H/I provides a single score that quantifies the risk distant recurrence, while H/I alone predicts benefit from extended endocrine therapy (EET). In multiple EET trials, we have shown that hormone receptor-positive (HR+) breast cancer (BC) patients with H/I-high biomarker expression benefit from EET, while those with H/I-low expression do not benefit from such therapy. Previous protein-protein interaction (PPI) dysregulation (dysreg) analysis of H/I-low BC tumors with drug-response-associated dysreg in BC cell lines revealed a significant correlation with response to two PIK3CA inhibitors, suggesting that PIK3CA pathway may represent an exploitable therapeutic vulnerability for H/I-low BC patients. However, given that PIK3CA is frequently mutated in ER+ tumors, the PPI dysreg analysis may merely reflect enrichment of PIK3CA genomic alterations within the H/I-Low BCs. Thus, to determine if a genetic abnormality within the H/I-low BCs accounts for the correlation with PIK3CA inhibitor drug response in BC cell lines, we performed targeted DNA sequencing of H/I-high and H/I-low BC tumors. Methods: DNA was extracted from 44 H/I-high and 30-H/I-low BC samples using a Qiaqen DNeasy Blood & Tissue Kit. Samples were then prepared using the Archer VariantPlex kits according to a modified protocol and sequenced in batches on the Illumina NextSeq platform. To determine if a genetic abnormality within H/I-low BCs accounts for the PPI dysreg correlation with PIK3CA drug response, the magnitude of the sample's drug associated PPI dysregs was compared to its mutational status. Geneset enrichment (GSEA) functional profiles between BC tissue PPI dysregs and BC cell line drug response-associated PPI dysregs, identified two PIK3CA inhibitors as potential therapeutic drugs for H/I-low tumors. For each

PIK3CA drug, the set of leading-edge genes associated with the genesets important to the observed correlation were isolated. Z-score transformed PPI dysreg count data across the BC samples was used to calculate the average dysreg scores for each sample based on the drug-associated leading-edge genes. The samples were sorted based on scores associated with each drug and GSEA was run on each ranked list looking for an association between the dysreg magnitude and PIK3CA mutation status. Results: Targeted DNA sequencing identified copy number variants for in H/I-high and low tumors, the most common of which are: ERBB2 (3/44 H/I-high; 1/30 H/I-low; p: 0.642), FGF19 (3/44 H/I-high; 1/30; p: 0.642), CCND1 (3/44 H/I-high; 1/30 H/I-low; p: 0.642). Sequencing identified a similar distribution of single nucleotide variants (SNVs) between the H/I-high and H/I-low groups. The most common SNVs identified in order of prevalence are PIK3CA (18/44, H/I-high; 6/30, H/I-low; p: 0.078), TP53 (12/44 H/I-high; 6/30 H/I-low; p: 0.585), CDH1 (4/44 H/I-high; 5/30 H/I-low; p: 0.471), BRCA2 (4/44 H/I-high; 2/30 H/I-low; p: 1). No significant difference in mutational prevalence was identified between the H/I-high and H/I-low BCs. No-significant associations between the PPI dysreg magnitude of the drug-associated leading-edge genes and PIK3CA mutational status was observed (AZD6482 FDR=0.736 and A66 FDR=0.95). Conclusion: No significant genetic alteration, including PIK3CA mutational status, was identified between H/I-high and H/I-low groups. Thus, protein-protein interaction (PPI) dysregulation analysis identifies H/I-low BC tumors as those that are predicted to response to PIK3CA inhibitors independent of PIK3CA mutational status.

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Anthony John lafrate, MD, PhD: Invitae: Receipt of Intellectual Property Rights / Patent Holder (Ongoing); Kinnate Biopharma: Consulting Fees (e.g., advisory boards) (Ongoing); Repare Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing)

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7:00 AM - 8:15 AM

P2-03-06

Real world treatment of node negative low and intermediate recurrence score breast cancer

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Introduction: Patients younger than 50 years old with node negative hormone receptor (HR) positive her2 negative breast cancer and oncotype Dx recurrence scores (RS) under 16 do not benefit from adjuvant chemotherapy. Those with a RS between 16-25 may have a marginal benefit from the addition of adjuvant chemotherapy, however a similar benefit may be achieved with adjuvant ovarian function suppression (OFS). The aim of this study is to describe real world treatment patterns and outcomes of premenopausal node negative patients with low and intermediate RS, with an emphasis on adjuvant OFS, endocrine therapy (ET), and menopausal status during adjuvant treatment. Methods: We retrospectively reviewed the records of all node negative patients under 50 years old who were sent for oncotype testing between 2008 and 2018. One hundred and sixty-five patients with low or intermediate RS were included in our analysis. Continuous variables were described using medians and interquartile range (IQR). Categorical variables were described as frequencies and percentages. Differences between categorical variables were analyzed with the chi squared test and survival was analyzed using the Kaplan-Meier method. The cox proportional hazards model was used to test the effect of multiple factors on survival. Breast cancer specific survival (bcss) was defined as the time to first breast cancer recurrence (local recurrence, second breast cancer, distant recurrence) and distant disease-free survival (ddfs) was defined as the time to any distant recurrence. Results: The median age was 44 (41-47) and median RS was 17 (14-20). Median follow-up time was 82 (61-108) months. One hundred and three (62.4%) patients had low clinical risk as defined in TailorX and 136 (82.4%) had intermediate RS. Fourteen (8.5%) patients with nodal micrometastases were also included. Only 5 (3%) patients received adjuvant chemotherapy and 74 (44.8%) received adjuvant OFS. Of the 91 (55%) of patients who did not receive OFS, 21 (23%) went into menopause or underwent subsequent oophorectomy while on adjuvant ET. One hundred and three (62.4%) patients received adjuvant tamoxifen alone, 16 (9.7%) received an aromatase inhibitor alone, and 40 (24.2%) underwent an endocrine switch with all but 1 beginning treatment with tamoxifen. There were no significant differences in clinical risk or RS risk group between patients that received and did not receive OFS. There were 22 (13.3%) bcss recurrences. Twelve (7.2%) patients had a local recurrence, 5 (3%) patients had second breast cancers, and 5 (3%) had a distant recurrence as their first recurrence. Overall, only 6 (3.6%) patients had a distant recurrence. Both OFS and ET type were not significantly associated with bcss or ddfs. On univariate analysis menopause during ET was significantly associated with improved bcss (HR= 0.2, 95% CI 0.05-0.85), however on multivariate analysis it was no longer significant. Conclusion: With only 6 (3.6%) distant recurrences over a median follow-up of over 6.5 years node negative premenopausal women with low or intermediate RS treated in our institution show an excellent prognosis regardless of treatment type. Our results support the evidence that most of these patients do not need chemotherapy and suggests that

most patients do not require OFS as well. Additional data examining the relationship between gene expression profiles and OFS benefit are needed to help guide OFS treatment in premenopausal patients who do not require chemotherapy.

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Multi-parametric algorithm integrating on-treatment Ki67 value and standard clinicopathological variables to predict risk of recurrences for women > 70 years old with early ER+HER2- tumours in POETIC trial

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Background: Prognosis in older patients with breast cancer (BC) is worse compared to younger patients. No robust and specific tool to predict the risk of recurrence (TTR) for women aged 70 and over is likely due to the lack of representation of this group in the data from clinical trials. In the POETIC trial, of estrogen receptor-positive (ER+) and mainly human epidermal growth factor receptor 2 negative (HER2-) BC (88%), peri-operative aromatase inhibitor (POAI) did not improve treatment outcome, but patients with low baseline Ki67 value (Ki67B) or low POAI-induced Ki67 value (Ki67_2wk) had good outcome with standard of care therapy (usually adjuvant endocrine therapy (adjET) with the addition of chemotherapy as clinically indicated). In this study, we sought to develop a multi-parametric algorithm, named Ki67Cal, by integrating Ki67_2wk value with tumour characteristics to predict TTR for patients > 70 years old (yr) with early ER+HER2- BC treated with adjET only.

Methods: Within POETIC, 39% (n=1744) of the randomised patients (n = 4480) were >70 years old. There were 813 patients aged > 70yr, with ER+HER2- BC, randomised to POAI treatment and treated with adjET only. A power calculation indicated that 811 such patients were sufficient to develop a prediction model that minimized overfitting, allowed up to 8 predictors, for predicting 5-years TTR with a median follow-up of 5.24 years and an overall event rate per 1000 person-years = 0.027, and provided an anticipated performance in terms of model fit $R^2 = 0.08$ (Riley et al. *BMJ* 2020). A three-fold cross-validation approach was applied; an optimal list of features was selected in the training set (n = 538, events = 70); the agreement between expected and observed outcomes from the algorithm on the validation set (n = 275, events = 37) was evaluated by calibration plot. Multivariable Ridge Cox Regression model of significant parameters was built on the dataset merging training and validation datasets (n = 813) for precise estimates of the coefficients of parameters. A subset of post-POAI samples (n = 99) was gene expression profiled with Nanostring to allow pseudo-Oncotype, pseudo-EndoPredict, and RUO-Prosigna scores calculated (Buus et al. *npj Breast cancer* 2021). The risk groups classified by the Ki67Cal and gene-expression assays (GEP) were compared.

Results:

Within this cohort, the 5-year TTR was 34.5% (C.I. 24.9-47.9) for those with a high Ki67_2wk ($\geq 10\%$) and 12.3% (C.I. 9.1-16.7) in those with a high Ki67B that was suppressed to Ki67_2wk < 10%. The significant features were Ki67_2wk, sampling type (core vs. excision) at surgery, and pathological variables (tumour size, grade, and nodal status) for the final Ki67Cal algorithm. Stratifying patients into five groups (quintiles) by Ki67Cal identified 60% of patients with TTR of < 5% at 5yrs, and 20% of patients with TTR of > 30% at 5yrs.

As an exploratory analysis, the risk groups by Ki67Cal and GEP were compared (Table 1). To

date, these assays are optimized to be used on untreated ER+HER2- samples; there were fairly good agreements between the high-risk group defined by Ki67Cal with pseudo-EndoPredict and RUO-Prosigna respectively, and low-risk groups by Ki67Cal with Prosigna probably because Prosigna scores are driven by proliferation score.

Conclusion:

The relatively poor outcome of patients >70yrs in POETIC emphasizes the need for prognostic tools that identify patients who may be treated with endocrine therapy alone or conversely should be considered for additional therapy. Ki67Cal provides a simple tool that identified very low-risk and high-risk patients in 80% of patients with ER+HER2- BC.

Table 1: Comparison of the risk groups defined by Ki67Cal algorithm with the three commonly used gene-expression assays (pseudo-EndoPredict, pseudo-Oncotype and RUO-Prosigna) applied on the post-peri-operative aromatase inhibitor samples.

	Risk Groups as defined by Ki67Cal algorithm									
	High risk		High-Moderate		Moderate		Moderate-Low		Low	
	N	%	N	%	N	%	N	%	N	%
	42	100	21	100	14	100	12	100	10	100
Pseudo-EndoPredict										
High	38	90.5	18	85.7	10	71.4	8	66.7	7	70
Low	4	9.5	3	14.3	4	28.6	4	33.3	3	30
Pseudo-Oncotype: Low: < 18; Intermediate: >= 18 & <= 31; High : > 31										
High	13	31	4	19	3	21.4	0	0	1	10
Intermediate	21	50	10	47.6	5	35.7	5	41.7	3	30
Low	8	19	7	33.3	6	42.9	7	58.3	6	60
RUO-Prosigna										
High	34	81	5	23.8	0	0	0	0	0	0
Intermediate	8	19	14	66.7	8	57.1	4	33.3	1	10
Low	0	0	2	9.5	6	42.9	8	66.7	9	90

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Maggie Chon U Cheang, PhD: AstraZeneca: Contracted Research (Ongoing); Eli Lilly: Contracted Research (Ongoing); Veracyte: Consulting Fees (e.g., advisory boards) (Ongoing), Royalty (Ongoing)

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7:00 AM - 8:15 AM

P2-03-08

Deconstructing the molecular characteristics of ER+ HER2+ early breast cancer in the POETIC trial using multiplex immunofluorescence and gene expression profiles

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Background

POETIC was a phase III clinical trial, with patients randomised 2:1 to 2-week perioperative aromatase inhibitor (POAI) vs control for postmenopausal women with oestrogen receptor positive (ER+) early breast cancer (BC) (Smith et al., *Lancet Oncology* 2020). Our previous study on POETIC trial patients with ER+ human epidermal growth factor receptor 2 positive (HER2+) BC suggested both HER2 enriched subtype (HER2-E) and immune enrichment pre-POAI (baseline, B) are main drivers of poor early response to POAI (Bergamino et al., 2022). However, some patients with HER2-E or immune enriched BC at B still showed good response to POAI. In this study, we aim to further investigate a sub-cohort of ER+ HER2+ BC from the POETIC trial, including a subset of aforementioned HER2-E tumours, to further explore the multi-modal molecular characteristics of the tumours resistant to POAI.

Methods

Proliferation rate was assessed as percentage of cancer cells stained by Ki67. Patient POAI response was determined by Ki67 reduction at 2 weeks of treatment. A sub-cohort of 37 patients were selected based on response and classified as poor responders (PR, reduction < 30%, n=18), good responders (GR, reduction > 90%, n=11) and good responders with HER2-E BC at B (GR, reduction > 65%, n=8). Paired B and post-POAI (surgery, S) samples were taken from each patient of the sub-cohort. Multiplex immunofluorescence (mIF) was performed on these samples, measuring the immune cell densities in stroma and tumour compartments using five biomarkers: CD3 (all T cells), CD20 (B cells), CD68 (Macrophages), FOXP3 (regulatory T cells), and CD3 FOXP3 co-expression. The samples were also profiled using Breast Cancer 360TM (NanoString, BC360), covering the expressions of 758 genes and 46 biological signatures. Wilcoxon test, hierarchical clustering and spearman correlation test were performed to compare the tumour characteristics of GR and PR.

Results

In this study, two B and four S samples were not achievable for mIF experiments due to low tumour content. At B (n = 35), among the five mIF biomarker measurements in stroma and tumour, only the stromal CD3 density was significantly different between GR (median = 0.0013) and PR (median = 0.0003, p = 0.041). In GR, HER2-E BC at B were separated into immune-high and immune-low groups with mIF biomarkers at B; the immune-high group was more likely to change into luminal subtypes post-POAI, while the immune-low group remained HER2-E. After POAI, the density changes in five mIF biomarkers in stroma and CD68 in tumour were all significantly higher in PR than GR (Table 1, n of paired samples = 62). The BC360 signatures of BC p53 (p < 0.001), BC proliferation (p < 0.001), LumB (p < 0.001) and HER2-E correlation coefficients (p < 0.001) were significantly downregulated in GR after POAI, while LumA correlation coefficients (p < 0.001) were notably increased.

Conclusions

Our results suggest that for this sub-cohort, increased stromal immune response is associated with poor response to 2-week POAI in ER+ HER2+ early BC. HER2-E GR display visible immune heterogeneity at B. Lower-risk BC characteristics were exhibited in GR after the 2-week treatment. Further integrating mIF imaging data and additional digital spatial profiling are ongoing to reveal additional characteristics of ER+ HER2+ BC and tumour microenvironment predicting POAI resistance.

Table 1

		Medians of 2-week density changes in mIF biomarkers (log2)		Wilcoxon Tests
		GR(n=15)	PR(n=16)	P-value
Stroma	CD3	-0.2343	1.1174	0.014 *
	CD20	0.4860	2.4950	0.0096 **
	CD68	-0.1948	2.0509	0.033 *
	FOXP3	-2.0699	0.2008	0.0072 **
	CD3 FOXP3	-1.5506	0.5818	0.0093 **
Tumour	CD3	-0.4499	0.2201	0.26
	CD20	1.4441	0.5708	0.95
	CD68	-0.3396	0.7716	0.0027 **
	FOXP3	-1.7718	-0.5633	0.11
	CD3 FOXP3	-1.4749	0.0198	0.15

List of medians of log2 fold changes in mIF biomarker densities between GR and PR among the 62 paired samples, and Wilcoxon test p-values.

Disclosure(s):

Xixuan Zhu, MRes: No financial relationships to disclose

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P2-03-10

DNA replication licensing is associated with resistance to CDK4/6 inhibitors in ER-positive breast cancer

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Background: The use of CDK4/6 inhibitors (CDK4/6i) has led to a remarkable progress in the treatment of advanced ER-positive (+) breast cancer (BC). The fact that both CDK4/6i and endocrine therapy (ET) target cell-cycle G1-S transition suggests some overlap of resistance mechanisms. However, clinical variability in response to CDK4/6i in patients progressing on ET suggests the involvement of additional or unique resistance mechanisms. Using bioinformatics analyses of clinical and preclinical data, we now identified genes involved in DNA replication licensing, in particular, excess MCM2 as a new mechanism of resistance to CDK4/6i. Methods: Gene expression data from the neoadjuvant NeoPalAna trial of the CDK4/6i palbociclib (Palbo) and the aromatase inhibitor (AI) anastrozole in ER+ BC was downloaded from Gene Expression Omnibus (GSE93204). Response to AI and Palbo was obtained using the published Ki67 immunohistochemistry data and cutoff on biopsies post treatment. Gene Set Enrichment Analysis comparing tumors with different sensitivity to AI vs. Palbo was performed using the Gene Ontology related to DNA replication, DNA repair, and DNA damage checkpoint. The DNA replication gene set was further sub-assigned by their selective role in origin licensing, firing, elongation, replication repair, and checkpoint regulation. A series of bioinformatics analyses was applied on five ER+/HER2-negative BC cell lines with gene expression and DepMap (from CCLE) and Palbo sensitivity data (from GDSC). Two ER+ BC cell models (MCF7 and T47D) and their estrogen deprivation (mimicking AIs)-resistant (EDR) derivatives were used for further

studies including RNA-seq, Palbo sensitivity (data from PMID: 33536276), and chromatin fractionation assays. Results: We found that the DNA replication-associated gene set, comprising > 80% genes outside the Rb-loss gene signature, was significantly enriched in baseline biopsies of Palbo-resistant (PalboR) tumors from patients in the NeoPalAna trial. Of the DNA replication genes, the subset of genes involved in origin licensing were preferentially enriched in PalboR vs. AI-resistant tumors. Similarly, the enrichment of genes involved in replication initiation was also seen in ER+/HER2-negative BC cell lines with a decreased response to Palbo. Notably, these PalboR cell lines showed a reduced vitality to shRNA knockdown of the replication initiation genes compared to randomly selected other genes or the Rb-loss gene set. Based on the modeling of DepMap gene dependency score and Palbo sensitivity, we nominated minichromosome maintenance 2 (MCM2), the key origin licensing factor, as the top gene that is essential for PalboR cell survival. Additionally, using our previously reported MCF7-EDR and T47D-EDR cell models with increased or decreased sensitivity to Palbo compared to their parental lines, respectively, we observed a corresponding decrease or increase in the expression of origin licensing genes and MCM2 in EDR vs. parental lines. Decreased Palbo sensitivity in the EDR cells was associated with sustained MCM2 chromatin loading and reduced expression of genes including the cyclin-dependent kinase inhibitor p21. Ongoing studies investigate whether elevated MCM2 levels confer resistance to CDK4/6i by resolving replication stress. Conclusions: Our strategic bioinformatics analyses reveal that excess DNA replication licensing is associated with CDK4/6i resistance in clinical and preclinical settings upon resistance to estrogen deprivation. Among the replication initiation-associated genes, MCM2 plays a potential role in conferring CDK4/6i resistance via sustaining origin licensing and suppressing p21. Our study provides a new avenue via lens of replication licensing to explore novel mechanisms and therapeutic opportunities in CDK4/6i resistance.

Disclosure(s):

Sarmistha Nanda, MS: No financial relationships to disclose

Martin J. Shea, Ph.D.: No financial relationships to disclose

Rachel Schiff, PhD: MacroGenics: Advisory Committee (Ongoing); Patent (filed and owned by Baylor College of Medicine): Pending patent application # PCT/US21/70543 (Ongoing); Puma Biotechnology: Contracted Research (Ongoing); Wolters Kluwer/UpToDate: Royalty (Ongoing)

C. Kent Osborne, MD: Gene Tex: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

Mothaffar Rimawi, MD: Daiichi Sankyo: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); F. Hoffmann-La Roche Ltd.: Contracted Research (Ongoing), Third-party writing assistance for this abstract, furnished by Sunaina Indermun, BPharm, PhD, of Health Interactions, was provided by Roche (Ongoing); Genentech: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); MacroGenics: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer: Contracted Research (Ongoing); Seattle Genetics: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

Xiaoyong Fu, MD., PhD: No financial relationships to disclose

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P2-03-11

Differential Long-Term Benefit from Adjuvant Tamoxifen Therapy in Estrogen Receptor (ER)-Positive/Human Epidermal Growth Factor Receptor 2 (HER2)-Negative Premenopausal and Postmenopausal Breast Cancer Patients

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Background: Tamoxifen is a standard endocrine therapy for both pre- and postmenopausal ER-positive breast cancer patients. Patients with ER-positive disease have a long-term risk of distant recurrence, thus, long-term follow-up studies are essential to understand true treatment benefit. Clinically used tumor characteristics are prognostic 5-10 years after primary diagnosis, however, whether these characteristics are predictive of long-term tamoxifen benefit is largely unexplored. Therefore, we aimed to determine the long-term tamoxifen therapy benefit by the clinically used tumor characteristics in pre- vs postmenopausal patients in the Stockholm tamoxifen (STO)-trials with 20-years complete follow-up.

Methods: Secondary analysis of 1242 ER-positive/HER2-negative patients from the STO-trials, randomized to at least 2 years of 40 mg tamoxifen vs no endocrine therapy (control). Premenopausal lymph node-positive patients were allocated to chemotherapy as standard of care and postmenopausal high-risk patients were further randomized to chemotherapy vs radiotherapy. Tumor immunohistochemical analysis was recently conducted. Complete 20-year follow-up was obtained from Swedish high-quality registries. Long-term distant recurrence-free interval (DRFI) was assessed by multivariable Cox proportional hazard regression and time-varying analysis using flexible parametric modelling.

Results: Premenopausal patients showed significantly improved long-term DRFI from tamoxifen vs control if they were lymph node-negative (Hazard Ratio [HR]=0.46; 95% CI, 0.24-0.87), PR-positive (HR=0.61; 95% CI, 0.41-0.91), or of genomic low risk (HR=0.47; 95% CI, 0.26-0.85), see Table.

In postmenopausal patients, significantly improved long-term DRFI from tamoxifen vs control was seen for all good prognosis tumor characteristics, i.e. small tumor size ($pT \leq 20$ mm: HR=0.55; 95% CI, 0.39-0.77), tumor grade 1-2 (HR=0.55; 95% CI, 0.41-0.73), lymph node-negative (HR=0.44; 95% CI, 0.30-0.64), PR-positive (HR=0.60; 95% CI, 0.44-0.80), Ki-67-low ($< 15\%$: HR=0.51; 95% CI, 0.38-0.68), and genomic low risk (HR=0.53; 95% CI, 0.37-0.74), see Table. Also, postmenopausal patients with large tumor size ($pT > 20$ mm: HR=0.64; 95% CI, 0.44-0.94) and PR-negative tumors (HR=0.51; 95% CI, 0.32-0.81) showed significant long-term tamoxifen benefit.

Time-varying analysis in premenopausal patients indicated that tamoxifen therapy benefit diminished over time. Significant tamoxifen benefit until year 5, 10, and 15 after primary diagnosis was observed for PR-positive, lymph node-negative, and genomic low-risk patients, respectively. Postmenopausal patients had a significant long-term tamoxifen benefit if they had tumors of small or large tumor size, tumor grade 1-2, lymph node-negative status, PR-positive status, low Ki-67 levels, or genomic low risk.

Conclusions: This study suggests a differential long-term tamoxifen therapy benefit in pre- vs postmenopausal patients. Clinically defined low-risk postmenopausal patients have long-term tamoxifen benefit, whereas the benefit is absent or diminish over time for premenopausal patients. Improved long-term prognostic and endocrine therapy predictive markers in premenopausal breast cancer patients with poor prognosis and long life-expectancy is needed, which could involve molecular tools.

Long-term tamoxifen benefit in premenopausal and postmenopausal breast cancer patients by the clinically used tumor characteristics.

Clinically used tumor characteristics		Trial arm	Premenopausal patients (n=381)	Postmenopausal patients (n=861)
			HR (95% CI)	HR (95% CI)
Tumor size	pT ≤ 20 mm	Tamoxifen	0.74 (0.46-1.18)	0.55 (0.39-0.77)
		Control	1.00 (Ref)	1.00 (Ref)
	pT>20 mm	Tamoxifen	0.84 (0.46-1.52)	0.64 (0.44-0.94)
		Control	1.00 (Ref)	1.00 (Ref)
Tumor grade	1-2	Tamoxifen	0.73 (0.46-1.14)	0.55 (0.41-0.73)
		Control	1.00 (Ref)	1.00 (Ref)
	3	Tamoxifen	0.94 (0.45-1.93)	0.95 (0.56-1.61)
		Control	1.00 (Ref)	1.00 (Ref)
Lymph node status	Negative	Tamoxifen	0.46 (0.24-0.87)	0.44 (0.30-0.64)
		Control	1.00 (Ref)	1.00 (Ref)
	Positive	Tamoxifen	0.96 (0.60-1.53)	0.73 (0.52-1.03)
		Control	1.00 (Ref)	1.00 (Ref)
PR status	Positive	Tamoxifen	0.61 (0.41-0.91)	0.60 (0.44-0.80)
		Control	1.00 (Ref)	1.00 (Ref)
	Negative	Tamoxifen	1.83 (0.36-9.22)	0.51 (0.32-0.81)
		Control	1.00 (Ref)	1.00 (Ref)
Ki-67	Low (<15%)	Tamoxifen	0.78 (0.49-1.24)	0.51 (0.38-0.68)
		Control	1.00 (Ref)	1.00 (Ref)
	Medium/high (≥15%)	Tamoxifen	0.68 (0.36-1.30)	0.75 (0.46-1.24)
		Control	1.00 (Ref)	1.00 (Ref)
Genomic risk	Low	Tamoxifen	0.47 (0.26-0.85)	0.53 (0.37-0.74)
		Control	1.00 (Ref)	1.00 (Ref)
	High	Tamoxifen	0.81 (0.41-1.58)	0.72 (0.47-1.10)
		Control	1.00 (Ref)	1.00 (Ref)

Multivariable Cox proportional hazard regression analysis of 20-year distant recurrence-free interval (DRFI) for patients with ER-positive/HER2-negative tumors, comparing patients randomized to tamoxifen vs patients randomized to no endocrine therapy (control). Adjusted for age, randomization year, tumor size, tumor grade, lymph node status, PR status, Ki-67 status, chemotherapy, radiotherapy, and type of surgery.

Disclosure(s):

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7:00 AM - 8:15 AM

P2-03-12

Impact of adjuvant endocrine therapy (ET) omission in ER+ breast cancer (BC) treated with neoadjuvant chemotherapy (NAC)

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Background: Adjuvant endocrine therapy (ET) in ER+ breast cancer (BC) reduces local, distant, and contralateral BC events and improves overall survival (OS). Furthermore, decreased adherence or omission of ET increases the risk of death. However, in ER+ pts with early-stage BC treated with NAC who have a pathologic complete response (pCR), the importance of adjuvant ET may be called into question. We sought to examine the impact of ET omission on the survival of pts with ER+ BC treated with NAC, according to pCR vs residual disease.

Methods: We queried the National Cancer Database (NCDB) 2010-2018 for female pts with stage I-III ER+ BC treated with NAC followed by surgery. pCR was defined as ypT0/ypTis, ypN0. The percent receiving adjuvant ET and the impact of adjuvant ET omission on overall survival (OS) in patients with and without pCR were assessed separately based on HER2 expression. OS was analyzed with adjuvant ET as a time-dependent covariate using Cox proportional hazards regression.

Results: We identified 34,394 pts treated with NAC for ER+ BC (28,434 ER+/HER2-, 5960 ER+/HER2+). Pts with ER+/HER2+ BC were less likely than pts with ER+/HER2- BC to have received adjuvant ET (61.6% vs 88.8%, $p < 0.001$). Overall, 4505 (13.1%) had pCR (9.1% of ER+/HER2- and 32.0% of ER+/HER2+). Within each subtype, pts with pCR were significantly less likely to start adjuvant ET after surgery than pts with residual disease (78.4% vs 89.8% for ER+/HER2- and 46.5% vs 68.7% for ER+/HER2+, each $p < 0.001$), Table 1. Regarding those with residual disease, pts with ER+/HER2+ BC were less likely than ER+/HER2- BC to receive adjuvant ET (68.7% vs 89.8%, $p < 0.001$). Median follow-up was 4.4 years. Among pts with

pCR, 5-year OS was 93.2% (95% CI: 92.1-94.4%) for ER+/HER2- BC and 94.3% (95% CI: 93.1-95.5%) for ER+/HER2+ BC (p=0.08), while among patients with residual disease 5-year OS was 81.7% (95% CI: 81.1-82.2%) and 85.7% (95% CI: 84.5-86.9%) for the two subtypes respectively (p< 0.001). On multivariable analysis, omission of adjuvant ET was significantly associated with poorer OS in patients with residual disease for both ER+/HER2- BC (adjusted HR 1.72, p< 0.001) and ER+/HER2+ BC (adjusted HR 1.63, p< 0.001). In contrast, omission of adjuvant ET was not significantly associated with OS in patients with pCR, regardless of HER2 status (ER+/HER2- adjusted HR 1.28, p=0.20; ER+/HER2+ adjusted HR 1.13, p=0.54), Table 1.

Conclusions: In pts receiving NAC for ER+ BC, those with ER+/HER2+ disease were less likely to have received adjuvant ET compared to ER+/HER2- patients, regardless of pCR. In pts with residual disease after NAC, omission of adjuvant ET was associated with significantly higher risk of death. These data provide strong support for interventions to increase utilization of ET, especially for patients with residual disease following NAC. The observation that ET omission did not impact OS in pts with ER+ BC who achieve pCR following NAC is hypothesis generating and may have implications for future de-escalation trials for this subset of patients.

Table 1. Differential use of adjuvant endocrine therapy by subtype and pCR and the impact on overall survival

			2-year OS (95% CI)	5-year OS (95% CI)	8-year OS (95% CI)	Overall Survival Hazard Ratio (95% CI) for no adjuvant endocrine therapy (No Adj ET) vs Adj ET	
						Unadjusted	Adjusted*
ER+/HER2- (n=28,434)	pCR n=2599 (9.1%)	Adj ET n=2037 (78.4%)	97% (96-98%)	94% (92-95%)	90% (88-92%)	1.20 (0.83-1.72) p=0.33	1.28 (0.88-1.87) p=0.20
		No Adj ET n=562 (21.6%)	97% (96-98%)	92% (90-95%)	88% (83-93%)		
	Residual disease n=25,835 (90.9%)	Adj ET n=23,211 (89.8%)	95% (95-95%)	83% (82-84%)	73% (72-74%)	1.87 (1.73-2.03) p<0.001	1.72 (1.58-1.87) p<0.001
		No Adj ET n=2624 (10.2%)	86% (84-87%)	72% (70-74%)	64% (61-67%)		
ER+/HER2+ (n=5960)	pCR n=1906 (32.0%)	Adj ET n=886 (46.5%)	99% (98-100%)	95% (94-97%)	91% (89-93%)	1.19 (0.81-1.74) p=0.38	1.13 (0.77-1.66) p=0.54
		No Adj ET n=1020 (53.5%)	98% (97-99%)	94% (92-96%)	90% (87-94%)		
	Residual disease n=4054 (68.0%)	Adj ET n=2784 (68.7%)	97% (97-98%)	88% (86-89%)	79% (77-81%)	1.61 (1.35-1.91) p<0.001	1.63 (1.37-1.94) p<0.001
		No Adj ET n=1270 (31.3%)	93% (91-94%)	81% (78-84%)	72% (68-76%)		

Adj ET – adjuvant endocrine therapy
*Adjusted for age, comorbidity score, PR status, cT category, cN status, grade, and, in those without pCR, the extent of residual disease (ypT category and ypN category).

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

P2-03-13

Breast Cancer Index (BCI) identifies fewer patients with high risk of late recurrence and high likelihood of benefit from extended endocrine therapy with invasive lobular compared to invasive ductal carcinoma

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Background: Invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC) are the first and second most common histologic subtypes of breast cancer. Both IDC and ILC present distinguishing clinicopathologic features that contribute to differences in response to treatment and long-term prognosis. BCI is a validated gene expression assay that provides the risk of overall (0-10y) and late (5-10y) distant recurrence (DR) and predicts the likelihood of benefit from extended endocrine therapy (EET). In this analysis, BCI results between groups of HR+ ILC and IDC breast cancer patients were compared. Methods: The BCI Clinical Database for Correlative Studies is an IRB-approved de-identified database containing >50 clinicopathologic and molecular variables from cases submitted for BCI testing in clinical practice (N=19,126). Molecular variables include BCI Prognostic score, HOXB13/IL17BR ratio (H/I), and molecular grade index (MGI). Clinicopathologic variables were abstracted from pathology reports when available. Chi-squared tests and Kruskal-Wallis tests were used to compare categorical and numeric factors, respectively, between IDC and ILC subgroups. Kaplan-Meier survival analysis and Cox proportional hazards regression were used to analyze BCI Predictive performance in the lobular patients from IDEAL study. Results: The current study included 3814 patients submitted for BCI testing during years 4-7 post-diagnosis with available histologic subtype data (80.5% IDC; 13.2% ILC; 3.0% mixed; 3.3% other). Among those with either ductal (n=3072) or lobular (n=504) carcinomas (71% node-negative and 29% node-positive), patients with ILC were older compared to IDC (>70 y: 17% vs 12%). Clinically, ILC was generally less aggressive than IDC (Grade 3: 7% vs 21%; lymphovascular invasion: 9% vs 20%; HER2+: 2% vs 13%; Ki67 % positive stained cells: 29% vs 46%; p< 0.001 for all comparisons), with the exception that ILC had larger tumors than IDC (T2/T3: 46% vs 24%) due to its unique histology. This was

consistent with BCI Prognostic results showing fewer ILC patients at high risk for late DR compared to IDC (43% vs 55%, $p < 0.001$). BCI (H/I) showed a similar trend with fewer patients with High Likelihood to benefit from EET (39% vs 43%) although the difference was not statistically significant ($p = 0.169$). The combination of BCI prognostic and predictive results revealed that more ILC patients were classified as Low Risk/Low Likelihood of benefit (43% vs 38%) and fewer were called High Risk/High Likelihood of benefit (25% vs 35%) ($p < 0.001$) compared to IDC. The IDEAL BCI translational study included 142 ILC patients with 9.3 years of median follow-up. Similar to the BCI Clinical Database results, ILC was associated with less aggressive disease than IDC (Grade 3: 18% vs 41%; HER2+: 11% vs 24%). 39% and 61% of ILC patients were classified as BCI (H/I)-High and -Low, respectively. Given the small sample size, BCI (H/I)-High showed a non-significant absolute benefit of 11.9% (HR=0.44, 95% CI 0.09-2.14; $p = 0.298$) and BCI (H/I)-Low showed no benefit (HR=2.63, 95% CI 0.70-9.93; $p = 0.138$). An analysis of the 3-way interaction among treatment, biomarker and histology showed a non-significant p-value of 0.28, suggesting BCI (H/I) provides similar predictive information in ILC as in the overall population. Conclusion: BCI identified a smaller proportion of patients with ILC at High Risk of late DR and High Likelihood of benefit from EET compared to IDC. Data from the IDEAL translational study showed that while fewer patients with ILC were identified as BCI (H/I)-High, they still derived similar absolute benefit compared to the overall cohort, while those classified as BCI (H/I)-Low derived no benefit from EET.

Disclosure(s):

Otto Metzger, MD: Abbvie: Contracted Research (Ongoing); Alliance for Clinical Trials in Oncology: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Cascadian Therapeutics: Contracted Research (Ongoing); Eisai: Contracted Research (Ongoing); Grupo Oncoclinicas: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing), Travel, Accommodations, Expenses (Ongoing); Invitae: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Merck: Honoraria (Ongoing); Pfizer: Contracted Research (Ongoing); Resilience Care: Consulting Fees (e.g., advisory boards) (Ongoing); Roche/Genentech: Contracted Research (Ongoing); Sanofi: Receipt of Intellectual Property Rights / Patent Holder (Ongoing); Susan G. Komen for the Cure: Contracted Research (Ongoing)

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12/7/2022

7:00 AM - 8:15 AM

P2-03-14

Tumor-agnostic measurement of ctDNA levels in first line ER+, HER2- metastatic breast cancer patients as a marker for survival

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INTRODUCTION

Circulating tumor cell (CTC) count and levels of circulating tumor DNA (ctDNA) have proven their individual prognostic value in metastatic breast cancer (MBC). Whereas CTCs can be quantified by enumeration, levels of ctDNA are often expressed as the variant allele frequency of the dominant mutation. The modified fast aneuploidy screening test-sequencing system (mFAST-SeqS) estimates ctDNA-load by measuring chromosomal aneuploidy instead of mutations. The mFAST-SeqS method is cheap and provides a comprehensive overview of the tumor genome without prior knowledge on genomic tumor aberrations. Previously, we showed in a small MBC cohort (n=50), heterogeneous with regard to subtype and line of treatment, that the mFAST-SeqS-derived genome-wide aneuploidy score (GWA-score) was an independent prognostic biomarker (1). Our current aim was to provide evidence for the prognostic value of GWA-score in a homogeneous cohort of estrogen receptor positive (ER+), HER2 negative (HER2-) MBC patients, starting first line treatment with an aromatase inhibitor.

MATERIALS & METHODS

CTCs were enumerated using the CellSearch-system (Menarini) and screened for ctDNA fraction using mFAST-SeqS in ER+, HER2- MBC patients, starting with first line aromatase

inhibitors. CTC-count was divided into high (CTChigh) and low (CTClow) using the validated cut-off of 5 CTCs/7.5 ml blood; similarly GWA-score was divided in high (GWAhigh) and low (GWAlow) based on the previously described cut-off of 5 (2). PFS and OS were estimated using Kaplan-Meier. Cox regression was used for uni- and multivariable analysis.

RESULTS

One hundred and thirty-four patients were included in this analysis. Mean age was 68 (range 40-90). Median follow up was 26 months. Sixty-five samples had both scores low and 30 both high, 25 samples were CTChigh/GWAlow and 14 were CTClow/GWAhigh. PFS and OS were not significantly different between CTChigh versus CTClow groups (p=0.07 and p=0.26, median PFS 15 vs 24 months, median OS 45 vs 49 months). However, PFS and OS were significantly different between GWAhigh versus GWAlow groups (p < 0.01 for both, median PFS 11 vs 24 months, median OS 31 vs 51 months). In multivariate analysis, GWA-score was a significant prognostic factor for both PFS and OS while presence of visceral disease was also prognostic for OS (table 1).

CONCLUSIONS

In patients treated with aromatase inhibitors in the first line of treatment, GWA-score was an independent prognostic marker for a worse PFS and OS and may have added value beyond CTC-count.

1. Verschoor, N., et al., Abstract P2-01-17: Circulating tumor cell count and levels of circulating tumor DNA are complementary prognostic biomarkers in metastatic breast cancer - A pilot study. Cancer Research, 2022. 82(4_Supplement): p. P2-01-17-P2-01-17.
2. Belic, J., et al., mFast-SeqS as a Monitoring and Pre-screening Tool for Tumor-Specific Aneuploidy in Plasma DNA. Adv Exp Med Biol, 2016. 924: p. 147-155.

Table 1

	PFS				OS			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age	0.99 (0.97-1.01)	0.15			1.02 (0.99-1.04)	0.17		
DFI	1.00 (1.00-1.00)	0.59			1.00 (1.00-1.00)	0.40		
Visceral disease (Y/N)	1.39 (0.90-2.15)	0.13			2.09 (1.23-3.55)	<0.01	2.35 (1.37-4.02)	<0.01
CTCs>5 (Y/N)	1.49 (0.96-2.31)	0.08	1.25 (0.79-1.97)	0.35	1.34 (0.80-2.26)	0.27	1.09 (0.62-1.93)	0.76
GWA>5 (Y/N)	2.19 (1.40-3.40)	<0.01	2.06 (1.30-3.27)	<0.01	2.08 (1.20-3.42)	<0.01	2.21 (1.25-3.93)	<0.01

Uni- and multivariate Cox regression for PFS and OS

Disclosure(s):

Noortje Verschoor, n/a: No financial relationships to disclose

Jaco Kraan, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-03-15

Retrospective study using database for the effectiveness of medroxyprogesterone acetate in patients with ER-positive/HER2-negative postmenopausal advanced breast cancer: An additional analysis of the JBCRG-C06 Safari study

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Background: Only old evidence exist to back up the use of medroxyprogesterone acetate (MPA) in endocrine therapy. Therefore, this study aimed to explore the factors that influence the time to treatment failure (TTF) of MPA in real world settings as late-line treatment following aromatase inhibitors and fulvestrant.

Methods: This was a cohort study that used the database of the Safari study, on estrogen receptor-positive (ER+) post-menopausal advanced breast cancer previously treated with fulvestrant (UMIN000015168). We created Kaplan-Meier curves for TTF treated with MPA. Further, univariate and multivariate analyses were performed using a Cox hazard model of the clinicopathological factors involved in the TTF of MPA.

Results:

First, we made Kaplan-Meier curves by treatment line for MPA in TTF analysis population 1 (n = 244), excluding HER2+ and HER2 with unknown status. The median TTF for MPA was 8.2 months (95% CI 5.1–14.9) for first- and second-line treatments, 3.0 months (95% CI 2.5–3.9) for third-line treatment, and 4.1 months (95% CI 3.5–5.0) for fourth or later treatment lines. The first- and second-line treatments had significantly longer TTF than the third-line treatment (P < 0.001) and fourth-line or later treatments (P < 0.001). No difference in TTF was observed between the third and fourth or later treatment lines. Similar results were obtained in the analysis population 2 (n = 203) for TTF, excluding cases in which MPA was considered to have been used in palliative care. The median TTF for MPA was 7.9 months (95% CI, 5.1-16.0) for first- and second-line treatments, 3.0 months (95% CI 2.8–4.6) for third-line treatment, and 4.3 months (95% CI 3.7–5.6) for fourth or later treatment lines. The first- and second-line treatments had significantly longer TTF than the third-line treatment (P < 0.001) and the fourth-line or later treatments (P < 0.001). No difference in TTF was observed between the third and fourth or later treatment lines.

Second, Table 1 shows the clinicopathological factors involved in the TTF of MPA. In univariate analysis, long DFI (≥ 6 years), small nuclear or histological grade, and the presence of visceral metastases correlated with significantly long TTF (P < 0.05). Whereas PgR, adjuvant chemotherapy, and adjuvant endocrine therapy did not affect the TTF of patients treated with MPA. However, in the multivariate regression analysis, only longer DFI (≥ 6 years) was correlated with a significantly longer TTF.

Third, we compared the clinicopathologic factors in the groups that received MPA as the fourth or later treatment lines and achieved a TTF of more than 1 year with those that did not. There were no characteristic clinicopathological factors distinct between the two groups.

Conclusion: In actual clinical practice, patients treated with MPA alone as the fourth or subsequent treatment lines showed a TTF of 4 months, suggesting that there is merit in using MPA even in late treatment lines, especially in patients with long DFI and those who are difficult to treat with other antineoplastic agents.

Table 1. Univariate and Multivariate analyses to investigate association between clinicopathological factors and TTF of MPA (n = 170)

	Univariate analysis		Multivariate analysis		Multiple regression analysis	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
		[overall P-value]		[overall P-value]		[overall P-value]
Age						
< 64 years	Reference					
≥ 64 years	0.90 (0.66–1.24)	0.53				
DFI*						
0	1.05 (0.66–1.66)	0.84	1.00 (0.61–1.64)	1.00	1.05 (0.66–1.66)	0.84
< 6 years	Reference	[0.007]	Reference	[0.17]	Reference	[0.007]
≥ 6 years	0.60 (0.42–0.85)	0.004	0.71 (0.49–1.03)	0.07	0.60 (0.42–0.85)	0.004
Nuclear or histological grade†						
Grade 1	Reference	[0.02]	Reference	[0.29]		
Grade 2	1.39 (0.90–2.15)	0.14	1.31 (0.83–2.08)	0.25		
Grade 3	1.63 (0.92–2.90)	0.10	1.33 (0.73–2.41)	0.35		
Visceral metastasis						
no	Reference		Reference			
yes	0.67 (0.48–0.93)	0.02	0.74 (0.53–1.04)	0.09		
PgR†						
negative	Reference	[0.46]				
positive	0.93 (0.65–1.33)	0.68				
Adjuvant chemotherapy						
no	Reference					
yes	0.80 (0.58–1.09)	0.15				
Adjuvant endocrine therapy						
no	Reference					
yes	0.79 (0.57–1.11)	0.17				

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Quantifying estrogen and progesterone receptor status in early-stage invasive lobular carcinoma of the breast: associated factors and outcomes in an institutional series

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Background: Recent guidelines regarding estrogen (ER) and progesterone (PR) receptor testing from the American Society of Clinical Oncology and College of American Pathologists defined a new reporting category of ER-low positive breast cancer for tumors with 1-10% ER expression by immunohistochemistry (IHC). The clinical implications of ER-low positivity are incompletely understood, especially in invasive lobular carcinoma (ILC), the second most common type of breast cancer. Given the rarity of low-ER positivity in ILC, we evaluated tumor features and outcomes associated with a spectrum of ER/PR positivity in a monoinstitutional ILC cohort. Methods: We analyzed cases of stage I-III ILC with available IHC reports. Based on prior published categories in ILC, we classified ER as low, medium, or high as defined by ER staining of 10–69%, 70–89%, and $\geq 90\%$ respectively. PR negative, low, and high tumors were defined by 0%, $< 20\%$, or $\geq 20\%$ staining respectively. We used chi-squared tests, t-tests, and Cox proportional hazards models in Stata 16.1 to evaluate associations between ER/PR categories including clinicopathologic variables and event-free survival (EFS). Results: Of 744 cases, 24 (3.2%) were ER negative and 10 (1.3%) were ER-low positive as defined by 1-10% positive staining. 713 remaining cases had ER positivity $\geq 10\%$ and comprised the cohort categories of ER low, medium, and high for this study (11.2%, 15.0%, and 73.8% respectively).

In 751 cases with PR data, 122 (16.2%) were PR negative, 145 (19.4%) were PR low and 483 (64.3%) were PR high. ER high status was significantly associated with older age (mean 56.7, 56.7, and 60.6 years in ER low, medium, and high respectively, $p=0.0005$). ER low was associated with PR negative and low status (42.3% were PR neg/low and ER low, versus 37.4% with ER medium and 29.9% in ER high, $p=0.045$), and more likely to have overexpression of HER2 (9.7%, 9.0%, and 2.9% ER low, medium, high, respectively, $p=0.002$). ER low tumors were more likely to be grade 1 than ER medium or high (41.8%, 29.8% and 24.5% respectively, $p=0.025$), and have positive surgical margins (39.4%, 35.9% and 23.9% respectively, $p=0.002$). ER status was not associated with Ki67, stage, body mass index (BMI), lymphovascular invasion, lobular carcinoma in situ (LCIS), pleomorphic histology, local therapy, or chemotherapy use. In contrast, PR high was significantly associated with younger age (57.6 versus 63.5 years in PR low, $p< 0.0001$). PR low was associated with HER2 overexpression (8.6% versus 3.2% in PR high, $p=0.002$). PR low cases were more likely to present at higher stages (15.8% stage III versus 10.1% stage III in PR high, $p=0.032$), to be pleomorphic (16.8% versus 8.2%, $p< 0.001$), and to receive chemotherapy (30.8% versus 23.1%, $p=0.022$) but were less likely to have associated LCIS (64.0 versus 74.2%, $p=0.004$). PR status was not associated with Ki67, BMI, lymphovascular invasion, local therapy, or surgical margins. In a Cox proportional hazards model adjusting for age, stage, grade, pleomorphic histology, and chemotherapy use, ER category was not associated with EFS but both PR negative and PR low status each had significantly worse EFS compared to PR $\geq 20\%$ (HR 3.5, 95% CI 1.8-6.7, $p< 0.001$ for PR negative, and HR 2.0, 95% CI 1.1-3.5, $p=0.015$ for PR low). The estimated cumulative 5-year EFS for patients with ER low, medium, and high tumors was 87.1%, 93.4%, and 90.1% respectively. The estimated cumulative 5-year EFS for patients with PR negative, low, and high tumors was 78.9%, 90.2%, and 92.7% respectively. Conclusions: Using ILC-specific categories for ER expression, we found associations between ER category and clinicopathologic variables but not with EFS. In contrast, PR negative and low status was associated with worse EFS. These findings highlight the importance of exploring the spectrum of ER/PR activity within ILC, a classically strongly hormone receptor-positive tumor type, using more quantitative methods.

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Elle Clelland, BS: No financial relationships to disclose

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P2-03-17

Fluoroestradiol (FES) and Fluorodeoxyglucose (FDG) PET imaging in patients with ER+, HER2+ or HER2- metastatic breast cancer

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Fluoroestradiol (FES) and Fluorodeoxyglucose (FDG) PET imaging in patients with ER+, HER2+ or HER2- metastatic breast cancer

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Background: 18F-Fluorodeoxyglucose (FDG) has long been used for measuring tumor glycolytic activity in clinical PET imaging. The FDA recently approved 18F-Fluoroestradiol (FES) (Cerianna) as a PET imaging tracer for characterizing disease in patients with estrogen-receptor positive (ER+) breast cancer. As FES PET enters clinical practice it is important to establish its utility in the full population of hormone-receptor positive patients, including for patients with human epidermal growth factor 2 (HER2)-overexpressing tumors. Patients with HER2-positive metastatic breast cancer have historically been treated with combination cytotoxic and HER2-directed therapy, with the understanding that HER2 is the primary driver in this disease state. This retrospective study examined uptake in matched lesions for both FES and FDG PET and compared activity in patients with HER2 positive versus HER2 negative metastatic breast cancer.

Methods: Patients were selected from the UW research database who had a history of biopsy-proven primary ER+ breast cancer as well as FES and FDG PET scans within 30 days. We examined FDG and FES scans and recorded SUVmax in up to 16 matched lesions between the two scans. Patients were also divided by HER2 status (+/-). In addition, a subset of patients who underwent at least 2 paired FDG and FES scans were reviewed.

Results: 270 matched FDG and FES scans were analyzed in 216 patients with history of ER+, and HER2+ or HER2- breast cancer who were not part of an ongoing clinical trial. 158 (73%) had ductal disease, 38 (18%) had lobular disease. 183 (85%) had HER2- breast cancer. Of the 33 patients who had HER2+ breast cancer, 28 (85%) had ductal carcinoma. 40 patients underwent serial scans, allowing tracking over multiple timepoints. A total of 1323 metastatic sites were recorded (average = 5/scan (range 1,16)), with the majority (71%) representing bony lesions. No difference in quantitative FES or FDG avidity was observed between soft tissue and osseous sites. FES and FDG SUVmax were similar among patients with either HER2- or HER2+ breast cancer (Table 1). Among 40 patients with multiple paired FDG and FES scans, 26 (65%) had 2 scans while the remaining 14 had 3, with FES avidity remaining stable over time. There was no correlation between FES or FDG scans and HER2 status.

Conclusion: In a cohort of ER+, HER2+ and HER2- patients undergoing concurrent FDG and FES PET scans, FDG and FES activity was similar regardless of HER2 status. FES uptake in both HER2- and HER2+ patients and stability over time in serial scans suggest that HER2 does not affect ER density. This suggests that in many patients with so-called "triple positive" disease, endocrine therapy may offer a powerful primary rather than ancillary tool in select patients. FES combined with FDG PET may offer utility in predicting and assessing response to therapy in this patient population.

Table 1. FES and FDG uptake in patients with HER2- or HER2+ disease

Table 1. FES and FDG uptake in patients with HER2- or HER2+ disease

FES SUVmax	HER2- (n=1139 lesions)	HER2+ (n=184 lesions)
Mean	4.1	3.4
Min	0.1	0.3
Max	22.8	13.7
FDG SUVmax		
Mean	5.1	4.4
Min	1.1	1.5
Max	26.7	11.6

Disclosure(s):

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7:00 AM - 8:15 AM

P2-03-18

Clinical use of Breast Cancer Index for prediction of late breast cancer recurrence and prediction of benefit in extended endocrine therapy: A single institution experience

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Background: The decision to extend adjuvant endocrine therapy beyond five years is often individualized. Breast Cancer Index (BCI) (Biotheranostics, Inc.) is a validated multigene-expression tissue-based analytic tool used in early hormone-positive breast cancer to predict the response to extended endocrine therapy, based on the HOXB13/IL17BR ratio (H/I ratio), and prognosis 5-10 years after diagnosis, based on the molecular grade index (MGI) and H/I ratio. It is presumed that if BCI shows a high likelihood of benefit from endocrine therapy (BCI-high), the treating clinician would recommend extended adjuvant endocrine therapy and if the primary prediction shows a low likelihood of benefit (BCI-low), the clinician would recommend discontinuation of therapy; however, this may not always be practiced. The Clinical Treatment Score post-5 years (CTS5) is a validated clinicopathologic tool that provides a calculated risk assessment of late distant recurrence (LDR). Clinicians may use the calculated CTS5 score in deciding whether to extend adjuvant endocrine therapy and forego additional prognostic testing, such as BCI. The aim of the study is to understand how clinicians integrate BCI results into medical decision making and to determine the correlation with CTS5 scores in making the decision to offer extended endocrine therapy. Methods: This is a single institution retrospective study. All patients within Henry Ford Health System who had BCI testing ordered, between April 2016 and January 2022, were included. Recommendations regarding extended endocrine therapy were collected. CTS5 scores were calculated based on patient's age, tumor size, tumor

grade, and number of involved lymph nodes. If available, the 21-gene recurrence scores (Oncotype-DX) and Ki-67 scores were collected for additional comparison. Results: A total of 165 female patients were included in this study. The average age at diagnosis was 58.5 ± 10.4 years old; 116 (70%) were Caucasian, 35 (21%) were African American; 132 patients (80%) were post-menopausal. The decision regarding extending endocrine therapy was concordant with BCI predictive results in 93.3% of patients; endocrine therapy was continued in 87% of patients in the BCI-high group and discontinued in 95% of patients in the BCI-low group ($p < 0.001$). In comparing the categorical results of BCI predictive scores (low vs. high) and the CTS5 results (low vs. intermediate vs. high) univariate analysis did not detect a statistically significant relationship. In comparing BCI prognostic LDR risk percentage with the CTS5 LDR (5–10 year) risk percentage, a statistically significant, but weak, positive correlation was observed (Pearson correlation coefficient of 0.38487, $p\text{-value} = < 0.0001$). The odds of a BCI-high primary prediction were 1.031 (95% CI: 1.005, 1.057) times higher for every-one percentage increase in Ki-67 ($p\text{-value} = 0.0172$), 1.052 (95% CI: 1.003, 1.057) times higher for every one-unit increase in Oncotype-DX score ($p\text{-value} = 0.0353$) and 1.232 (95% CI: 1.24, 1.351) times higher for every-one percentage increase in BCI prognostic LDR risk assessment ($p\text{-value} < 0.0001$). No statistically significant association was found between the BCI predictive score and age, race, stage, lymph node involvement, and HER2 receptor positivity. Conclusions: This single-institution study revealed that clinicians make decisions regarding extended endocrine therapy that are usually concordant with BCI predictive results. CTS5 results weakly correlate with BCI prognostic results but may not provide conclusive information to support a clinical decision. For patients with early hormone-receptor positive breast cancer the BCI tissue-based analysis may influence a decision regarding extending endocrine therapy.

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P2-03-19

The efficacy of neoadjuvant endocrine therapy during the waiting period for surgery in postmenopausal hormone receptor positive breast cancer

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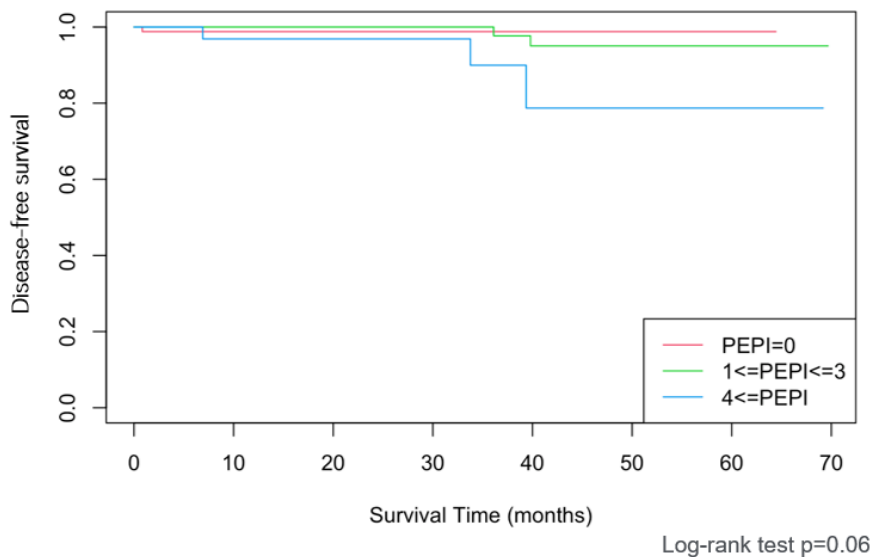
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Background: Although neoadjuvant endocrine therapy has been used to improve breast conservation rate, its prognostic relevance is unknown. The search for a valid prognostic factor equivalent to pCR in neoadjuvant chemotherapy is a current challenge in neoadjuvant endocrine therapy. In this study, we investigated the efficacy of short term neoadjuvant endocrine therapy utilizing the waiting period for surgery and the prognostic factor including Preoperative Endocrine Prognostic Index (PEPI) score.

Patients and Methods : A total of 269 postmenopausal women with hormone receptor-positive, HER2-negative breast cancer was treated with endocrine therapy with non-steroidal aromatase inhibitor during the waiting period for surgery between October 2012 and November 2021. Of the entire 269 patients, 92 and 177 patients had anastrozole and letrozole, respectively. The primary endpoint was change in tumor size by ultrasound and Ki67 before and after short-term endocrine therapy. The secondary endpoint was prognosis of patients divided by PEPI score which was calculated using tumor size, lymph node metastasis, Ki67, and ER Allred score. This study was approved by the institutional review board of Teikyo University.

Results: Median age was 68 years old (range, 41-89). ER and PgR was positive in 266 (98%) and 232 (86%) of the entire 269 patients, respectively. Median tumor size was 1.65 cm (range, 0.4-7.5). Seventeen (6.3%) pts were clinically node-positive. Patients with histological grade I tumor were 190 (70.6%). The median duration of endocrine therapy was 39 days (range, 2-88). Average pretreatment Ki67 expression was 10% (range, 0-90). Tumor diameter was significantly decreased to 1.43cm (range,0.45-5.83) after short-term endocrine therapy ($p=0.01$). The Ki67 expression was significantly decreased to 3.0% (range, 0-85) after endocrine therapy ($p< 0.01$) and only five patients (1.9%) showed marked increase in Ki-67 expression. PEPI score 0, 1-3 and ≥ 4 was found in 83 (30.9%),147 (54.7%) and 39 patients (14.5%), respectively. After the median observation period of 928 days, patients with PEPI score ≥ 4 showed worse disease-free survival (Figure) compared with patients with PEPI score 0 and 1-3 ($p=0.06$). In terms of mortality, patients with PEPI score ≥ 4 had worse overall survival than patients with PEPI score 0 and 1-3 ($p=0.07$).

Conclusions: These results suggested that neoadjuvant endocrine therapy during the waiting period for surgery might be effective in reducing the size and Ki67 expression level and PEPI score might be useful in predicting the prognosis of postmenopausal hormone receptor positive breast cancer patients.



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P2-03-20

Clinical profiling and comprehensive analysis of candidate genes related to breast cancer estrogen receptor intratumour heterogeneity

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1. Background and Aim

Breast cancer has the highest incidence among the world's population. One third of patients diagnosed with early breast cancer progressed into metastatic outcomes due to the inherent heterogeneity and evolutionary features of tumors.

The main clinical manifestation is the discordance of receptor expression in metastases. ESR1 the estrogen receptor(ER) encoding gene, has been proved affected ER expression.

Nevertheless, the correlation between ER transformation and the somatic mutation profiles in breast cancer metastatic lesions remains unclear. Availability of advanced high-throughput technologies, and the development of bioinformatics tools has greatly accelerated our cognition of the molecular basis of cancer.

In this study, we aimed to evaluate the frequency, clinical characteristics and prognostic value of ER receptor conversion between primary and first metastatic lesions in 115 patients whose primary ER status are positive. We also compared the results of NGS of 42 patients and explored latent genes related to ER discordance in expression.

2.Method

Qualified metastatic tumor tissue sequencing information was available for 42 patients. Samples were accessed using the FoundationOne CDx assay (Foundation Medicine, Cambridge, MA, USA) panel including 733 tumor related genes. High frequency mutant genes were defined as the genes count more than 4 times in each group. All data were analyzed using SPSS 25.0 software (Chicago, IL, USA). Pearson's chi-squared (χ^2) test, Fisher's exact test, were used to test the associations between different variables. The Cox proportional hazard models was used to evaluate the relationship between KMT2C mutation and Disease free survival (DFS) in the patients cohorts. The results with $p < 0.05$ were considered statistically significant.

3.Results and Conclusions

All 115 patients (primary ER status is positive) were divided into two groups, 70(60.87%) patients ER status remained positive while 45(39.14%) patients ER status transformed into negative. The histological type ($p=0.008$) and DFS ($p=0.004$) were significantly different in two subgroups. There were no significant correlations between the age at the time of diagnosis, BMI classification, menopausal status, surgery, histological grade, tumor size, lymph node status, metastasis, Ki67, adjuvant radiotherapy, neoadjuvant, metastasis site before second biopsy, first treatment after recurrent and first PFS after rebiopsy.

Univariable analysis of DFS proved metastasis to be distinct risk factor for poor survival (hazard

ratio [HR] > 1, p = 0.001). By contrast, neoadjuvant proved to be protective factor for better survival (hazard ratio [HR] < 1, p < 0.001) . The surgery, histological type, histological grade, tumorsize, metastasis, neoadjuvant, first treatment after recurrent, first PFS after rebiopsy were subsequently analyzed with the multivariable Cox analysis. Metastasis (HR > 1 , p=0.007) and neoadjuvant (HR < 1 , p<0.001) remained independent prognostic factors of DFS.

We compared the differentially mutated genes in the ER differential expression BC patient groups. Mutations in TP53 (n=24) and PIK3CA (n=19) occurred most frequently in both groups and account for 57.14% and 49.23% separately. Notably, mutations in KMT2C (n=6) was detected in ER+ to – subgroup and accounted for 37.5%. According to the results of NGS, the distribution of KMT2C mutations was different among the two cohorts. We identified the mutation in codon 321 was the hot spot of KMT2C in our patient cohort. Next, we used the Kyoto Encyclopedia of Genes and Genomes (KEGG) database to analyze the enriched pathways of KMT2C. KEGG pathway analysis revealed that patients with KMT2C mutations harbored significantly more mutations in genes involved in the Ubiquitin mediated proteolysis and Lysine degradation signaling pathway.

Table.1 Patients' basic clinicopathological characteristics among two groups

			ER remained positive	ER transformed into negative	P value
Patients number	Total	115	70(60.87)	45(39.14)	/
Age at Diagnosis	<50	74 (64.3)	47(67.14)	27(60.0)	0.435
	≥50	41 (35.7)	23(32.86)	18(40.0)	
BMI	< 18.5	10(8.7)	6(8.57)	4(8.89)	0.225
	18.5-24	57(49.6)	32(45.71)	25(55.56)	
	>24	42(36.5)	30(42.86)	12(26.67)	
	Unknown	6(5.2)	2(2.86)	4(8.89)	
Menopausal status	Premenopausal	29(25.2)	15(21.43)	14(31.11)	0.407
	Postmenopausal	81(70.4)	51(72.86)	30(66.67)	
	Unknown	5(4.3)	4(5.71)	1(2.22)	
Surgery	Modified radical mastectomy	91 (79.1)	54(77.14)	37(82.22)	0.927
	Mastectomy	13 (11.3)	9(12.86)	4(8.89)	
	Breast-conserving surgery	6(5.2)	4(5.71)	2(4.44)	
	Unknown	5(4.3)	3(4.29)	2(4.44)	
Histological type	IDC	99(86.1)	60(85.71)	39(86.67)	0.008
	ILC	6(5.2)	2(2.86)	4(8.89)	
	Others	2(1.7)	0	2(4.44)	
	Unknown	8(7.0)	8(11.43)	0	
Histological grade	I	3(2.6)	0	3(6.67)	0.072
	II	80(69.6)	49(70.0)	31(68.89)	
	III	7(6.1)	3(4.29)	4(8.89)	
	Unkonwn	25(21.7)	18(25.71)	7(15.56)	
Tumorsize	T1	23(20.0)	13(18.57)	10(22.22)	0.599
	T2	53(46.1)	35(50.0)	18(40.0)	
	T3	11(9.6)	5(7.14)	6(13.33)	
	T4	28(24.3)	17(24.29)	11(24.44)	
Lymphnodestatus	N0	31(27.0)	19(27.14)	12(26.67)	0.671
	N1	35(30.4)	23(32.86)	12(26.67)	
	N2	20(17.4)	10(14.29)	10(22.22)	
	N3	15(13.0)	8(11.43)	7(15.56)	
	Unknown	14(12.2)	10(14.29)	4(8.89)	

Table 2. Univariate and Multivariate Analysis Between Clinicopathological Characteristics and DFS of 115 BC patients

Table 2. Univariate and Multivariate Analysis Between Clinicopathological Characteristics and DFS of 115 BC patients

Characteristics	Univariate Analysis			Multivariate analysis		
	HR	95%CI	P value	HR	95%CI	P value
Age at Diagnosis						
<50	1	1				
≥50	0.939	0.626-1.408	0.76			
BMI						
<18.5	1	1				
18.5-24	1.249	0.605-2.576	0.548			
>24	1.418	0.679-2.961	0.353			
Unknown	1.498	0.527-4.258	0.448			
Menopausal status						
Premenopausal	1	1				
Postmenopausal	0.996	0.639-1.552	0.987			
Unknown	1.412	0.541-3.686	0.481			
Surgery						
Modified radical mastectomy	1	1		1	1	
Mastectomy	1.494	0.792-2.819	0.215	1.448	0.703-2.944	0.306
Breast-conserving surgery	1.214	0.528-2.792	0.647	1.235	0.462-3.303	0.675
Unknown	0.75	0.269-2.092	0.583	1.034	0.230-4.660	0.965
Histological type						
IDC	1	1				
ILC	0.829	0.354-1.937	0.664	0.696	0.268-1.811	0.458
Others	0.452	0.107-1.912	0.28	0.35	0.038-3.215	0.353
Unknown	1.413	0.652-3.065	0.381	1.153	0.453-2.933	0.766
Histological grade						
I	1	1				
II	1.885	0.589-6.034	0.285	1.618	0.452-5.793	0.46
III	2.049	0.526-7.978	0.301	1.419	0.311-6.489	0.651
Unkonwn	1.624	0.481-5.480	0.435	2.11	0.498-8.932	0.311
Tumorsize						
T1	1	1				
T2	1.281	0.772-2.127	0.338	1.725	0.95-3.131	0.073
T3	2.054	0.988-4.269	0.054	1.995	0.812-4.902	0.132
T4	1.005	0.559-1.806	0.988	1.071	0.48-2.39	0.866
Lymphnodestatus						
N0	1	1				
N1	1.062	0.642-1.758	0.814			
N2	1.221	0.682-2.188	0.501			
N3	1.231	0.638-2.376	0.536			
Unknown	0.731	0.363-1.470	0.379			
Metastasis						
M0	1	1		1	1	
M1	3.818	1.695-8.598	0.001	3.905	1.44-10.593	0.007
Unknown	0.764	0.383-1.524	0.445	1.089	0.421-2.814	0.861
Ki67						
<14	1	1				
≥14	1.377	0.765-2.477	0.286			
Unknown	0.795	0.413-1.528	0.491			
Adjuvantradiotherapy						
yes	1	1				
no	1.076	0.727-1.592	0.715			
Unkonwn	0.602	0.183-1.976	0.402			
Neoadjuvant						
no	1	1		1	1	
yes	0.4	0.245-0.653	<0.001	0.353	0.199-0.625	<0.001
Metastasis Site before second biopsy						
with liver metastasis	1	1				
without liver metastasis	0.921	0.623-1.361	0.679			
First treatment after recurrent						
with chemotherapy	1	1		1	1	
without chemotherapy	0.76	0.497-1.162	0.205	0.653	0.401-1.064	0.087
Unkonwn	1.035	0.446-2.398	0.937	1.129	0.445-2.866	0.798
ER discordant						
no	1	1				
yes	1.198	0.809-1.775	0.368			
First PFS after rebiopsy						
<6month	1	1		1	1	
≥6month	0.721	0.461-1.126	0.15	0.694	0.412-1.168	0.169
Unkonwn	0.699	0.403-1.213	0.202	0.648	0.349-1.203	0.169

Table 3. Mutated Genes Rank and patients number

	Only ER + to + (26)	Only ER + to – (16)	In both groups (42)
Mutated Genes Rank and patients number	ESR1(7) CDK12(6) MYC(5)	KMT2C(6) FGF19(3) FGF4(3) FGFR1(3)	TP53(24) PIK3CA(19) ERBB2(9) NF1(9) CCND1(8) FGF3(8)

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Xi Wang, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-03-21

Chemotherapy is not mandatory in premenopausal, node-positive, HR+HER2- breast cancer patients

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Background: The RxPONDER trial demonstrated that chemotherapy improves survival in premenopausal, node-positive, HR+HER2- breast cancer patients irrelative of genomic risk. However, the rate of ovarian function suppression (OFS) was under 20%, questioning whether hormone therapy with OFS would be sufficient in genomic low risk patients. The survival outcome of premenopausal, node-positive, HR+HER2- breast cancer patients were retrospectively reviewed, to investigate the non-inferiority of only hormone therapy with OFS in this population. We also retrospectively reviewed patients who underwent genomic multigene assay in this population. Patients and methods: Breast cancer patients who underwent primary surgery between 1990 – 2013 at Asan Medical Center were retrospectively reviewed in this study. Patients who were 50 years old or younger, HR+HER2- breast cancer and T2/3N0 or T1/2N0 were included. Premenopausal patients who underwent the MAMMAPRINT® test between January 2018 – April 2021 were also reviewed and analyzed. Recurrence was defined as locoregional recur and distant metastasis. Disease-free survival (DFS) and distant

metastasis-free survival (DMFS) was analyzed using the Kaplan-Meier survival analysis and log-rank test. Results: A total of 6,220 patients who were 50 years or younger underwent primary breast cancer surgery for HR+HER2- breast cancer between 1990 – 2013. Among them, 762 patients were T2/3N0 and 1,283 patients were T1/2N0. Most of the patients (N=1,652, 80.8%) underwent chemotherapy. Among patients who only had hormone therapy, 48 (12.2%) patients only had tamoxifen and 345 (87.8%) patients had tamoxifen with OFS (TAM+OFS). The median follow-up was 107 months. The 8-year DFS was 87.2% in the chemotherapy group, compared to 90.2% in the TAM+OFS group (log-rank test p-value 0.499). The 8-year DFMS had no significant difference also between the chemotherapy and TAM+OFS group also (90.7% vs. 93.5% retrospectively, log-rank test p-value 0.184). DFS and DMFS did not differ in the subgroup analysis of T2/3N0 and T1/2N0 too. A total of 270 premenopausal patients underwent the MAMMAPRINT® test for HR+HER2-, N1 breast cancer between Jan 2018 – April 2021. Among them, 136 (50.4%) patients had low genomic risk and 134 (49.6%) had high genomic risk. Among the low genomic risk patients, 17 (19.9%) patients had only tamoxifen, 107 (78.7%) had TAM+OFS and 1 (0.7%) patient had aromatase inhibitor. The median follow-up period was 26 months. There were seven recurrence events, 2 distant metastasis and 5 locoregional recurrences. Among the low genomic risk patients, 1 patient had lung metastasis and 1 patient had local recurrence. Both patients had only TAM+OFS. Conclusion: In this study, TAM+OFS showed no significant survival difference compared to chemotherapy in premenopausal, HR+HER2- patients. Patient selection is essential to omit chemotherapy in this population. The predictive value of genomic multigene assay for chemotherapy in premenopausal, HR+HER2-, node positive patients warrant further evaluation. Several clinical trials are being prepared to answer this question.

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7:00 AM - 8:15 AM

P2-03-22

Assessment of the relationship between duration of treatment with hormonal therapy and the detection of ESR1 mutations in hormone-receptor positive, HER2 negative, breast cancer

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Background Hormonal therapeutic agents such as the selective estrogen receptor modulator, tamoxifen, as well as the aromatase inhibitors (AIs), anastrozole, exemestane, and letrozole, are a mainstay in the treatment of patients with hormone-receptor positive (HR+) breast cancer. Despite the effectiveness of hormonal therapy in the treatment of patients with HR+ breast cancer, acquired resistance to both AIs and tamoxifen does occur, often associated with mutations of the estrogen receptor 1 (ESR1). Although the acquisition of ESR1 mutations in patients with HR+ breast cancer treated with hormonal therapy has been established as a mechanism of resistance, there is a paucity of data on the relationship between the duration of treatment with hormonal therapies and the development of ESR1 mutations. Using a cohort of patients with HR+ breast cancer who underwent next generation sequencing (NGS) as part of routine clinical care, we aim to assess the relationship between the duration of exposure to aromatase inhibitors and the detection of ESR1 mutations. The results of this study will further our understanding of ESR1-mutations and provide insight into strategies to optimize therapy for patients with HR+ breast cancers. Methods This is a retrospective analysis of patients 18 years of age or older treated at a single academic cancer center in the USA, diagnosed with HR+, HER2-negative breast cancer and who have received somatic NGS as part of clinical care over a six-year period through July 2019. Demographic, disease-related, and treatment related variables were collected along with genomic testing variables (ie. ESR1-mutation status) for each patient who met the inclusion criteria. Two patient groups were formed on the basis of ESR1-mutation status (present vs. absent) and compared on the basis of duration of treatment with AI, and other clinical and demographic categories. Results A total of 247 patients who were diagnosed with HR-positive, HER2-negative breast cancer and received NGS were identified and are included in this analysis. A total of 138 (56%) patients were assessed via tissue based NGS and 109 (44%) by liquid biopsy. The median age at time of sequencing was 58 years [57 years (ESR1-absent) vs. 60 years (ESR1-present); $p=0.009$]. The majority of

patients were white (83%) and post-menopausal (57%). Invasive ductal carcinoma was the most common histological type (82%). Nearly all (96%) patients had stage IV disease at time of sequencing and ESR1 mutations were found exclusively in those with stage IV disease. ESR1 mutations were identified in 62 patients (25%). The median duration of treatment with aromatase inhibitors prior to testing was 19.3 months in both groups (ESR1 mutations absent vs. detected). There was no difference in prior tamoxifen use between groups (absent 43%, present 48%; $p=0.48$). In patients tested by tissue based NGS, ESR1 mutations were more frequently detected in metastatic sites (28% vs. 13%; $p=0.03$). Twenty-two patients for whom NGS did not identify an ESR1 mutation prior to July 2019 received subsequent NGS testing. Of these 22 patients, six (27%) had ESR1 mutations detected by subsequent NGS. In these six patients, ESR1-mutations were detected by NGS a median of 2.2 years (range 1.7 years to 2.6 years) after prior NGS. Conclusion There was no difference in duration of treatment with aromatase inhibitor therapy in patients with ESR1 mutations vs. those without ESR1 mutations detected by NGS. Patients with ESR1 mutations tended to be older. Although the detection of ESR1 mutations is associated with acquired therapy resistance and progression on treatment, a longer duration of treatment may make the emergence of ESR1 mutations more likely. These counterbalancing factors may have contributed to the results reported here.

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7:00 AM - 8:15 AM

P2-03-23

Retrospective evaluation of outcomes in a real-world, prospective cohort using EndoPredict: Results from the Charité registry

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Background: EndoPredict is a prognostic and predictive gene expression assay that provides an EPclin risk score, which can be used to identify individuals with low enough risk of distant breast cancer recurrence that they may forgo chemotherapy. In clinical studies, EndoPredict has been validated to predict risk of distant recurrence up to 15 years and chemotherapy benefit. To date, real-world studies evaluating patient outcomes after prospective EndoPredict testing have been limited. Here, we report on outcomes collected via survey from patients enrolled in a registry created to generate real-world evidence from over 800 patients routinely tested with EndoPredict at Charité University Hospital Berlin. Methods: Female patients with hormone receptor positive, HER2 negative primary breast cancer with up to three positive lymph nodes who received prospective EndoPredict testing at Charité University Hospital Institute of Pathology between 2011 and 2016 were contacted to complete a survey for participation in this study. Surveys included questions on treatment and recurrence history. Patient demographics, clinical characteristics of the cancer, and EndoPredict results were retrieved from Charité records. All patients received EndoPredict test results before decision making on systemic treatment. After testing, treatment included either adjuvant endocrine therapy or adjuvant endocrine therapy plus adjuvant chemotherapy, and may have included radiotherapy. Cox proportional hazards models were fit with binary EPclin risk category (high, low) or continuous EPclin risk score predicting 5-year distant recurrence or recurrence of any kind. Analyses were performed across all survey responses, and in subsets of patients stratified by adjuvant chemotherapy treatment. Kaplan-Meier estimates of 5-year risk of recurrence were also calculated. Results: 842 patient survey responses were returned with informed consent and met study inclusion criteria. The median age at diagnosis was 54 years (IQR 49, 63), and across survey responses, 63.5% (N=535/842) of patients were lymph node negative, 60.9% (N=513/842) were T1, and 43.9% (N=370/842) were treated with adjuvant chemotherapy. Among included patients, 49.5% (N=417/842) were classified as EPclin low-risk and 50.5% (N=425/842) were high-risk. The concordance between EPclin risk category and chemotherapy status was 0.89 with 5.5% (N=23/417) of EPclin low-risk and 81.6% (N=347/425) of EPclin high-risk patients receiving treatment with chemotherapy. In the subset of patients not treated with adjuvant chemotherapy (N=472/842, 55.7%), continuous EPclin score was a significant predictor of distant recurrence (N=469; HR: 4.34, 95% CI 1.75-9.58); $p = 2.4 \times 10^{-3}$), and recurrence of any kind (N=468; HR: 3.39, 95% CI 1.61-6.58); $p = 1.9 \times 10^{-3}$). In EPclin low-risk patients treated with endocrine therapy alone, there was a low risk of 5-year distant recurrence (1.6%, 95% CI 0.7%-3.4%). In EPclin high-risk patients the risk of distant recurrence at 5 years was 6.8% (95% CI 2.6%-17.4%) in patients without chemotherapy and 3.6% (95% CI 2.1%-6.3%) in patients treated with chemotherapy. In an exploratory subgroup analysis in patients with node negative and node positive disease, risk of 5-year distant recurrence in EPclin low-risk patients without chemotherapy was 1.3% (95% CI 0.5%-3.5%) and 2.4% (95% CI 0.6%-9.2%), respectively. Conclusion: In this real-world cohort of patients with prospective routine testing with EndoPredict, EPclin scores were a significant predictor for patient-reported outcomes. Patients with EPclin low-risk scores had a low risk of 5-year distant recurrence even in the absence of chemotherapy treatment. This real-world result supports previous clinical studies demonstrating that patients with EPclin low-risk scores can safely forgo chemotherapy.

Disclosure(s):

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Paul Jank, n/a: Myriad Genetics Inc.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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12/7/2022

7:00 AM - 8:15 AM

P2-03-24

Predictors of Incomplete Ovarian Function Suppression (OFS) in Adolescent and Young Adult (AYA) Women with Hormone Receptor Positive (HR+) Breast Cancer

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Authors: Apoorva Anandan, MD (1,2), Trinetri Ghosh (3), Jiwei Zhao (3), Kari Wisinski, MD (1,2) (1) Department of Medicine, Section of Hematology/Oncology, University of Wisconsin-Madison School of Medicine and Public Health, Madison, WI (2) University of Wisconsin Carbone Cancer Center, Madison, WI (3) University of Wisconsin Department of Biostatistics and Medical Informatics Madison, WI Background: A combined analysis of the SOFT/TEXT trials demonstrated an overall survival (OS) benefit to endocrine therapy in addition to OFS compared to endocrine therapy alone, further establishing the importance of adequate OFS in premenopausal women with HR+ breast cancers. Factors associated with inadequate OFS are ambiguous, but younger age, type of chemotherapy, high body mass index (BMI), and time from treatment completion seem to be important. Additionally, data remains limited regarding whether monitoring of OFS should be routinely performed and optimal timing of hormone levels. We sought to identify predictors of inadequate OFS among an AYA population of hormone receptor positive breast cancer receiving OFS at our institution. Methods: A retrospective, descriptive study was conducted looking at AYA patients (pts) aged 18-39 with a diagnosis of HR+ breast cancer who previously and/or currently received oncologic care for management of their breast cancer at the institution. Data was collected from pts diagnosed between 2000-2022. Patients who had previously received or are currently receiving OFS in the adjuvant and/or metastatic setting were included in the study. Data was collected regarding age, BMI, chemotherapy regimen received in the neoadjuvant and/or adjuvant setting, type, dose, and frequency of ovarian suppression, number of times estradiol was monitored, and frequency of estradiol levels >20. This was used as the cut off based on a comprehensive review of data consistently categorizing levels >20 as not to be postmenopausal. Results: 74 AYA patients who received OFS were included with median age of 28 (range 20-39) and average BMI 27.7 (range 15-45). 70% of the population was Caucasian, 10% African American, and 20% Hispanic. Estradiol levels were monitored in 46 of the 74 pts (62%). The frequency of estradiol monitored ranged from 1-22 times. 16 out of the 46 (35%) pts had estradiol checked only once, 10 (22%) twice, and 16 (35%) four or more times. 22 out of 46 pts (48%) had estradiol levels

>20 when checked at least once. 9 out of 22 (41%) had estradiol >20 when checked more than four times. Out of 74 pts, 36 received OFS every month (49%), 32 received OFS every three months (43%). Only 4 out of 74 pts (5%) switched from monthly to every three months, meanwhile only 1 (1%) switched from every three months to monthly. 18 out of the 36 pts (50%) receiving monthly OFS had estradiol levels checked with 9 (50%) having estradiol >20. Meanwhile, 20 out of the 32 pts who received OFS every 3 months (63%) had estradiol levels checked with 10 (50%) having estradiol >20. The average age of pts with estradiol >20 was 33.6 while the average BMI of those with estradiol >20 was 29.2. Finally, 64 out of 74 pts (86%) received chemotherapy in the neoadjuvant and/or adjuvant setting. 41 out of 64 (64%) had estradiol levels checked. 18 out of 41 (44%) had estradiol >20. Discussion: Our data indicates a high degree of clinician variability in monitoring estradiol levels in AYA pts treated with OFS. Lack of adequate OFS was seen in nearly half of pts in this cohort. Higher BMI and young age may be predictors of lack of adequate ovarian suppression, supporting the findings of other studies. An algorithm for routine monitoring of estradiol may improve outcomes with OFS especially in young pts or those with a high BMI.

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Apoorva Anandan, MD: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-03-25

Pilot study to evaluate circulating tumor DNA (ctDNA) to PET/CT imaging using 18F-Fluorodeoxyglucose (FDG) and 18F-Fluoroestradiol (FES) PET/CT imaging as biomarkers in patients with metastatic breast cancer

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Background: 18F-FES is an FDA-approved estrogen analogue PET imaging tracer (Cerianna) which measures tumor estrogen receptor (ER) expression at multiple tumor sites simultaneously and predicts response to endocrine therapy. 18F-FDG is a commonly used glucose PET imaging tracer which measures glycolytic metabolic activity in tumors. Elevated plasma ctDNA has been associated with an increased risk of relapse and can identify actionable genomic alterations. This pilot research study explored the relationship between somatic copy-number variants (CNVs) and cell-free DNA mass using low-pass-whole-genome (LPWG) ctDNA in the blood to FES and FDG PET/CT findings with both qualitative and quantitative image analysis in metastatic breast cancer patients.

Methods: Two(2) 10ml Streck tubes were collected from 20 patients with metastatic ER+ breast cancer +/-30 days of their FDG-PET/CT scan (n=19) or their FES-PET/CT scan (n=9). 8 patients had both scans. Somatic mutations were assessed using comprehensive genomic profiling of tissue samples from 19 patients using the clinically validated UW-Oncoplex assay. Qualitative analysis included detection of LPWG ctDNA, presence of PIK3A mutations in tissue, and intensity of uptake in PET/CT imaging. LPWG ctDNA of blood samples evaluated ctDNA mass and CNVs that comprised at least 8% of total ctDNA. Total lesion glycolysis (TLG) in FDG scans and total lesion estrogen receptors (TLER) in FES scans were calculated using a dedicated workflow in MiM software (MiM Software Inc. Cleveland OH). Quantitative analysis included the circulating fraction (ctDNA), PET/CT SUVmax of the index lesion, number of lesions, TLG and TLER. For TLG, the threshold for determining measurable lesions was calculated using liver SULmean + 1.5*SD. The threshold for TLER was calculated using SUVmean of the mediastinal blood pool. The ctDNA fraction and the number of lesions for both FDG and FES were each ranked into 3 categories. FDG and FES data (SUVmax of index lesion, # of lesions, and TLG or TLER) were correlated to the calculated ctDNA fraction values. TLG and TLER were also correlated to each other.

Results: ctDNA was classified as no ctDNA present (n=9), ctDNA present (n=8) and indeterminate (n=3). Average neoplastic ctDNA fraction was 0.114 (range 0.03-0.423). PIK3A mutations were: 10 absent and 9 present. Ranked categories for ctDNA fraction, FDG TLG and FES TLER are shown in Table 1. Table 2 shows results of FDG and FES analysis and correlation with ctDNA. Ranked ctDNA findings correlated with both the FDG number of lesions (R2=0.69) and TLG (R2=0.83), but not the SUVmax of the index lesion (R2=0.29). Correlation decreased for ctDNA versus FES number of lesions (R2=0.51), TLER (R2=0.61), and SUVmax of index lesion (R2=0.16). TLG and TLER significantly correlated with the 8 patients that had both an FDG and FES PET/CT scan (R2=0.77).

Conclusions: In this pilot study, FDG TLG showed a significant correlation with ctDNA. There is an encouraging association with ctDNA fraction and number of FDG lesions and with ctDNA fraction and extent of FES avid disease (TLER) in the 9 patients that had FES.

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Table 1. Categorical rankings for qualitative analysis of ctDNA, TLG and TLER

Table 1. Categorical rankings for qualitative analysis of ctDNA, TLG and TLER

ctDNA ranked categories (1-3) n=20 samples		
1 (low) n=6	0.000	0.085
2 (intermediate) n=8	0.085	0.108
3 (high) n=6	0.108	0.424
Categories of # of lesions from FDG TLG (1-3) n=19 scans		
1 (low) n=6	0	4
2 (intermediate) n=6	4	25
3 (high) n=7	25	142
Categories of # of lesions from FES TLWE (1-3) n=9 scans		
1 (low) n=1	0	4
2 (intermediate) n=4	4	25
3 (high) n=1	25	175

Table 2. FDG and FES imaging results and correlation with ctDNA

Table 2. FDG and FES imaging results and correlation with ctDNA

	# of FDG Lesions n=505	Total Lesion Glycolysis (TLG) SUVmean*mL	FDG SUVmax (index lesion)	# of FES Lesions n=408	Total Lesion Estrogen Receptor (TLER) SUVmean*mL	FES SUVmax (index lesion)
Mean (range)	28 (0-142)	1113.8 (0-6446)	9.2	45 (1-175)	1463.8 (15.2-6840.4)	12.1 (2.7-18.6)
Pearson correlation with ctDNA (R ²)	0.69	0.83	0.29	0.51	0.61	0.16

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7:00 AM - 8:15 AM

P2-04-01

Immunoexpression of markers related to the HER2 pathway in cases of pure positive her2 breast carcinoma treated with trastuzumab

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Introduction: Breast cancer is a heterogeneous disease with well-defined molecular subtypes and variable clinical behavior. The overexpressed HER2 subtype represents approximately 20% of all breast carcinomas. It is associated with a poor prognosis, increased risk of systemic and brain metastases, and poor overall survival until the advent of anti-HER2 therapies, such as trastuzumab. Its introduction into clinical practice has improved the prognosis in cases of breast cancer with overexpressing of pure HER2. However, some cases develop resistance to this drug. Objectives: To evaluate immunoexpression of possible markers involved in the HER2 pathway in breast carcinoma with overexpressing of pure HER2 treated with trastuzumab. Methods: We included 90 patients diagnosed with pure positive HER2 breast carcinoma treated with trastuzumab at the IBCC and HSP/Unifesp public hospitals between 2009 and 2018. Through immunohistochemistry, markers involved in the HER2 pathway (MUC4, IGF-1, IGF-1R, EGFR, p21, p27, p53, p16, cyclin D1, PTEN, CDK4, Bcl-2, VEGF, AR, MDM2, and TNF α) were analyzed samples paraffin-embedded of tumor and compromised lymph nodes and then, correlated with clinicopathological variables. The statistics were performed using the SPSS® software, version 25, from the company IBM, values equal to or less than 0.05 were considered significant ($p \leq 0.05$). To verify possible associations between the clinical-pathological variables and the analyzed markers, Pearson's X2 test, and Fisher's exact test were used; for survival analysis, the Kaplan-Meier method was used. Results: Treatment resistance of pure HER2-positive breast cancer cases after trastuzumab treatment was 40%; the OS of this series was 4.13 years (95% CI 5.1 - 12.5) and the DFS was 3.6 years (95% CI 5.1 - 13.1). In the tumor

samples it was possible to determine potential markers of good prognosis: cyclin D1 with nuclear grade ($p=0.049$) and recurrence ($p=0.038$); IGF-1 with tumor size ($p= 0.015$) and death ($p= 0.046$); p16 with response to treatment ($p= 0.016$); PTEN with response to treatment ($p= 0.050$) and death ($p= 0.030$). The results also showed possible markers of poor prognosis such as p53 with SBR GH ($p= 0.003$) and GN ($p= 0.048$); and IGF-1R with compromised lymph node ($p=0.016$). In compromised lymph nodes samples, the correlations showed TNF α with tumor size ($p=0.043$); and CDK4 with the response to treatment ($p=0.011$) as possible markers of good prognosis; only p53 with GH SBR grade ($p= 0.045$) maintained its potential for poor prognosis. Conclusions: In tumor samples, it was possible to demonstrate that the markers: cyclin D1, IGF-1, p16, and PTEN had the potential for a good prognosis panel and p53 and IGF-1R for worse. In samples of compromised lymph nodes, p53 remained as a marker of poor prognosis, while TNF α and CDK4 of good prognosis.

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7:00 AM - 8:15 AM

P2-05-01

Addressing barriers to adherence and quality of life among women recommended to receive chemoprevention for breast cancer prevention

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Aims: While women with breast cancer may have increased survival when compared to other cancers, aggressive, multi-modal treatments are often required with significant impact on quality of life and economic cost, highlighting the importance of breast cancer prevention and screening. For the estimated 10 million women in the United States who meet high-risk criteria for breast cancer, evidence-based interventions may be implemented to reduce risk, including long-term chemoprevention. Engaging in preventative care requires a healthy woman to navigate a complicated decision-making process involving the woman's perception of risk, access to information about risk and prevention strategies, access to care, social support, and the financial ability to manage cost of preventive care. Even with substantial evidence supporting chemoprevention for risk reduction, there is significant lack of uptake and adherence, especially among racial and ethnic minorities and underserved women. Given the missed opportunity for breast cancer prevention that this represents, it is critical to characterize the experience of women with chemoprevention to improve uptake and adherence to chemoprevention. Our aims were to explore the patient experience of women recommended to receive chemoprevention for breast cancer prevention. **Methods:** Sampling from a unique high-risk specialty care setting, we interviewed a diverse cohort of thirty women recommended to receive chemoprevention for breast cancer to learn about their experience in single semi-structured qualitative interviews. Content analysis was used to describe their experience and identify barriers to chemoprevention uptake and adherence. The MDASI-Breast was used to capture patient reported symptom burden at the time of interview. **Results:** Mean participant age was 54.6 years (range 34-87 years); 44.0% Hispanic; 20.0% Black; 81.0% receiving a selective estrogen receptor modulator, 19% receiving an aromatase inhibitor. Mean time since initiating chemoprevention was 14.0 months (range 1.1-49.3 months). At the time of the interview, women reported multiple symptoms, with the most severe reports of fatigue (mean severity 3.77, SD 2.91), sleep disturbance (mean severity 2.90, SD 2.47), problems with memory (mean severity 2.48, SD 2.07), drowsiness (mean severity 2.23, SD 2.14), and decrease in sexual interest or activity (mean severity 2.09, SD 2.38). In qualitative interviews, women reported barriers to preventive care related to symptom burden, access to care, access to accurate information, lack of understanding of breast cancer risk, and financial concerns. Content analysis found 20 symptoms related to both risk and preventive treatment, with 8 symptoms reported by $\geq 20\%$ of women. All women described distress related to their risk, with 23.8% of women describing sadness related to their risk. In addition, 33.3% of women reported distress related to the impact of their own risk on their family, primarily on their children. Women (23.8%) described breast changes that were present when their risk was identified, such as a lump or pain. Treatment-related symptoms varied based on type of endocrine therapy received and history of surgery and included sleep disturbance (23.8% of women), pain (28.6%), hot flashes/night sweats (33.3%), fatigue (28.6%), and joint stiffness or soreness (23.8%). Women shared ways in which symptoms impacted daily functioning, work, relationships, and ability to enjoy life. **Conclusions:** Women at risk for breast cancer recommended to receive chemoprevention experience multiple barriers to adherence including symptoms related to their risk and preventive care, access to care and accurate information, and financial burden. Interventions are needed to improve access to care and symptom management.

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P2-05-02

Potential Empowerment and risk of Genetic Counseling with Genetic Breast cancer risk assessment in Personalized Health Care : Prospective Cohort Study using Genetic Counseling Outcome Scale (GCOS-24)

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【Introduction】 Personalized health care is recommended for the prevention and early detection of breast cancer. Advances in technology have made it possible to estimate genetic risk, PGV (pathogenic/likely-pathogenic germline variant) or PRS (polygenic risk score), in practice. However, linkage after risk assessment to personalized health care is still developing. One of the issues is how to tell the result especially in case of newly diagnosed PGV after Genetic Panel Testing or PRS. In this study, we evaluated genetic counseling (GC) using an established patient-reported outcome measure for clinical genetics services scale (Genetic Counseling Outcome Scale²⁴ (GCOS24)) at genetic counseling for disclosure the results of the previous study, and examined the association with management after GC. **【Method】** We performed targeted sequencing for 11 breast cancer-related genes using peripheral blood DNA from 1995 female breast cancer patients. Of 1995 cases, 101 patients were PGV carriers, who were candidates of this study. Participants were referred to the Clinical Genetics unit, Kyoto University Hospital from 10 institutions (January 2018-March 2022). GCOS24 and relating questionnaires were asked before and after GC. GCOS24 is a scale consisting of 24 items that assess five factors: decision control, cognitive control, behavioral control, emotional regulation, and hope. (In light of the current status of hereditary breast cancer care in Japan, 23 items were used.) Each item is rated on a scale of 1-7 points, for a total score of 23-161. In addition, we reviewed medical records to evaluate the post-GC management. **【Results】** Of the 101 cases, 38 cases were enrolled. The reasons of 63 not-enrolled cases were: 30 cases without follow-up (deaths or transfer to another hospital), 11 cases already diagnosed in clinical practice, 18 cases that did not wish to know their results, and 4 cases whose hospital were developing for hereditary breast cancer care. Median age at the time of genetic GC was 55 (min-max 30-83) years. Details of PGV cases were: BRCA2 23 cases, BRCA1 2, PALB2 4, PTEN 3, TP53 3, ATM 1, CHEK2 1 and NF1 1. GCOS24 after GC were improved than before GC. (Average 99 (min-max 17-124) vs 114 (91-138), Mean difference 23.9, 95% Confidence intervals (CI) 29.6 to 18.3). Thirty patients (79%) had higher increase in scores than 10.3, which was the previously reported Minimum Clinically Important Difference (MCID) of this scale. In all items except 4 items (#6,11,13,21), GCOS24 after GC were significantly improved than before GC. In post-GC management, 8 patients received or planned RRSO (risk reducing salpingo-oophorectomy) among 25 BRCA1/2 cases. There was a case with dysplastic cells detected in the resected ovary. After GC, average of GCOS24 in RRSO cases was 120 (95% CI 110 to 129), while average of GCOS24 of other BRCA1/2 cases was 110 (95% CI 104 to 116). On the other hand, two patients stopped visiting to the hospital because of fear after GC. Average of GCOS24 of 15 junior-high/high school graduate cases were 111 (95% CI 105 to 117), while average of GCOS24 of 23 college graduate cases were 117 (95% CI 111 to 122). **【Discussion】** In patients diagnosed with hereditary breast cancer by genetic panel testing, GC worked well except for 4 items. These 4 items (#6,11,13,21) were related to emotion. This study revealed there was also a risk to reject surveillance due to fear, suggesting that it is necessary to provide psychological support in some cases. Although the limitation of this study is the small number of cases, GCOS24 were high in RRSO cases, suggesting that GC played

an important role when proceeding with intervention. We believe that the findings are helpful for the future implementation of genetic panel testing or PRS testing in healthy subjects for personalized health care.

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

P2-05-03

Perceived Guideline Clarity & Deferral to Patient Preferences impact guideline concordant care for breast cancer screening in women age 40-49

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Background: Canadian and US Task Forces recommend against routine mammography screening for women age 40-49 at average breast cancer risk on the basis that harms outweigh the benefits. Both cite the importance of supporting women's individualized decisions based on the relative value placed on potential benefits and harms of screening (2, 4). Population-based data reveal that screening rates in this age group are influenced by the woman's primary care provider (PCP), suggesting some providers refer more often than others. This highlights the need to explore PCP perspectives on screening and how this informs clinical behaviour.

Methods: Qualitative semi-structured interviews were performed by phone with PCPs in Ontario, Canada. Interviews were structured using the Theoretical Domains Framework (TDF) to explore determinants (barriers/facilitators) of three screening-related behaviours: 1) conducting a risk assessment; 2) discussion regarding benefits and harms; and 3) making a decision regarding referral for mammographic screening.

Analysis: Interviews were transcribed and analyzed iteratively until saturation was reached. Two independent researchers coded all transcripts deductively both by behaviour and according to TDF domain. Findings that did not fit within a TDF code were coded inductively. Data were then grouped by screening behaviour and the associated codes were used to generate descriptive narratives of the determinants influencing PCP behaviour.

Results: Eighteen physicians (mean age 48, 72% identified female) were interviewed. Table 1 outlines the determinants of the three screening behaviours. Analysis of inductive codes revealed two key contextual themes that influenced behaviours and moderated TDF codes: perceived guideline clarity (a lack of clarity on which behaviours (if any) were guideline-concordant) and deferral to patient preference (patient decision regarding screening without a complete discussion of benefits and harms). PCPs who perceived that the guidelines stated definitively that screening was not recommended had improved knowledge of harms and stronger beliefs about capabilities to educate patients about why screening was not recommended routinely. Deferral to patient preference seemed to occur when PCP's knowledge was low and/or if they were impacted by experience of a younger woman diagnosed with breast cancer, which often led to anticipated regret (TDF domain: emotion).

Discussion/Conclusion: Low knowledge related to formal breast cancer risk assessment, combined with a tendency to over-estimate benefits of screening relative to harms could explain some inappropriate variation in practice. All 3 PCP screening behaviours appeared to be affected by both perceived guideline clarity and deferral to patient preferences. These may all be effective targets for future interventions to address variation in care.

Table 1: Unique Barriers and Facilitators of Three Screening Behaviours

Table 1: Unique Barriers and Facilitators of Three Screening Behaviours					
Behaviour 1: Risk Assessment		Behaviour 2: Informed Discussion		Behaviour 3: Guideline Concordant Decision/Mammography Referral	
Facilitators	Barriers	Facilitators	Barriers	Facilitators	Barriers
	<ol style="list-style-type: none"> 1. Knowledge of risk factors & risk assessment tools 2. Skills to synthesize risk 3. Beliefs about consequences: tools don't guide management 	<ol style="list-style-type: none"> 1. Beliefs about capabilities / Skills for discussion to support patient choice 2. Professional Role to inform patients 	<ol style="list-style-type: none"> 1. Knowledge – incomplete knowledge of benefits and harms 2. Beliefs about Consequences: discussion of screening harms will sway patients against screening 	<ol style="list-style-type: none"> 1. Beliefs about capabilities to explain why screening not recommended 	<ol style="list-style-type: none"> 1. Knowledge / Beliefs about consequences: Overestimate benefits + underestimate harms of screening 2. Emotion: past experience & belief that screening would have changed outcome 3. Social Influence: radiology guidelines, patient concerns about cancer risk 4. Environment: actions of radiology departments to accept all referrals

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7:00 AM - 8:15 AM

P2-05-04

Safety of Breast MRI under General Anesthesia

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INTRODUCTION: Breast MRI (bMRI) has become a standard of care (SOC) modality for both screening and diagnostic work-up of breast disease (1-2). Despite availability of larger bores,

claustrophobia remains the most common reason for patients declining MRI (3). Anesthesia service can offer sedation during MRI improving patients' acceptance. However, unlike routine MRI, bMRI is performed with patient positioned prone. Our anesthesiologists observed patients' expectation of receiving general anesthesia, without understanding the risks associated with sedation/anesthesia in this particular setting and no prior trials of oral anxiolysis. **OBJECTIVE:** This project retrospectively reviewed bMRI exams with sedation for image quality and potential complication to identify areas for intervention such as provider education on anesthesiology risks in the bMRI environment and the implementation of an institution-approved oral anxiolysis program. **METHODS:** Patients receiving bMRI exams with sedation/anesthesia at a large academic cancer center were identified from the existing institutionally approved Report Imaging Quality Issue database after receiving institutional approval for this quality improvement project with waiver for consent obtained from Institution Review Board. Patient demographics, imaging data, and clinical notes were reviewed by two board certified breast radiologists with over 15 years of experience in MRI interpretation. Safety reports were reviewed in consensus between two radiologists and lead anesthesiologist for MRI department. **RESULTS:** Of 4844 bMRI exams, 33 were performed with sedation/anesthesia. Mean age was 60 years (range 37-77), with mean body mass index of 34 (range 21-45). Reason for anesthesia included claustrophobia in 13 (40%) patients, pain in 6 (18%), and 14 not clearly documented (42%). Eighteen of 33 (55%) exams were rated as poor quality, 7 (21%) as average, and 8 (24%) good or diagnostic. Most common reasons for poor quality included motion from snoring or pain and poor fat suppression due to body habitus. In 11/33 (33%), repeat imaging with still poor quality was documented in technologists' comments. Length of exam appointment ranged from 52 – 155, average 90 minutes. Only one case documented facial bruising due to prone positioning and one case of positioning requiring up to 7 staff. **DISCUSSION:** Availability of on-site anesthesia has enabled some patients to receive bMRI. These patients present to MRI with expectation of sedation/anesthesia without understanding risks or prior trial of anxiolysis and most have a challenging body habitus contributing to difficulty in prone positioning and decreased image quality while under sedation/anesthesia. Development of an oral patient anxiolysis program and provider education may improve image quality and reduce utilization of anesthesia.

Disclosure(s):

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P2-06-01

Improving the health of women on Aromatase Inhibitors: A pilot controlled dietary and exercise intervention trial

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Background: In spite of aromatase inhibitors reducing risk of recurrence and mortality, painful side effects often cause women to discontinue use of the drug. Side effects of aromatase

inhibitors include joint and muscle pain, loss of bone mineral density, and impairment of heart functioning. Discontinuation of aromatase inhibitors due to these side effects occur in up to 40% of breast cancer survivors, and consequently risks of recurrence and mortality increase. Objective: We developed two interventions designed to reduce inflammation, alleviate pain and stabilize bone mineral density. Methods: We are currently conducting a pilot parallel intervention trial that is targeted toward alleviating side effects from aromatase inhibitors through dietary and exercise controlled interventions lasting for three months. The dietary intervention is an anti-inflammatory Mediterranean diet designed to decrease inflammation and lessen joint and muscle pain. Participants randomized to the Mediterranean dietary intervention are exclusively consuming food provided by Territory Foods®, an outside food preparation and delivery service, local to Los Angeles. Our exercise intervention is designed to mobilize the joints, and strengthen and reduce bone loss. Participants are visiting the UCLA Kinross gym for three days per week and are undergoing tailored exercise sessions delivered from personal trainers following our bone strengthening intervention protocol. Anthropometric measures, muscle strength, DXA scanning of bone mineral density, peripheral arterial tonometry, pulse wave velocity and biomarkers of inflammation, bone turnover and heart functioning are conducted at baseline, mid- and end of intervention. Results: Our trial is targeted to accrue 20 participants. Thus far we enrolled six participants, with three participants completing the trial. Analysis is ongoing and preliminary results will be presented at the San Antonio Breast Cancer Symposium in December, 2022. Post intervention reports from participants have noted a reduction in pain symptoms, moderate weight loss and increase in muscle strength.

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12/7/2022

7:00 AM - 8:15 AM

P2-06-02

A randomized controlled trial of soy isoflavone intake on mammographic density among Malaysian women

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Introduction: Soy intake is associated with lower breast cancer risk in observational studies of Asian women, but clinical trials of soy isoflavone (ISF) supplements report no effect on biomarkers of breast cancer risk among Caucasian women. To date, there are no such trials among Asian women living in Asia. We conducted a three-armed, randomized controlled trial (RCT) to assess the effects of one-year intervention of soy isoflavone supplements (100mg/day) or soy isoflavones through diet (50mg/day) on mammographic density (MD) change among peri- and postmenopausal Malaysian women. Methodology: Healthy women

between 45-65 years old were enrolled between November 2018 and December 2019 at a private tertiary hospital in Malaysia. Women were randomly assigned into the 100mg/day ISF Supplement arm, 50mg/day ISF Diet arm, or Control arm. Dense area was assessed from digital mammograms conducted at enrolment and after 12 months. We compared absolute and relative change in dense area over the study period by study arm using Kruskal Wallis tests. Results: Of the 118 women who received the intervention, 91 women completed the study whilst 27 women (23%) were lost to follow up. After 12 months of intervention, women in the ISF Supplement arm observed a marginally larger decline in dense area (-1.3cm²), compared to women in the ISF Diet arm (-0.5cm²) and Control arm (-0.8cm²), but this difference was not statistically significant (p=0.479). Notably, these effects appear to be stronger and limited to women who enrolled within 5 years of menopause, where up to 6cm² decline in MD was observed in the ISF Supplement arm, compared to < 1.0cm in the Control arm (p=0.131). Conclusion: This RCT demonstrates a possible causal association between soy ISF intake and lower breast cancer risk among Asian women, specifically around the time of menopause, but these findings will require confirmation in a larger trial.

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P2-06-03

Dietary exposure to acrylamide and breast cancer risk: results from the NutriNet-Santé cohort

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Background: Acrylamide is classified as a probable human carcinogen by the IARC but epidemiological evidence on the carcinogenicity of acrylamide from dietary sources is limited. This study aimed to investigate the associations between dietary acrylamide and breast cancer risk in the NutriNet-Santé cohort. Methods: This prospective cohort study included 80,597 French women (mean [SD] age at baseline: 40.8 [14] years) during a mean (SD) follow-up of 8.8 (2.3) years. Acrylamide intake was evaluated using repeated 24h dietary records (n= 5.5 [SD 3.0]), linked to a comprehensive food composition database. Associations between acrylamide intake and breast cancer risk (overall, premenopausal and post-menopausal) were

assessed by Cox hazard models adjusted for known risk factors. Results: The mean (SD) dietary acrylamide intake was 30.1 (21.9) µg/d (main contributors: coffee, potato fries and chips, pastries and cakes, and bread). During follow-up, 1016 first incident breast cancer cases were diagnosed (431 premenopausal, 585 postmenopausal). A borderline significant positive association was observed between acrylamide intake and breast cancer risk overall (HRQ4 vs Q1= 1.21 [95% CI: 1.00-1.47]) and a positive association was observed with premenopausal cancer (HRQ4 vs Q1= 1.40 [95% CI: 1.04-1.88]). Restricted cubic spline analyses suggested evidence for non-linearity of these associations, with higher HR for intermediate (Q2) and high (Q4) exposures. Receptor-specific analyses revealed a positive association with estrogen receptor-positive breast cancer, which represented 86% of total cancer cases. Acrylamide intake was not associated with post-menopausal breast cancer. Conclusions: Results from this large prospective cohort study suggest the potential deleterious role of dietary acrylamide in breast cancer etiology, especially in premenopausal women, and provide new insights that should encourage further mitigation strategies to reduce the content of acrylamide in food.

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P2-06-04

Effects of BMI velocity on outcomes in patients with metastatic breast cancer in the Dallas Metastatic Breast Cancer Study

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BACKGROUND: The Dallas Metastatic Breast Cancer Study (DMBCS) is a clinical database that was established in 2021 at a single academic medical system to track patient demographics, associated pathology, treatments, and other variables that are not widely available in the Surveillance, Epidemiology, and End Results (SEER) Program for metastatic breast cancer (MBC). One of many ongoing studies as part of the DMBCS is to investigate how weight loss after diagnosis affects outcomes in MBC patients. Although previous studies have shown that significant weight loss is associated with poorer outcomes in certain cancer types, little is known about its role in breast cancer. **METHODS:** 139 patients who were diagnosed with MBC between 2009-2021 were included in this data collection. BMI at the time of diagnosis of MBC and within 6 months of death or last follow-up were recorded. BMI velocity was calculated by dividing the difference between BMI at diagnosis and BMI at time of death (or last follow-up) by the number of months between initial diagnosis and time of death (or last follow-up). The BMI velocity represents the rate at which patients lost or gained weight during their disease course. A negative BMI velocity indicates weight loss, and a positive BMI velocity indicates weight gain over the defined period. The absolute value of the BMI velocity indicates how rapidly someone gains or loses weight. The association of BMI velocity on the primary outcome (overall survival (OS) and progression-free survival (PFS)) was assessed using Cox proportional hazard (PH) model. Adjusted hazard ratios (HR) with 95% confidence intervals were computed using the multivariable Cox PH model. **RESULTS:** At the time of diagnosis of MBC, 40% were obese and 33% were overweight. At the time of death or last follow-up, 27% were obese and 31% were overweight. The mean BMI velocity was -0.13 per month. Contrary

to previous studies that have shown a negative effect of obesity on OS, we found that obesity at the time of diagnosis of MBC did not statistically worsen OS and PFS. However, compared to patients who had negative BMI velocities, improved OS (lower hazard ratio) was noted for patients with stable or increasing BMI velocities (HR = 0.53; 95% CI = 0.32-0.88, p = 0.014). A greater rate of weight loss was also associated with worse OS (HR = 0.23; 95% CI = 0.12 - 0.47, p < 0.001) and PFS (HR = 0.29; 95% CI = 0.16 - 0.52, p < 0.001). Improved PFS was seen for patients with stable or increasing BMI velocities in the unadjusted analysis (HR = 0.65; 95% CI = 0.42 - 0.99, p = 0.047). CONCLUSION: Our study found that contrary to previously published results in patients with early-stage breast cancer, obesity did not statistically worsen OS or PFS. However, the rate of weight loss, which we defined as BMI velocity, is associated with higher mortality in MBC. Our findings can be applied to clinical practice when advising MBC patients regarding healthy changes in weight during their disease course. BMI velocity could be used as a prognostic indicator to predict outcomes in patients with MBC. In future studies, we aim to quantify the amount of weight loss that is associated with worse outcomes.

Disclosure(s):

Mir Lim, MD: No financial relationships to disclose

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Anna Moscovitz, MD: No financial relationships to disclose

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P2-07-01

Hydroxytyrosol, a Component of Olive Oil for Breast Cancer Prevention in Women at High Risk

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Background Breast cancer is the most frequently diagnosed cancer in women in developed countries with increased incidence in women at high risk such as those with strong family history, BRCA mutations, atypical hyperplasia etc. Chemoprevention with drugs like tamoxifen and aromatase inhibitors come with challenges of intolerance and limited efficacy in estrogen receptor negative breast cancers. The purpose of our study was to evaluate the effects of hydroxytyrosol (HT), a component of olive oil on mammographic breast density reduction, which is a validated surrogate biomarker for breast cancer prevention as well as to explore on-target effects on Wingless-related integration site (Wnt) pathway, and alterations in key pathways of proliferation, DNA damage repair and stem cell function. **Methods** This study was conducted using 25mg/day oral dose of HT for 12 months in both pre- and post-menopausal women who are at increased risk of breast cancer with Gail 5-year risk score ≥ 1.67 and/or $> 10\%$ probability of BRCA mutation and had declined standard chemoprevention. These women underwent annual mammograms as well as had the option to have a biopsy of normal breast tissue before and after HT. Maximum volumetric breast density (Max VBD%) was assessed quantitatively using Volpara software (VIS 3.2) and the annualized percent decrease in max VBD% between baseline (BL) and end of treatment (EOT) with HT was analyzed in the study. RNA was extracted from the breast biopsies and RNA sequencing (RNA-Seq) and multiplex analysis of 28 proteins using NanoString nCounter analysis was performed to compare the BL with EOT samples. **Results** A total of 61 women were screened for the trial, 51 were enrolled and 41 patients completed the study. Median age for the study population was 54 years (range

35-76 years). There were 26 patients with paired BL and EOT mammograms. There were 14 patients with paired BL and EOT breast biopsies and seven patients with only BL and seven with only EOT biopsies. Mammographic density as measured by max VBD% showed a non-significant change of -0.038%, $p = 0.49$. However, on subgroup analysis in women 60-years or older, the mean decrease in max VBD% was - 3.7% ($p = 0.0391$), especially in those with high baseline mammographic density ($> 10\%$ baseline max VBD%). RNAseq data was generated from 15 BL and 17 EOT samples and pathways were confirmed by NanoString. Our bioinformatics pipeline identified 190 transcripts that were upregulated and 90 that were downregulated in EOT vs. BL by at least 1.5 fold. Reactome pathway R-HSA-195721 (Signaling by WNT) is identified as the top pathway enriched with EOT downregulated genes. On further review of the expression profiles, 82 of 261 member genes had p -value < 0.05 for EOT vs. BL, among which only 4 were upregulated and 78 were downregulated in EOT samples. These 82 genes were highly interactive with each other, with 379 high confidence protein-protein interactions (PPIs) (confidence score > 0.7 from STRING database) involving 81 out of 82 genes. In addition, mitotic telophase/cytokinesis ($p = 0.004$), ATM signaling ($p = 0.007$) were some pathways that were upregulated whereas, NOTCH signaling ($p = 0.007$), oxidative stress induced senescence ($p = 0.0001$) pathways were downregulated in EOT vs. BL. Conclusions Hydroxytyrosol, a component of olive oil did not show a decrease in breast density in the intention to treat population but showed some reduction in breast density in women 60-years of age and above, especially in those with high baseline breast density. HT showed on target effects by affecting Wnt signaling pathway, as well as decrease in proliferation. This study lays the foundation for future larger studies in exploring a natural compound such as HT for chemoprevention of breast cancer.

Disclosure(s):

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P2-07-02

Effects of different duration of prophylactic antibiotic use on unplanned reoperation in breast cancer patients undergoing implant-based breast reconstruction: A retrospective study with overlap weighting analysis

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Abstract Background: Some special consensus recommended the duration of perioperative antibiotic prophylaxis was within 24 hours postoperatively in breast cancer undergoing postmastectomy implant breast reconstruction. However, surgeons in practice favored to prolong the duration. The aim of this study was to estimate the effects of duration of antibiotics on major adverse outcomes in real clinical practice setting with diverse population using overlap weighting model. **Methods:** In this retrospective study, patients with breast cancer undergoing breast implant reconstructions were collected in Fudan University Shanghai Cancer Center from 1 January 2008 to 31 December 2021. Cases were divided into two groups according to the duration of perioperative antibiotic prophylaxis: short-term group (≤ 24 hours) and long-term group (>24 and ≤ 48 hours). The primary outcomes were unplanned reoperations and complication-related unplanned reoperations. Unplanned reoperation was defined as debridement, expander removal without prosthesis implantation, expander removal and expander implantation, prosthesis removal and prosthesis implantation, prosthesis removal, prosthesis removal and expander implantation. By reviewing the patients' detailed medical history, all unplanned reoperations were divided into non-complication-related unplanned reoperations and complication-related unplanned reoperations. Non-complication-related

unplanned reoperations included: patients voluntarily gave up continuing reconstruction, suspected recurrence of cancer, changed reconstruction methods, unsatisfactory appearance, and unknown reasons. Complication-related unplanned reoperations included: infection, exposure of prosthesis or expander, poor wound healing, rupture of expander, necrosis of skin flap, bleeding. The secondary outcomes were infections that required intervention. It was defined as both met with white blood cells elevation and physician antibiotic prescription during outpatient follow-up. To adjust confounders, propensity score overlap weighting was used, and subgroup analysis and sensitive test were conducted to demonstrate the robustness of results. A P value less than 0.05 was considered statistically significant. Results: In 4367 cases of unilateral implant reconstructions, 4128 (95%) were included in this study. Among them, 1689 were expander implantation, 1124 were prosthesis implantation and 1315 were expander removal and prosthetic implantation. At inclusion, only 283 cases (6.9%) received antibiotics prophylaxis ≤ 24 hours, 3090 cases (74.9%) with duration > 24 and ≤ 48 hours, and 755 cases (18.3%) with duration > 48 hours. Of them, 230 cases (5.6%) underwent unplanned reoperation, including 131 (3.2%) complication-related unplanned reoperations, and 99 (2.4%) non-complication-related unplanned reoperations. And there were 110 cases (2.7%) with infections that required intervention. In unweighted or weighted data set, short-term antibiotic use did not significantly increase the risk of adverse outcomes, including unplanned reoperation, complication-related unplanned reoperation, and infection required intervention, compared with long-term antibiotic use with or without patients with duration more than 48 hours. Most subgroup analysis showed no evidence of heterogeneity of the effects of duration of antibiotic use on adverse outcomes. Conclusion: In clinical setting with diverse population, prolong antibiotic prophylaxis with more than 24 hours is not necessary to reduce major adverse outcomes, even in some critical conditions. Appropriating and accessible prophylactic initiatives should be developed and implemented with shorten the duration of antibiotic prophylaxis and minimized adverse outcomes. Key words: perioperative antibiotic prophylaxis, breast cancer, postmastectomy implant reconstruction, unplanned reoperation

Disclosure(s):

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P2-08-01

Licochalcone A from licorice reprograms metabolic and antioxidant pathways in the breast leading to a tumor preventive environment.

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Background: Increased adiposity is a risk factor for postmenopausal breast cancer. It is often accompanied by chronic low-grade inflammation and elevated levels of reactive oxygen species, which drive breast tumorigenesis. Risk reducing drugs such as selective estrogen receptor modulators and aromatase inhibitors, which have demonstrated efficacy, have had a significantly low acceptance among women at high risk for breast cancer. This hesitancy is mainly due to the adverse side effects of these medications such as vasomotor symptoms, osteoporosis, thromboembolism, and uterine cancer. Therefore, alternative strategies with lower toxicity and greater acceptability are needed. We have previously shown that licochalcone A (LicA) from licorice (*Glycyrrhiza inflata*), which has osteogenic effects, suppresses aromatase expression and activity, enhances the activity of detoxifying enzymes, and reduces estrogen genotoxic metabolism in cell lines and animal models. However, its effects on the breast tissue of high-risk women are understudied. We hypothesize that LicA creates a tumor preventive environment in the breast by locally modulating adipogenesis and antioxidant/anti-inflammatory responses leading to decreased proliferation. Methods: We prepared microstructures from fresh tissue of contralateral unaffected mastectomy specimens of 6 postmenopausal women with incident unilateral breast cancer. We exposed these to DMSO (control) and LicA (5 μ M) for 24 h. Employing total RNA sequencing, we examined differential gene expression between treated and control samples. Up-regulated and down-regulated genes were analyzed using Enrichr gene ontology (GO) pathway analysis. Enriched pathways with combined enrichment scores > 4 and FDR < 0.05 were considered statistically significant. Metabolism flux analysis was performed (FDR < 0.05). Live cell imaging to monitor proliferation of pre-malignant DCIS.COM, DCIS.COM/ER+ PR+; and malignant MDA-MB-231 (ER- PR-), MCF-7 (ER+ PR+), MCF-7aro, and BRCA1 defective HCC-1937, and HCC3153

cells was conducted using IncuCyte. Single versus repeated dosing of various concentrations of LicA were also evaluated. Results: We observed significant ($P < 0.05$) upregulation up to 8-fold of antioxidant genes, consistent with significant upregulation of NRF2, the major regulator of antioxidant pathways. This was accompanied by significant ($P < 0.05$) downregulation of NF- κ B dependent inflammatory pathways. In addition, we observed the significant ($P < 0.05$) downregulation, ranging from 4 to 32-fold of cholesterol biosynthesis and transport, steroid hormone biosynthesis, as well as lipid metabolism genes, consistent with the profound downregulation of SREBF1 and SREBF2, which encode the master regulator of adipogenesis, SREBP. Metabolic flux results demonstrated a robust increase ($FDR < 0.05$) in the pentose phosphate shunt and NAD(P)H generation without enhancing ribose 5 phosphate formation, confirming an antioxidant and anti-proliferative environment. Likewise, LicA suppressed proliferation of pre-malignant and malignant cells dose- and time-dependently. Repeated dosing of lower concentrations of LicA ($< 10 \mu\text{M}$) demonstrated sustained antiproliferative effects even in the aggressive cancer cell lines. Conclusion: Our data suggest that LicA can generate a tumor-preventive breast microenvironment by reprogramming metabolic pathways involved in steroid and lipid homeostasis and antioxidant responses. These observations along with its low toxicity, suggest that LicA is a good candidate for further investigation as a breast cancer prevention agent.

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Atieh Hajirahimkhan, PhD: No financial relationships to disclose

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An Emerging Technology for Breast Cancer Detection - Preliminary Data of Breast Cancer Detection using Novel Low Dose Positron Emission Mammography

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Purpose: To investigate the feasibility of low-dose Positron Emission Mammography (PEM) to identify breast cancer. **Materials and Methods:** In an REB-approved ongoing clinical trial, which started in December 2019, all newly diagnosed women with breast cancer who had not undergone neoadjuvant chemotherapy and consented to the study were randomly assigned independently of their mammographic breast density, tumor size, and histopathology cancer subtype to perform PEM using a novel organ-targeted PET system (Radialis PET Imager, Radialis Inc., FDA cleared to image and measure the distribution of injected positron-emitting radiopharmaceuticals) with either 1mCi, 2mCi or 5 mCi of 18F-FDG. The PEM images acquired 1 and 4 hours after 18F-FDG administration were reviewed in consensus by two fellowship-trained breast radiologists blinded to cancer location. PEM imaging features of known malignancies and additional PEM findings were recorded and correlated with histopathology as the ground truth. **Results:** Our cohort comprised 22 women with a median age of 51 years (range 32-85) with 88 completed bilateral sets of images where 23 cancers (18 invasives, and 5 in situ) were present. The median invasive cancer size on surgical pathology was 28 mm (range: 3-120). Out of 18 invasive cancers, the only PEM images that did not visualize cancer (2 invasive lobular cancers and 2 in-situ cancers) were acquired with the lowest dose of 18F-FDG (1 mCi). A total of 6 (27.3%) subjects received 1mCi 18F-FDG with 5 invasive cancers, 7 (31.8%) of patients received 5 mCi 18F-FDG with 7 invasive cancers, and 9 (40.9%) of patients received 5 mCi 18F-FDG with 6 invasive cancers. A total of 3 false-positive images of benign findings were also present. No additional cancers were identified exclusively by PEM. The PEM performance was similar following an additional 3-hour interval for radiotracer uptake. **Conclusion:** This preliminary data results show the feasibility of invasive breast cancer detection with a decreased 18F-FDG dose, possibly due to the novel PEM system detectors increasing the sensitivity to radiotracer and the perceived spatial resolution by the visual assessment. Larger-scale clinical trials are required to consolidate our preliminary findings. **Clinical Relevance:** A novel organ-targeted PET system enables the detection of invasive breast cancer using low-dose PEM, potentially emerging as a promising novel imaging tool.

Disclosure(s):

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7:00 AM - 8:15 AM

P2-09-02

Noninvasive Detection of Lymph Node Involvement in Subjects with Human Epidermal Growth Factor Receptor 2 Positive (HER2+) Breast Cancer using the MagSense® HER2 Test Reagent – A First-In-Human Phase 1 Study

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Introduction Iron oxide nanoparticles have been used in preclinical and clinical research as imaging agents for decades because of their magnetic properties and their known safety profile. We have been developing the MagSense® HER2 Test Reagent (MSH2TR), a formulation of anti-human epidermal growth factor receptor 2 (HER2) conjugated iron oxide nanoparticles, for the noninvasive detection of metastatic lymph nodes to aid in staging of HER2 positive (HER2+) breast cancer patients. Currently, nodal staging requires a patient's lymph nodes to be surgically removed or biopsied for histopathological examination. MSH2TR is currently being investigated in a first-in-human phase I study in subjects with HER2+ primary breast cancer who, in the judgment of the investigator, have a likelihood of lymph node metastasis. Methods This phase I study is designed to be a preliminary proof-of-principle study with the primary objective of achieving an initial assessment of the safety and tolerability of the MSH2TR injectable imaging agent. A secondary objective of the study is the confirmation that the route of administration is effective in allowing the imaging agent to reach the patient's lymph nodes. The exploratory objectives of the study include a comparison of the two imaging modalities: magnetic resonance imaging (MRI) and a novel proprietary technology called magnetic relaxometry (MRX), to standard clinical tissue histopathology. The exploratory objectives are expected to provide a preliminary assessment as to whether the MagSense® HER2 imaging agent, when used with one or both imaging modalities, might be able to provide a non-invasive alternative to nodal biopsy. All eligible subjects receive a 30mg injection of MSH2TR into the subareolar interstitial tissue or area near and around the primary tumor. MRI of the axilla are performed before and 24 to 72 hours after MSH2TR injection followed by core biopsy or dissection of the suspected lymph node tissue as per standard of care (SOC) procedures for histopathology assessments and also for ex vivo MRX measurements using the MagSense® Relaxometry Instrument. Review of the MRI scans and histopathology are performed in respective central laboratories. The study is currently enrolling in 4 clinical sites in Australia. Results From an interim evaluation of the first five patients that have completed the study, MSH2TR appears to be safe and well tolerated and no safety issues reported related to the imaging agent. The imaging agent, as administered, is reaching the lymph nodes. The study

intends to enroll approximately 15 patients for the preliminary efficacy assessment. Safety and efficacy results from available patients' data will be presented. Conclusion Available data to date from the ongoing phase I study show that the MagSense® HER2 imaging agent, as administered, appear to be safe and drains to the axillary lymph nodes within the timeframe of interest. Further data collection is ongoing for the preliminary evaluation of efficacy.

Disclosure(s):

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P2-09-03

Quantification of HER2 expression and spatial biology using computational pathology: A cross-assay validation study in breast cancer

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Background Conventional pathologic scoring of HER2 by IHC is proven to distinguish potential responders to trastuzumab but has not been effective for next generation antibody drug conjugates (ADCs) such as trastuzumab deruxtecan (T-DXd), which is capable of bystander killing. Several alternative approaches have been deployed to measure HER2, including immunofluorescence and mRNA sequencing. We have developed a novel and fully automated computational pathology technique, Quantitative Continuous Scoring (QCS), to quantify the level and distribution of HER2 from digitized HER2 IHC slides in an objective, quantifiable, and reproducible manner on a per-cell basis [Gustavson et al., SABCS 2020]. To further validate this approach, we performed a systematic multi-omic comparison of QCS to orthogonal methods of HER2 quantitation on a cohort of primary and metastatic breast cancer cases (N=30). Methods HER2 was evaluated using three independent methods on serial tissue

sections obtained from 30 archival FFPE breast cancer samples distributed over the full range of HER2 expression, from 0 to 3+. HER2-IHC staining (clone 4B5, Roche Tissue Diagnostics) was performed using standard methods and cases were scored by two pathologists using CAP/ASCO guidelines and H-scores were assigned. We performed FISH (HER2 IQFISH pharmDx [Dako]; PathVysion HER-2 DNA Probe Kit [Vysis]), mRNA quantification of ERBB2 transcript levels (Nano String), and immunofluorescence (IF; HER2 clone 29D8, CST). Imaged with Vectra (Akoya) and analyzed with Halo (Indica). QCS readouts were generated from the above-mentioned digital images of IHC slides by using a fully automated image analysis pipeline; readouts included per-cell staining intensity measurements of membranes and cytoplasmic sub-compartments in terms of optical density (OD) [Van der Laak, JQCS 2000], which were aggregated to a single slide-level score. Additionally, using the OD measurements and the cell locations, a Spatial Proximity Score (SPS) was computed, summing the percentage of cells with $OD \geq 10$ (corresponding to the limit of visual detection of IHC staining) as well as the percentage of cells with $OD < 10$ within a prespecified radius ($25\mu\text{m}$) of a neighboring cell with $OD \geq 10$. Results Our analysis demonstrated that QCS-based scoring correlates with orthogonal measurements used in this study. Comparing protein-based assays, the observed Pearson correlation was $R=0.88$ between QCS median membrane OD and IHC H-scores, $R=0.86$ with IF-based HER2 mean cell expression intensity, and $R=0.85$ with IF-based H-scores. Correlation with transcriptomic profiling was $R=0.81$ for OD vs. mRNA, however ERBB2 transcript levels did not distinguish between HER2 0, 1+, and 2+ FISH negative cases, while QCS was able to do so. Correlation between protein-based and nucleic-acid based assays were numerically worse, with $R=0.64$ for OD vs. FISH. All samples (including those with HER2 IHC scores of 0 and H-Scores < 10) had at least ~20% of cells with quantifiable HER2 expression by OD, the presence of which was confirmed using IF. For cases in the lowest quartile of HER2 expression by OD, SPS identified 20-50% additional HER2-null cells that were in close proximity to HER2-expressing cells that may be vulnerable to bystander killing. Conclusion QCS-based scoring is consistent with orthogonal protein-based measurements across the range of HER2 expression. Most importantly, QCS derived-spatial analysis features identify additional patients in the lower end of HER2 expression that might be highly relevant for ADC response prediction, particularly if a drug exerts bystander activity. Further clinical verification and validation on large cohorts is needed. Footnote: This study was approved by the IRB at MSKCC.

12/7/2022

7:00 AM - 8:15 AM

P2-10-01

Correction of gradient non-linearity in multi-site multi-vendor Breast DWI: initial characterization and evaluation of effects on quantitative tumor ADC measures

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Background

Diffusion-weighted imaging (DWI) is an MRI technique that does not require a contrast agent and can provide quantitative information on tissue microstructure in the form of calculated metrics such as the apparent diffusion coefficient (ADC), which reflects the mobility of tissue water. Initial studies have shown promising results evaluating changes in tumor ADC to predict treatment response in breast cancer patients receiving neoadjuvant chemotherapy¹.

One limitation of quantitative DWI is that MRI scanner gradient non-linearity (GN) results in spatially varying diffusion-weighting gradients, resulting in a bias in calculated ADC values². This effect increases for imaging at greater distances from the magnet isocenter, as required for breast imaging. GN effects are a concern for utilizing ADC as a biomarker of response or for diagnostic use in the clinical trial setting, as they may introduce confounding bias in ADC measures: across different patients, in the same patient at other time points, and between the ipsilateral and contralateral breasts. Previous work has demonstrated that GN effects can be corrected across leading clinical multiple MRI scanner vendors resulting in more accurate ADC values³.

The goal of this work was to implement multi-vendor GN correction (GNC) of DWI data acquired in breast cancer patients receiving neoadjuvant chemotherapy (NAC) from the

multicenter I-SPY 2/ACRIN-6698 trials and evaluate the effects of GNC on 1) cross-sectional tumor ADC values across multiple MRI scanner platforms and 2) on longitudinal changes of ADC values for treatment response evaluation.

Methods

This retrospective analysis utilized DWI data ($b=0, 800$ s/mm² or $b=0, 100, 600, 800$ s/mm²) acquired in women diagnosed with high-risk, stage II/III breast cancer. Patients were recruited from 19 institutions, and data included DWI from 11 different gradient systems from three leading MRI scanner vendors (General Electric, Philips, and Siemens), utilizing both 1.5T and 3T scanners. DWI data acquired before initiation of treatment (T0) and three weeks after the start of NAC (T1) were analyzed. A vendor-agnostic GN correction program³ utilizing vendor-supplied spherical harmonics for gradient characterization was used to generate GN-corrected ADC maps from the DWI data retrospectively corrected. Tumor regions of interest (ROIs) encompassing tissue appearing hyperintense on DWI ($b=800$ s/mm²) images and hypointense on corresponding ADC maps were defined on multiple DWI imaging slices encompassing the full extent of the tumor. The ROIs were applied to both uncorrected and GNC ADC maps. The uncorrected and GNC tumor ADCs were evaluated for mean, standard deviation, and percentage change resulting from GNC. Statistics were calculated for the entire cohort and separately for each MRI scanner gradient system. The effect of GNC on the mean ADC change from T0 to T1 was also evaluated.

Results

A cohort of 131 patients with 262 DWI exams was included in this analysis. Uncorrected and GN corrected mean tumor ADC and Std Dev are shown in Table 1. For DWI in the whole cohort, GNC reduced the tumor ADC from -9.04% to -0.03% from all the gradient systems across vendor platforms. GNC also decreased the Std Dev of ADC distribution from -8.70% to -4.06% from all systems. These align with previous published phantom results and the single vendor investigation.

Tumor ADC value changes measured between baseline (pre-treatment, T0) and after three weeks of treatment (T1) show a small impact from GNC correction (Table 2).

Discussion

This retrospective study of applying GN correction to DWI data acquired in the clinical trials from multiple imaging sites utilizing MRI scanners manufactured by different vendors demonstrated the effect of gradient correction on the tumor ADC measurement.

References

1. Newitt DC et al. JMRI 42(4):908-19, 2015
2. Malyarenko DI et al. Tomography 6(2): 86-92, 2020
3. Malyarenko DI et al. Tomography 1(2): 145-151, 2015

ADC value changes with and without GNC from multi-vendor and multi-gradient systems

	System	Field	# of Exams	Mean ADC (Without GNC) (10 ⁻³ mm ² /sec)	Mean ADC (With GNC) (10 ⁻³ mm ² /sec)	% Change in mean ADC from GNC	Std Dev of ADC (Without GNC) (10 ⁻³ mm ² /sec)	Std Dev of ADC (With GNC) (10 ⁻³ mm ² /sec)	% Change in ADC Std Dev from GNC
Vendor_1	System1	1.5T	128	1.03	0.93	-9.04%	0.127	0.120	-6.15%
	System2	1.5T	24	1.00	0.97	-2.55%	0.155	0.147	-4.91%
	System3	1.5T	12	1.13	1.05	-7.15%	0.113	0.106	-6.44%
	System4	3T	32	1.08	0.98	-8.78%	0.179	0.167	-6.00%
	System5	3T	4	1.03	1.00	-2.16%	0.179	0.158	-8.70%
Vendor_2	System1	1.5T	18	1.01	1.00	-0.61%	0.165	0.152	-6.91%
	System2	1.5T	4	0.99	0.98	-0.68%	0.129	0.111	-8.76%
	System3	3T	4	1.16	1.13	-3.00%	0.170	0.152	-6.06%
Vendor_3	System1	1.5T	26	1.03	1.03	-0.03%	0.148	0.137	-7.24%
	System2	3T	6	0.96	0.96	-0.96%	0.104	0.099	-4.06%
	System3	3T	4	0.92	0.89	-3.44%	0.150	0.145	-4.69%

GNC impacts on the initial longitudinal changes in tumor ADC from multi-vendor and multi-gradient systems

	System	Field	# of Exams	% Change of Mean ADC after three weeks of treatment (T1-T0) (Without GNC)	% Change of Mean ADC after three weeks of treatment (T1-T0) (With GNC)	% Change from GNC after initial treatment
Vendor_1	System1	1.5T	128	14.80%	14.81%	0.01%
	System2	1.5T	24	6.39%	6.28%	-0.12%
	System3	1.5T	12	19.77%	19.63%	-0.14%
	System4	3T	32	10.94%	11.09%	0.16%
	System5	3T	4	14.83%	15.40%	0.57%
Vendor_2	System1	1.5T	18	12.22%	12.25%	0.03%
	System2	1.5T	4	4.62%	4.61%	0.00%
	System3	3T	4	12.54%	12.99%	0.46%
Vendor_3	System1	1.5T	26	11.60%	11.64%	0.04%
	System2	3T	6	21.38%	21.31%	-0.07%
	System3	3T	4	8.79%	8.51%	-0.28%

Disclosure(s):

Jiachao Liang, PhD: No financial relationships to disclose

Lisa J. Wilmes, PhD: No financial relationships to disclose

Dariya Malyarenko, n/a: Philips Medical Systems (PMS): Coinventor on intellectual property assigned to and are managed by the Univ of MI licensed to PMS for the technology (Ongoing)

David C. Newitt, PhD: Kheiron Medical Technology: research support to an institution outside the submitted work (Ongoing)

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Thomas Chenevert, n/a: Philips Medical Systems (PMS): Coinventor on intellectual property assigned to and are managed by the Univ of MI licensed to PMS for the technology (Ongoing)

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7:00 AM - 8:15 AM

P2-10-02

Impact of neoadjuvant treatment on the accuracy of breast MRI and calliper in premenopausal ER-positive, HER2-negative, and node-positive breast cancer patients: Prospective phase III clinical trial

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Background: Improved understanding of factors affecting the accuracy of breast MRI after NST can lead to more tailored use of MRI in deciding surgical extent after NST. **Purpose:** To investigate whether the accuracy of magnetic resonance imaging (MRI) and caliper predicting residual tumor extent is affected by neoadjuvant treatment in estrogen receptor (ER) positive and HER2-negative, lymph node-positive, premenopausal breast cancer breast cancer. **Materials and Methods:** We analyzed the imaging and clinicopathologic data of 123 patients in phase 3, randomized clinical trial (NCT01622361), which compared neoadjuvant chemotherapy (NCT) with neoadjuvant endocrine therapy (NET) in estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2-), lymph node (LN)-positive, premenopausal breast cancer patients. In this study, we compared the largest size of MRI and Caliper after neoadjuvant treatment with one of pathology. **Results:** In patient with discrepancy in predicting response to NST, the measurement (MRI or caliper) that predict as non-response (SD or PD) was more accurate in both of NCT and NET group (ICC, Intraclass correlation coefficient, MRI; 0.84, 95% CI 0.616-0.942, Caliper; 0.75, 95% CI 0.303-0.931). The accuracy of MRI was better in NCT group than in NET group (ICC 0.86; 95% CI 0.626-0.956 for NCT, 0.47; 95%CI 0.133-0.708 for NET). The mean absolute discrepancies (largest size by MRI or caliper - largest size in pathology) for the MRI and Caliper were, respectively, -0.78cm and -1.04cm in NCT group and -0.44cm and -1.32cm in NET group ($p > 0.05$). The proportion of discrepancy $>1\text{cm}$ or $>0.5\text{cm}$ were not significantly difference between NCT and NET groups among MRI and Caliper. **Conclusion:** In ER-positive, HER2-negative, lymph node-positive breast cancer, both MRI and caliper tend to overestimate residual tumor size than pathology in NET group compare to NCT group. When MRI and caliper show discrepancy in predicting response to NST, the measurement (MRI or caliper) that predict as non-response (SD or PD) was more accurate in both of NCT and NET group. These factors should be considered for deciding the evaluation method of response and surgical decision after NST and surgical decision in this subgroup. **REGISTRATION:** ClinicalTrials.gov identifier: NCT01622361

Disclosure(s):

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Kyung Hae Jung, MD, MS, PhD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Celgene: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi-Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Ongoing); Everest Medicine: Consulting Fees (e.g., advisory boards) (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Third-party writing assistance for this abstract, furnished by Sunaina Indermun, BPharm, PhD, of Health Interactions, was provided by Roche (Ongoing); Takeda: Consulting Fees (e.g., advisory boards) (Ongoing)

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12/7/2022

7:00 AM - 8:15 AM

P2-11-01

Secondary endocrine resistance and high Ki-67 labeling index ($\geq 20\%$) in patients with low genomic risk identified by 21-gene recurrence score

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Introduction: Although breast cancer with high Ki-67 index are likely to have high genomic risk, some of these might have low genomic risk. In ER+HER2- breast cancer patients with low genomic risk identified by the 21-gene assay, we addressed a clinical significance of Ki-67 index in terms of recurrence-free survival (RFS). Methods: We retrospectively identified 2,295 patients with ER+HER2- breast cancer who underwent the 21-gene assay (Oncotype DX®). High Ki-67 LI was defined as 20% or greater, and low genomic risk was defined by recurrence score (RS) from the assay (< 26). Recurrence after 3 year was regarded as secondary endocrine resistance, which is defined as recurrence while on 2 years of adjuvant endocrine treatment. Results: In all patients, Ki67 index assigned 870 (38%) as the high and 1,425 (62%) as the low groups. Thirty percent (263/870) of the high Ki67 index had high genomic risk, whereas 84/1425 (6%) of the low Ki67 did. Among the patients with low genomic risk who did not receive chemotherapy (n=1,807), high Ki67 index was an independent poor risk factor for recurrence. Furthermore, recurrence after 3 years differed significantly according to Ki-67 index (P=0.003), whereas recurrence within 3 years did not differ (P=0.900). Multivariable analysis demonstrated high Ki67 index as a risk factor for recurrence after 3 years (hazard ratio 3.12;

95% confidence interval, 1.28–7.66). Conclusions: In ER+HER2- breast cancer with low genomic risk identified by 21-gene RS, high Ki67 index is associated with secondary endocrine resistance. Novel approach with CDK4/6 inhibitors is demanded to overcome secondary endocrine resistance in tumors with high Ki67/low genomic profile.

Disclosure(s):

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7:00 AM - 8:15 AM

P2-11-02

BIOMARKERS RELATED TO SURVIVAL BENEFIT IN THE TREATMENT OF METASTATIC LUMINAL BREAST CANCER (mBC) WITH CYCLIN 4/6 INHIBITORS (CDK 4/6i) PLUS ENDOCRINE THERAPY (ET)

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Treatment with CDK4/6i plus ET is the standard treatment for mBC with a significantly better progression free survival (PFS) and a long treatment duration response, although there's finally a progression. The expression of cyclin E and progesterone receptor had been related to survival, so analyzing of these potential biomarkers could help to select their effect in patients with a long treatment duration (> 20 months).
We evaluate 68 mBC treated with CDK4/6i plus ET as a clinical practice in a single institution.

Median age was 68 years, 27(39,7%) patients had de novo metastatic disease, 17 (25%) progressed during ET adjuvant, and 24 (35,3%) progressed after 5 years of ET. Forty-eight patients (70%) received CDK4/6i plus ET in first line and visceral disease was present in 40% of patients. The median expression by histoscore with immunohistochemistry of cyclin E (CycE) was 75,3 (4-97) and progesterone receptor (PR) 121.

Median PFS was 16 months (8,3- 23,6) with 45 events, 25 months in patients treated in first line and 12 months in second line (p: 0,0001). We analyzed 59 patients who had already completed CDK4/6i plus ET or had achieved a PFS more than 20 months, 40 (69%) in first line and 18 (31%) in second line. We summarized the related of expression of PR, CycE and this combination with PFS more than 20 month.

CONCLUSION

Treatment with CDK4/6i plus ET achieved long treatment duration in patients with low expression of cyclin E (OR 3,1 p:0,045), positive progesterone receptor (OR 3,89 p: 0023) and specially in patients with positive progesterone receptor and low expression of cyclin E (OR 7,22 p:0,016). Patients with negative progesterone receptor and high expression of cyclin E had a poor prognosis with a median disease-free survival of 6 months (2.8 – 9.2), so these patients required other treatment approaches to improve their outcomes.

DFS (MONTHS)	LINE OF TREATMENT		PROGESTERONE RECEPTOR		CYCLINE E	PROGESTERONE+CYCLINE	
	First line	> 1 line	positive	negative	Cycline E	PR>100+Cyc E<70	PR<100+Cyc E>70
<20 months	23 (57,5%)	15 (83%)	11 (47,8%)	25 (78%)	24(77%)	5 (38%)	17 (89%)
>20 months	17 (42,5%)	3 (17%)	12 (52%)	7 (22%)	7 (23%)	8 (62%)	2 (11%)
OR	3,69 (p:0,065)		3,89(p:0,023)		3,1 (p:0,045)	7,22 (p:0,016)	0,23 (p:0,02)

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P2-11-03

How to make decisions in ductal carcinoma in situ? The first study of clinical applicability of the MSKCC ductal carcinoma in situ nomogram in the prediction of local recurrence risk after breast conserving surgery in a Brazilian cohort

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ABSTRACT Introduction: Radiation therapy (RT) plays an important role in the management of patients with ductal carcinoma in situ (DCIS) of the breast, treated by breast conserving surgery (BCS). RT reduces significantly the risk of local recurrences (LR). Efforts are being, currently, to de-escalate RT in this scenario with individualized decision-makings. Several biomarkers and clinical tools were developed to predict the probability of LR and aid a tailored clinical decision. The aim of this study is to assess the potential of the MSKCC DCIS Nomogram, which combines clinical, pathologic, and treatment features to forecast LR after BCS for DCIS patients and assist physicians to recommend RT. Methods: Were enrolled into the study women with DCIS undergoing BCS, with clear surgical margins, and external RT from 1993 to 2018 at a specialized breast cancer service in São Paulo, Brazil. The data were collected from medical records. The MSKCC DCIS Nomogram was applied to the study population. Receiver operating characteristic curve were drawn and the area under the curve (AUC) of 10-year risk of LR evaluation was calculated. Results: 110 women were eligible. Eight patients had LR (7,3%), being 5 invasives (62,5%) and 3 in situ (37,5%). The follow-up mean time was 4.8 years. Time to recurrence was 9.6 years with a 10 years risk of LR of 10,3%. The MSKCC DCIS Nomogram 10-year risk estimates showed satisfactory correlation as regard to LR with the AUC of 0.61.

The nomogram is warranted for the 10-year risk LR prediction, and it may reinforce RT indication. Conclusions: The MSKCC DCIS Nomogram may identify patients with DCIS treated by BCS with high probability of LR, and therefore is a useful treatment decision aid for patients with DCIS and may assist the RT recommendation.

Disclosure(s):

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Effects of Intrinsic Subtypes and 21-gene Assay on the Early and Late Recurrence Risks in Patients with Early Stage HER2+ Breast Cancer: An Analysis of the North Central Cancer Treatment Group (NCCTG) N9831 (Alliance) Trial

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Background: We previously demonstrated that intrinsic subtypes were associated with prognosis for early recurrence risk in patients (pts) with early-stage HER2-positive (HER2+) BC treated with trastuzumab (H) in the N9831 trial. Here, we evaluated the prognostic value of Intrinsic subtypes and 21-gene assay and the risk of early and late recurrence in the N9831 trial. Methods: NanoString custom code set, which included PAM50 and housekeeping genes, was used to quantify mRNA and generated intrinsic subtypes and risk of recurrence (ROR) score from the N9831 trial in Arms A and C: Arm A chemotherapy alone and arm C concurrent H. Quantitative RT-PCR of 21 genes, calculation of the axis, including estrogen axis (ER, PGR, BCL2, SCUBE2), HER2 axis (GRB7, HER2), proliferation axis (Ki67, STK15, Survivin, CCNB1, MYBL2), invasion axis (MMP11, CTSL2), and recurrence score (RS) risk group assignment (RS group 1 and 2: RS < 31 and RS group 3: RS ≥ 31) were performed using Oncotype DX assay. Cox regression models for RFS were used for analysis. Early recurrence was defined as a recurrence that occurred at ≤ 5 years, and late recurrence was defined as recurrence at > 5 years. Results: A total of 783 patients (Arm A 409 and Arm C 374) were included in this analysis. Using multivariate Cox regression analysis to evaluate the risk of early recurrence in

patients who received chemotherapy alone in arm A, both invasion genes (MMP11 HR 1.23, 95%CI 1.05-1.44, p 0.01 and CTSL2 HR 1.36, 95%CI 1.1-1.69, p 0.005) and invasion axis (HR 1.64, 95%CI 1.26-2.13, p < 0.001) were associated with a higher rate of early recurrence. CD68 was associated with improved outcomes (HR 0.56, 95%CI 0.38-0.83, p 0.004). For the risk of early recurrence in patients treated with trastuzumab in arm C, ER (HR 0.85, 95%CI 0.74-0.97, p 0.02), PR (HR 0.78, 95%CI 0.64-0.94, p 0.008), and estrogen axis (HR 0.7, 95%CI 0.57-0.87, p 0.001) were associated with improved outcomes. Invasion axis (HR 1.61, 95%CI 1.08-2.41, p 0.02), Oncotype Dx risk group (3 vs. 1 and 2, HR 8.89, 95%CI 1.27-1124, p 0.02), and basal subtype (HR 2.77, 95%CI 1.1-5.95, p 0.03) were also significantly associated with worse outcomes. For risk of late recurrence, in arm A, ER (HR 1.22, 95%CI 1.04-1.44, p 0.02), PR (1.26, 95%CI 1.05-1.5, p 0.01), and estrogen axis (1.39, 95%CI 1.09-1.77, p 0.008) were associated with worse outcomes. Oncotype Dx risk group (3 vs. 1 and 2, HR 0.4, 95%CI 0.16-0.98, p 0.05) was associated with improved outcomes. However, neither individual gene, axis, nor intrinsic subtypes were associated with the risk of late recurrence in patients treated with trastuzumab. Conclusions: For risks of early recurrence, the invasion genes/axis were associated with increased risks of recurrence in patients with early-stage HER2+ BC regardless of trastuzumab treatment. Among patients treated with trastuzumab, ER genes/axis, Oncotype Dx risk group, and intrinsic subtype were prognostic for risks of recurrence in the first five years. For risks of late recurrence, ER genes/axis and Oncotype Dx risk group were prognostic but only in patients treated with chemotherapy alone. The ER genes/axis were associated with less recurrence in the first five years but worse after five years, reflecting a higher risk of late recurrence in ER/PR+ HER2+ BC patients treated with chemotherapy alone. However, none of the individual gene, axis, or intrinsic subtypes were associated with the risk of late recurrence in patients treated with trastuzumab. Therefore, future studies are needed to identify biomarkers for the risk of late recurrence in HER2+ BC patients treated with adjuvant trastuzumab. Support: BCRF-19-161; U10CA180821, U10CA180882, Genentech. <https://acknowledgments.alliancefound.org>; [Clinicaltrials.gov](https://clinicaltrials.gov) Identifier: NCT00005970

Disclosure(s):

Saranya Chumsri, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Terminated, September 15, 2021); Biotheranostic: Contracted Research (Terminated, April 12, 2022); Immunomedics: Consulting Fees (e.g., advisory boards) (Terminated, September 28, 2020); Merck & Co.: Contracted Research (Ongoing); Pfizer: Contracted Research (Ongoing); Rebiotix: Contracted Research (Ongoing); Salix: Contracted Research (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Terminated, March 10, 2022)

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P2-11-06

Plasma assay of methylated DNA markers (MDM) detects patients with metastatic breast cancer (MBC) compared to healthy controls and treated breast cancer patients with no evidence of disease

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Objective:

Aberrantly methylated DNA may be used to detect minimal residual disease or early recurrence in breast cancer. As a 1st step, we aimed to develop an MDM panel to delineate between healthy women, stage I-III breast cancer in remission with no evidence of disease (NED), and metastatic breast cancer (MBC).

Methods:

We prospectively enrolled patients into 3 groups: healthy controls (adult females with a normal mammogram in past 12 months with no history of breast cancer), NED [stage I-III breast cancer with no clinical evidence of recurrence 6 months - 3 years post-treatment (adjuvant endocrine therapy allowed)], and MBC (collected either at initial diagnosis of untreated metastatic disease or radiographic progression). DNA was extracted from 6 mL of plasma derived from blood collected in LBGard tubes (Exact Sciences Corp., San Diego CA), and was bisulfite-treated and assayed by target enrichment long-probe quantitative amplified signal (TELQASTM) method for a panel of 15 previously identified MDMs [Table], normalized by the control gene, B3GALT6. Areas under the receiver operating characteristic curve (AUC) were calculated for each MDM to assess discrimination of MBC from other groups. With 60 patients per group, we had greater than 80% power to detect a difference of 0.20 from the null AUC of 0.7.

Results:

We tested samples from 60 MBC (10 untreated, 50 recurrent), 60 NED, and 60 healthy women. The median age was 63 (IQR, 55-72) and was not different between groups. The NED group was all hormone-receptor (HR) positive, with 47 (78%) being human epidermal growth factor receptor 2 negative (HER2-) and 13 (22%) HER2+; 48 (80%) were stage I and 9 (15%) were N+. The MBC group had 35 (58%) patients with HR+/HER2- tumors, 11 (18%) HR+/HER2+, and 6 (10%) HR-/HER2-, 4 (7%) HR-/HER2+, with 4 (7%) unknown. Of the 41 MBC whose original stage and nodal status were known 9 (22%) were stage I and 22 (54%) were N+. The markers were able to discriminate between MBC and NED patient samples with AUCs from 0.97 to 0.72. AUCs for 10/15 MDMs (ITPRIPL1, EMX1, C17orf64, OSR2, TRIM67, CHST2, IFFO1, TRH, FAM59B, and MPZ) were >0.90. No difference in MDMs was observed between the healthy and NED groups.

Conclusions:

MDMs, assayed from plasma, appear highly discriminant for metastatic breast cancer cases in comparison to control patients with NED or healthy controls. Further clinical validation of this MDM panel in a larger cohort is warranted.

Table 1. Plasma MDM discrimination of metastatic breast cancer (MBC) from healthy controls and previously treated breast cancer patients with no evidence of disease (NED)

MDM	AUC (95% CI)	
	MBC vs healthy control	MBC vs NED
<i>ITPRIPL1</i>	0.96 (0.93-0.99)	0.97 (0.95-0.99)
<i>EMX1</i>	0.94 (0.89-0.99)	0.94 (0.90-0.99)
<i>C17orf64</i>	0.94 (0.89-0.99)	0.94 (0.89-0.99)
<i>OSR2</i>	0.93 (0.88-0.99)	0.94 (0.89-0.99)
<i>TRIM67</i>	0.93 (0.87-0.98)	0.93 (0.88-0.99)
<i>CHST2</i>	0.92 (0.86-0.98)	0.93 (0.87-0.98)
<i>IFFO1</i>	0.92 (0.86-0.97)	0.92 (0.87-0.98)
<i>TRH</i>	0.91 (0.86-0.97)	0.92 (0.86-0.97)
<i>FAM59B</i>	0.92 (0.86-0.97)	0.91 (0.85-0.97)
<i>MPZ</i>	0.90 (0.84-0.96)	0.90 (0.84-0.96)
<i>ODC1</i>	0.89 (0.81-0.96)	0.89 (0.81-0.96)
<i>C10orf125</i>	0.80 (0.72-0.88)	0.81 (0.73-0.89)
<i>CXCL12</i>	0.78 (0.69-0.87)	0.79 (0.70-0.88)
<i>CD1D</i>	0.77 (0.68-0.85)	0.76 (0.67-0.85)
<i>SPHK2</i>	0.73 (0.64-0.83)	0.72 (0.62-0.81)
<i>CALN1</i>	0.66 (0.56-0.76)	0.72 (0.62-0.81)

Disclosure(s):

Karthik V. Giridhar, M.D.: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-11-07

Association of PIK3CA mutations with efficacy in HER2-positive first-line metastatic breast cancer: a meta-analysis

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BACKGROUND

PIK3CA mutations have been shown to be associated with poor prognosis in HER2-positive breast cancer (BC). We combined data from three completed Phase III Roche-sponsored randomized trials of HER2-targeted therapy for the first-line treatment of HER2-positive metastatic BC (MBC); this allowed for exploration of the prognostic impact of PIK3CA mutations observed in the three individual trials across subgroups of interest.

METHODS

Data from CLEOPATRA (pertuzumab + trastuzumab + docetaxel [PHD] vs. placebo [Pla] + HD;

NCT00567190; N = 808), MARIANNE (HD vs. ado-trastuzumab emtansine [K] + Pla vs. K + P; NCT01120184; N = 1095), and PUFFIN (PHD vs. Pla + HD; NCT02896855; N = 243) were included. An individual patient data (IPD) meta-analysis was performed to test the association between PIK3CA mutation status in tumor tissue (mutated vs. wild type [WT]) and efficacy (progression-free and overall survival [PFS/OS]) in different biomarker and clinical subgroups. Confounder adjustment was conducted for age, Eastern Cooperative Oncology Group Performance Status, body mass index, treatment, disease type, and number of metastases (all at baseline). "Study" was included as a random effect in the IPD meta-analysis model to account for variability between studies.

A landmark analysis was conducted on fast and non-fast progressors (cutoff of >137 days [i.e., after six chemotherapy cycles]) from CLEOPATRA and PUFFIN only, since they include the current standard-of-care regimens (PHD), by using Day 137 as the landmark time with separate Cox proportional hazards models.

RESULTS

PIK3CA mutation data were available for 1905/2146 patients (89%; ~80% from primary tissue); mutation prevalence was 27% (n = 521). PIK3CA-mutated vs. WT in association with PFS in pooled treatment arms is shown in the table. OS data were consistent.

CONCLUSIONS

PIK3CA mutations were associated with a worse prognosis across subgroups of interest, including in fast and non-fast progressors, in the two PHD-containing studies as compared with the overall ITT population.

PIK3CA-mutated vs. WT in association with PFS in pooled treatment arms

	PFS events/ patients	Hazard ratio	95% CI	P value
<i>PIK3CA</i> -mutated vs. WT				
Overall ITT	1479/1883*	1.45	1.30–1.63	<0.001
Subgroup analysis for <i>PIK3CA</i> -mutated vs. WT				
HER2				
IHC				
2+	179/202	1.11	0.82–1.50	0.510
3+	1278/1656	1.43	1.26–1.62	<0.001
mRNA				
≤median	723/872	1.36	1.17–1.59	<0.001
>median	648/868	1.34	1.11–1.63	0.003
Gene ratio				
≤median	714/888	1.50	1.28–1.75	<0.001
>median	691/898	1.30	1.09–1.55	0.003
Hormone receptor				
Negative	637/820	1.33	1.12–1.58	0.001
Positive	796/999	1.58	1.36–1.85	<0.001
De novo MBC at first diagnosis				
Yes	667/862	1.58	1.33–1.88	<0.001
No	812/1021	1.32	1.14–1.54	<0.001
Landmark analyses				
Overall ITT				
CLEOPATRA	553/679	1.37	1.13–1.66	
PUFFIN	181/237	1.44	1.06–1.97	
Fast progressors				
CLEOPATRA	81/679	1.25	0.78–2.02	
PUFFIN	36/237	1.96	1.01–3.81	
Non-fast progressors				
CLEOPATRA	472/576	1.40	1.14–1.73	
PUFFIN	145/194	1.33	0.93–1.89	

Hazard ratio >1 indicates *PIK3CA* mutation associated with worse prognosis.

* Patients with *PIK3CA*, specific subgroup, and confounder variables available.

Disclosure(s):

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P2-11-08

Multimodal Prediction of Breast Cancer Recurrence Assays and Risk of Recurrence

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Background: Hormone receptor positive breast cancer constitutes about 70% of newly diagnosed early-stage disease in the United States, and gene-expression based recurrence assays such as Oncotype DX (ODX) are strongly recommended by guidelines to aid in treatment decisions. However, recurrence assays are costly, time-consuming, underutilized in low resource settings, and unavailable in developing countries. Deep Learning (DL) using hematoxylin and eosin (H&E) stained digital pathology has been shown to approximate gene expression patterns for multiple cancer types, and may provide a cost-effective, fast, and scalable method to predict risk of recurrence in community settings. **Methods:** We first developed a model for ODX using only DL on pathology, comprised of two Xception-based modules, trained on 1,039 slides from The Cancer Genome Atlas (TCGA) tessellated into 10x magnification image tiles. The first module predicts tumor likelihood, and was trained using pathologist annotations for tumor regions versus normal stroma. The second module was trained to predict ODX score, estimated from gene expression data within TCGA. Patient-level predictions were calculated by weighting the predicted recurrence score by tumor likelihood for all tiles within a slide. Separately, ODX score was predicted from clinical variables using the University of Tennessee Nomogram, which incorporates grade, progesterone receptor, size, age, and histologic subtype. Finally, we developed a combined model by fitting a logistic regression to the DL pathologic model and the clinical nomogram predictions. Performance of the clinical nomogram, pathologic, and combined models were then compared in a single-institution external validation cohort of patients diagnosed with breast cancer between 2006 and 2020, all of whom had the commercial ODX assay run. **Results:** We identified 428 cases for our diverse validation cohort (69% White, 24% Black, 6% Asian, and 3% Hispanic) with mean ODX score of 18. Chemotherapy was administered for 104 (24.3%) of patients, the remaining 323 (75.4%) received endocrine therapy alone. Area under the receiver operating characteristic curve (AUROC) for prediction of high ODX score (≥ 26) of the combined model was 0.83 (95% confidence interval [CI] 0.78 – 0.89) in the validation cohort, which was higher than either the DL pathology model (AUROC 0.80, 95% CI 0.75 – 0.85, $p = 0.026$) or the Tennessee nomogram (AUROC 0.77, 85% CI 0.70 – 0.83, $p = 0.003$). Performance was similar in Black (AUROC 0.86, 95% CI 0.78 – 0.94) and White (AUROC of 0.81, 95% CI 0.74 – 0.88) subgroups. The combined model was more accurate in prediction of recurrence-free interval in patients receiving endocrine therapy (hazard ratio [HR] 2.02 per standard deviation [SD], 95% CI 1.16 – 3.52, $p = 0.013$, Concordance [C]-index 0.75) than the clinical nomogram (HR 1.75 per SD, 95% CI 1.09 – 2.81, $p = 0.021$, C-index 0.68). No model was prognostic in patients receiving chemotherapy. Pathologist review of heatmaps of DL model predictions identified lymphovascular invasion, necrosis, high grade, and infiltrative borders as features contributing to model prediction of high risk. **Conclusions:** DL can improve on existing clinical prediction of breast cancer with low recurrence risk. This approach could improve the speed at which treatment decisions are made due to the time-consuming nature of genomic testing and simultaneously reduce the cost of care. Given the equal performance in racial subgroups, this approach has promise for application in global health settings where genomic assays are not widely available or are prohibitively expensive.

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P2-11-09

Association of 21-gene recurrence score with overall survival in phase 3 TAILORx trial

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Background: The 21-gene recurrence score (RS) assay is a prognostic measurement originally established for distant recurrence in estrogen receptor-positive and node-negative breast cancer. Retrospective studies and the Trial Assigning Individualized Options for Treatment (TAILORx; ClinicalTrials.gov NCT00310180) validated its significance besides testing chemotherapy benefit in patients with midrange RS (11-25). However, unclarity remains as to whether RS has comparable prognostic value for overall survival (OS) in the TAILORx trial population. Methods: Association between the recurrence scores (midrange or high-range 26-100 vs. low-range 0-10) and OS was evaluated in all eligible patients with clinicopathological and treatment information by multivariable Cox proportional hazards regression model including RS, tumor size, tumor grades, chemotherapy, endocrine regimens, surgery type, progesterone receptor and demographics. We also evaluated the association between RS and invasive disease-free survival (DFS), recurrence-free interval (RFI) or distant recurrence-free interval (dRFI) by multivariable Cox analysis. Results: Median follow-up was 95.5 (range 0.1 to 138.6) months for OS, 89.6 months (range 0 to 134.8) for DFS, 87.7 (range 0 to 134.8) months for RFI or 87.6 (range 0-134.8) months for dRFI. Compared with low score group, midrange and high-range scores were associated with RFI and dRFI, respectively ($P \leq 0.01$ each). However, midrange score was neither associated with OS (adjusted HR 1.15; 95% CI 0.87-1.52; $P=0.33$) nor associated with DFS (HR 1.16; 95% CI 0.97-1.38; $P=0.11$). High-range score was associated with DFS (HR 1.58; 95% CI 1.21-2.06; $P < 0.01$) and had a trend towards association with OS (HR 1.44; 95% CI 0.95-2.19; $P=0.08$). Conclusions: The data indicate that the recurrence scores provide independent prognosis for breast cancer recurrence at both distant and locoregional sites and for distant recurrence, respectively. High-range score is prognostic of disease-free survival, with the midrange score showing marginal association. Midrange and high-range recurrence scores do not provide independent prognostic information for overall survival in hormone receptor-positive, HER2-negative, node-negative breast cancer in the TAILORx trial population.

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P2-11-10

Validation of the Breast Cancer Index (BCI) prognostic models optimized for late distant recurrence in postmenopausal women with early-stage HR+ breast cancer in the TEAM trial

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Background: Women with HR+ breast cancer experience a persistent risk of distant recurrence (DR) even after completion of 5 years of adjuvant endocrine therapy, with more than 50% of DR occurring after 5 years (late DR). The prognostic genomic signatures currently being used in the clinic were not developed or optimized specifically for late DR. We have previously shown that the Breast Cancer Index (BCI) and BCIN+ prognostic models were significantly prognostic for risk of overall (0-10y) and late (5-10y) distant recurrence (DR) in N0 and N1 HR+ patients in the Tamoxifen and Exemestane Adjuvant Multinational (TEAM) trial. Here, the prognostic performance of the BCI and BCIN+ models with alternative cut-points optimized for late DR were evaluated in patients from the TEAM trial, who were free from DR for at least 5 years. Methods: BCI testing was performed blinded to clinical outcome. The pre-specified alternative cut-points 4.4 and 1.8 for BCI and BCIN+ models were determined previously from Trans-aTTom and IDEAL studies, respectively (ESMO 2021). Kaplan-Meier analysis and log-rank test were used to evaluate the prognostic significance of BCI/BCIN+ risk groups based on DR. Univariate and multivariate Cox models were used to estimate hazard ratios (HRs) and the associated 95% confidence intervals (CIs).

Results: 1285 HR+ N0 (median age 69.2, 54.2% T1, 92.5% G2-3, 21.3% chemotherapy) and 1762 N1 (median age 68.5, 49.7% T1, 80.8% G2-3, 42.6% chemotherapy) patients who remained free from DR at 5 years post randomization were included in the current analysis. For N0 patients, BCI identified 439 (34%) and 846 (66%) patients as low and high-risk with late 10-year DR rates of 3.8% (95% CI: 1.5-6.0%) and 9.1% (95% CI: 6.8-11.4%), respectively (HR: 2.6, 95% CI: 1.4-5.0; p=0.0025). For N1 patients, BCIN+ identified 287 (16%) and 1475 (84%) patients as low and high-risk with late 10-year DR rates of 3.4% (95% CI: 1.2-5.5%) and 12.3% (95% CI: 10.4-14.2%), respectively (HR: 3.5, 95% CI: 1.8-6.9; p< 0.0001). Similar results were observed in the HER2- patients. Notably, BCI/BCIN+ remained a statistically significant prognostic factor in the multivariate analysis after controlling for age, tumor size, grade, treatment. (Table).

Conclusions: Compared to the original BCI/BCIN+ models, the optimized BCI and BCIN+ models showed improved prognostic performance for identifying low-risk patients with a very low risk of late DR (< 4%), for both N0 and N1 patients. These results provide further validation

of BCI clinical utility as an aid in the decision-making for extended endocrine therapies for HR+ breast cancer, particularly in patients with N1 disease that may be spared extended endocrine treatment.

Nodal Status	Her2 Status	BCI/BCIN+ Status	10-year risk of DR % (95% CI)	Adjusted HR (95% CI)	P Value
N0	All Pts	Low	3.8 (1.5, 6.0)		
		High	9.1 (6.8, 11.4)	2.6 (1.4, 5.1)	0.0025
	Her2-	Low	3.2 (0.9, 5.3)		
		High	9.0 (6.4, 11.6)	3.2 (1.5, 6.9)	0.0020
N1	All Pts	Low	3.4 (1.2, 5.5)		
		High	12.3 (10.4, 14.2)	2.9 (1.4, 5.6)	<0.0001
	Her2-	Low	3.0 (0.8, 5.1)		
		High	12.4 (10.2, 14.4)	3.3 (1.5, 7.1)	0.0001

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P2-11-11

Computer analysis of nuclear morphology with Multiple Instance Learning Predicts Overall Survival for Node Positive Breast Cancer Patients from SWOG S8814: A Blinded Validation Study

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Background: Adjuvant chemotherapy is a common treatment for breast cancer patients with aggressive tumors, but imposes severe side effects. Although lymph node involvement is associated with higher likelihood of mortality, a subset of LN+ patients can survive without relapse, even without adjuvant chemotherapy. SWOG-8814 (S8814) was a randomized clinical trial of hormone receptor positive, LN+ post-menopausal women (pathologic stage T1-3N1-2) to compare patient outcome between endocrine therapy alone (tamoxifen), chemotherapy (cyclophosphamide, doxorubicin, and 5-fluorouracil) followed by 5 years of tamoxifen, and chemotherapy with concurrent tamoxifen. In this work, we evaluated the ability of a machine learning approach called multiple instance learning (MIL) to predict long-term overall (OS) and disease-free survival (DFS) in patients from the S8814 clinical trial via analysis of digitized H&E

tissue slides. Methods: The training set (St, n=121) consisted of digitized H&E Whole Slide Images (WSIs) of ER+ LN+ patients from ECOG-2197 - a clinical trial to compare patient outcome under chemotherapy with doxorubicin/docetaxel vs. doxorubicin/cyclophosphamide. For each WSI, the nuclei of ten tumor patches (2000x2000 pixels) were automatically segmented by a pretrained machine learning algorithm called Convolutional Neural Networks (CNN). The results of the CNN's segmentations were used to obtain ten corresponding feature vectors of 3963 features relating to nuclear morphology and spatial arrangement. Five top discriminative features (Haralick texture, Delaunay triangulation, orientation entropy, perimeter kurtosis, architecture) were identified by reliefF-MI feature filtering and forward selection on St. A Normalized Set Kernel Support Vector Machine classifier was trained on St to construct a MIL binary classifier (M+), which generates a continuous survival score to predict which patients would have >10-years of DFS and OS. The score cutoff that maximized F1 score on St was used to generate binary predictions of patient outcome. Blinded validation of the risk scores on S8814 was performed by SWOG. Results: M+ was significantly prognostic of OS in univariate analysis (HR=0.72, p=0.020, 95% CI= 0.55 – 0.95) on S8814. M+ stratifications remained statistically significant after multivariable analysis controlling for treatment, number of positive lymph nodes, and tumor size (HR = 0.71, p=0.017, 95% CI=0.54-0.94). M+ predictions did not achieve statistical significance for DFS in univariate analysis (HR=0.81, p=0.081, 95% CI 0.64-1.03) nor multivariable analysis (HR=0.81, p=0.080, 95% CI 0.63-1.03). M+ was not predictive of chemotherapy benefit for OS (p=0.88) and DFS (p=0.65). There was no correlation of the generated continuous score with Recurrence Score (r=-0.05), previously shown to be a predictive factor for chemotherapy benefit. Conclusion: Our findings demonstrate that nuclear morphology provides insight into overall survival in ER+ LN+ breast cancer patients. Future work will involve combining the MIL based morphologic predictor with other clinicopathologic factors to improve DFS risk stratification. Funding: Funding NIH/NCI grants U10CA180888, U10CA180819, U24CA196175; and in part by Genomic Health, INC. (now Exact Sciences Corp.)

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7:00 AM - 8:15 AM

P2-11-12

Pattern of distant relapse according to intrinsic molecular subtype in patients with HER2-positive breast cancer: a combined analysis of ShortHER, CherLOB, and two institutional cohorts.

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Background: All intrinsic molecular subtypes are represented among HER2-positive breast cancer, with implications on clinical outcome and treatment sensitivity. The impact of molecular subtypes on the pattern and site of relapse is largely unexplored.

Methods: 677 patients with HER2-positive early breast cancer from the Shorther trial (n=437), the CherLOB trial (n=84) and two Institutional cohorts (Istituto Oncologico Veneto IRCCS Padova n=39 and Hospital Clinic Barcelona n=117) were included. Only patients with available PAM50 intrinsic molecular subtyping were considered. We analyzed the incidence of distant relapse (at any site and at specific sites) as the first event. Cumulative incidence was estimated according to competing risk analysis (Fine and Gray's method). Competing risk regression was used to calculate the subdistribution Hazard Ratios (subHR) and their 95% Confidence Interval (CI).

Results: The distribution of molecular subtypes was: 130 LumA (19%), 75 LumB (11%), 347 HER2-e (51%), 46 Basal (7%), 79 Normal (12%). Median follow up was 8.4 years (95%CI 8.2-8.6).

The 10-yr cumulative incidence rates of distant relapse as first event were: LumA 7.9%, LumB 14.8%, HER2-e 14.7%, Basal 15.5%, Normal 10.4% (HER2-e vs LumA: SubHR 2.21, 95%CI 1.05-4.64, p=0.037).

Table 1 shows the 5-yr and 10-yr cumulative incidence rates of distant metastases at specific sites (as first event) according to intrinsic subtype.

HER2-e enriched and Basal tumors were more prone as compared to other subtypes to develop brain and lung metastasis as first event, respectively. Isolated brain metastases without extracranial disease occurred only in patients with HER2-e tumors. All brain metastases as first event occurred within 5 years from diagnosis. Bone-only disease as first event was less frequent in HER2-e and Basal subtype (subHR HER2-e vs LumA: 0.32, 95%CI 0.10-10.4. p=0.058).

Next, we analyzed the frequency of site-specific first metastasis among patients who experienced a distant metastasis as first event (n=77). Lung metastases were more frequent in Basal tumors (LumA 25.0%, LumB 20.0%, HER2-e 24.4%, Basal 71.4%, Normal 0.0%, p=0.037) and bone metastases were more frequent in Luminal tumors (LumA 100.0%, LumB 60.0%, HER2-e 31.1%, Basal 42.9%, Normal 57.1%, p=0.006). Among 45 HER2-e patients with a first distant relapse, 25.6% were diagnosed with a brain metastasis and 15.6% had brain-only disease.

Conclusions: Molecular subtypes influence the metastatic behaviour of clinically HER2-positive breast cancer. These results, if further validated, may have implication in planning personalized monitoring strategies.

Table 1.
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5-yr and 10-yr cumulative incidence rates of distant metastasis at specific sites (as first event) according to intrinsic subtype.

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12/7/2022

7:00 AM - 8:15 AM

P2-11-13

High PD-L2 Protein Expression in Cancer Cells is an Independent Marker of Unfavorable Prognosis in Luminal Breast Tumors

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Background PD-1 inhibitors have shown significant efficacy in triple negative breast cancer (BC), however, durable responses are less common in estrogen receptor-positive (ER+) BC. Better markers are therefore needed that will identify likely responders to PD-1 inhibitors among patients with luminal BC. While most efforts have focused on the immune checkpoint protein PD-L1, the alternative PD-1 ligand, PD-L2, has been largely overlooked. We aimed to

determine if PD-L2 is associated with unfavorable prognosis in ER+ BC. Methods PD-L2 protein levels in cancer cells and stromal cells were measured retrospectively by quantitative immunofluorescence histocytometry in tissue microarrays of therapy-naïve, localized or locoregional ER+ BC and correlated with progression-free survival (PFS). Evaluable tumor PD-L2 data were derived from a main study cohort A diagnosed between 1988-2005 (n=684) with extensive clinical and outcome data and from an independent validation cohort B diagnosed between 1992-2012 (n=273). Patients received standard-of-care adjuvant therapy without immune checkpoint inhibitors after tumor resection. Results Univariate analysis of the main cohort A revealed that high PD-L2 expression in cancer cells was associated with shorter PFS (HR=1.8; 95%CI:1.3-2.6; p=0.001), an observation that was validated in an independent cohort B (HR=2.3, 95%CI:1.1-4.8; p=0.026). Approximately one third of ER+ BC cases were classified as high PD-L2. After multivariable adjustment for common clinicopathological variables, high cancer cell levels of PD-L2 remained independently predictive of early recurrence (HR=2.0; 95%CI:1.4-2.9; p< 0.001). Sub-analysis of ER+ BC cases treated with adjuvant chemotherapy (n=197) suggested that high PD-L2 levels in cancer cells was associated with particularly increased risk of progression (multivariable HR=3.4; 95%CI:1.9-6.2; p< 0.001). The observed frequent expression of PD-L2 protein in BC provided scientific rationale for the design of our ongoing phase II clinical trial (NCT04243616) of neoadjuvant combined PD-1 inhibitor (cemiplimab; Regeneron Pharmaceuticals Inc) and chemotherapy in patients diagnosed with PD-L1+ and/or PD-L2+ BC. The primary objective of this trial is to assess pathologic responses to neoadjuvant treatment with secondary objective of assessing the correlation between PD-L1/PD-L2 status and tumor responses. Pathologist review of PD-L1 and PD-L2 expression in an initial set of ER+ tumors (n=15) screened for trial eligibility revealed frequent discordance between cancer cell positivity for PD-L1 and PD-L2 protein (PD-L1: median=0%; range 0-2% vs. PD-L2: median=18%; range < 1-60%) as well as immune cell positivity (PD-L1: median=5%; range 0-50% vs. PD-L2: median=0; range 0-50%). Conclusions In treatment-naïve ER+ breast tumors, high cancer cell expression of PD-L2 protein was an independent predictor of poor clinical outcome, with evidence of further elevated risk of progression in patients who received adjuvant chemotherapy. Preliminary analyses of ER+ tumors from our ongoing clinical trial showed frequent discordance between baseline PD-L1 and PD-L2 protein expression in both cancer cells and immune cells. Collectively, our analyses indicate that PD-L2 has prognostic value for ER+ BC, and our progress justify further studies to determine whether PD-L2, alone or in combination with PD-L1, may serve as a predictive marker of response to PD-1 inhibitors.

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P2-11-15

Focal ESR1 gene amplification is an independent prognostic marker in postmenopausal patients with endocrine-responsive early breast cancer

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Purpose: Estrogen receptor (ER) expression predicts response to endocrine therapy and is a prognostic biomarker. However, no ER-associated biomarker is able to identify patients with particularly favorable outcome among ER+ tumors. We investigated the value of ESR1 amplification in predicting long-term outcome in tamoxifen-treated postmenopausal women with early breast cancer with and without nodal involvement. Patients and Methods: 394 patients with ER+ breast cancer (235 node-negative, 159 patients node-positive), who had received adjuvant tamoxifen for 5 years in the prospective randomized ABCSG-06 trial, and in whom FFPE tumor tissue was available, were included in this analysis. ER alpha immunoreactivity was evaluated using the Allred score, while ESR1 gene amplification was evaluated by FISH analysis. Results: Focal ESR1 amplification was detected in 187 (47%) tumors, and was associated with a favorable outcome. After a median follow-up of 10 years, women with focal ESR1 amplification had a significantly longer distant recurrence-free survival (DRFS; adjusted HR 0.48; 95% CI 0.26-0.91; p=0.02) and breast cancer-specific survival (BCSS; adjusted HR 0.47; CI 0.27-0.80; p=0.01) compared to women without ESR1 amplification. The association between ESR1 amplification and improved DRFS and BCSS was only found in node-positive tumors, but not in nodal-negative tumors. ER alpha immunoreactivity, evaluated by Allred score, correlated significantly with focal ESR1 amplification (p< 0.0001; Chi-squared test), but without prognostic significance. Conclusion: We suggest focal ESR1 amplification as predictor of improved long-term outcome in postmenopausal women with node-positive ER+ early breast cancer.

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Computerized Measurements of Nuclear Morphology Features, Mitosis Rate, and Tubule Formation from H&E Images Predicts Disease-Free Survival in Patients with HR+ & LN+ Invasive Breast Cancer from SWOG S8814

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Background: Lymph node (LN) involvement is a strong indicator of poor prognosis for breast cancer (BC), with adjuvant chemotherapy remaining fundamental to management of these patients. SWOG S8814 was a Phase III randomized trial of postmenopausal patients with pathologic LN-positive BC who were hormone receptor positive (HR+). The objectives of the clinical trial were to compare disease free survival (DFS) and overall survival (OS) of 1) these postoperative patients treated with a combination of cyclophosphamide, doxorubicin, fluorouracil (CAF) plus tamoxifen versus tamoxifen alone; and 2) patients treated with CAF followed by tamoxifen versus CAF plus concurrent tamoxifen. In this study we sought to evaluate the potential of applying computational image analysis on whole slide images (WSI) for predicting DFS and OS in SWOG S8814. Methods: A cohort of 135 patients (N=53 DFS event) diagnosed with HR+ & LN+ BC from clinical trial ECOG 2197 was utilized as training set D1. Validation set D2 comprised 630 patients (N=260 DFS event, N=195 death) with HR+ & LN+ BC from SWOG S8814. Three deep learning models were employed to respectively detect nuclei, mitosis, and tubules in WSIs. Subsequently, a total of 1,810 features relating to nuclear morphology (e.g., spatial distribution, shape, texture, orientation), mitotic activity (e.g., mitosis hotspot, mitotic rates) and tubule formation (e.g., tubular nuclei distribution, ratio of tubule to non-tubule area) were extracted from each WSI. A lasso regularized Cox regression model (IbRiS) was trained on D1 to respectively identify four features from each of the feature categories (nuclei morphology, mitotic activity, and tubule formation) most strongly associated with DFS, a continuous risk score based on the selected features was then constructed. An optimal risk threshold was identified on D1 to dichotomize the risk scores into high vs. low risk of recurrence categories. Blinded validation of the machine learning model on SWOG S8814 using Cox regression was performed by SWOG to evaluate its performance in terms of DFS and OS. Results: In D2, patients identified as high risk of recurrence by IbRiS had a significantly worse prognosis in terms of DFS with hazard ratio=1.30 (p=0.039, 95% CI=1.01-1.66). IbRiS was also found to be significantly prognostic of OS with hazard ratio=1.38 (p=0.026, 95% CI=1.04-1.83). IbRiS was however, neither prognostic of DFS (HR = 1.20; 95% CI 0.93-1.54) nor OS (HR = 1.28; 95% CI 0.96-1.71) in multivariable analysis adjusting for treatment, tumor size, and number of positive nodes. IbRiS was also not a significant predictor of chemotherapy benefit (DFS p=0.45; OS p=0.25). Conclusion: We developed a prognostic model (IbRiS) based on the combined features of nuclear morphology, mitosis count, and tubule formation that can help further risk stratify HR+ & LN+ BC patients by only using H&E slides.

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Prognostic value of Trop2 expression levels in non-metastatic triple-negative breast cancer and correlation with other biomarkers

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Background: Since the development of anti Trop2 antibody-drug conjugates (ADC), Trop2 has been validated as a major therapeutic target for antibody-drug conjugates in metastatic triple-negative breast cancer (TNBC). However, very few data have been reported regarding the prognostic implication, or clinicopathological variables, associated with Trop2 expression levels in early TNBC. Our aim was to evaluate Trop2 expression and its prognostic value in a retrospective series of patients with non-metastatic TNBC and a long follow-up, characterized for Basal-like (BL) or molecular apocrine-like (MA) IHC profiles as well as TILs infiltrate, PDL1 expression and PIK3CA / PTEN mutations. Patients and methods: The analysis was performed in a series of 228 patients with non-metastatic TNBC treated in our center between 2002 and 2012 arrayed on 6 TMA. BL and MA profiles were defined as IHC CK5/6 and/or EGFR expression, and Androgen-receptor and FOXA1 IHC expression, respectively. Trop2 expression levels were tested for their association with baseline clinicopathological variables, and for Relapse-Free Survival (RFS) and Overall survival (OS). Trop2 IHC level of expression was evaluated using the ENZ-ABS380 mouse monoclonal antibody and the methodology described by Bardia et al. (*Annals of Oncology*, 2021) to quantify the membrane signal. First, we established a score grid, according to staining intensity (no labeling: 0; weak labeling: 1; moderate labeling: 2; strong labeling: 3). Then, for each sampled core, the percentage of labeled invasive tumor cells in each intensity was reported. The overall membrane expression was then calculated using the H-Score method ($3 \times \% \text{ of cells with labeling intensity } 3 + 2 \times \% \text{ of cells with intensity } 2 + 1 \times \% \text{ of cells with intensity } 1$). The scores obtained ranged from 0 to 300. Results: Median age was 58.2 years (range 28.5-89.1). 43.9% of tumors were classified

pT1 and 63.5% pN0. 83.8% of patients had ductal carcinomas. Histological grade 1-2 represented 22.7% of all tumors. A BL phenotype was observed in 68.1% of cases, and an MA profile in 39.4% of the cases. Adjuvant chemotherapy (ACT) was delivered in 74% of patients. We observed low Trop2 expression (H-Score < 100) in 12.3% of the cases (28/228 samples), moderate Trop2 expression (H-Score 100-200) in 28.9% of the cases (66/228 samples), and strong Trop2 expression (H-Score >200) in 58.8% of the cases (134/228 samples). We only identified 3 tumors without any Trop2 expression. Regarding baseline clinicopathological correlations, Trop2 levels were only found significantly associated with pT stage, pT1 tumors displaying more frequently high Trop2 scores compared to tumors \geq pT2 ($p=0.002$). No significant correlation was found between Trop2 expression levels and HER2 levels (0 vs. 1+/2+), BL or MA status. With a median follow-up of 9.7 years, Trop2 levels were not associated with RFS nor OS in univariate analysis. In multivariate analysis, poor RFS was associated with classical variables in the early TNBC setting: tumors \geq T2 stage (Hazard Ratio (HR) 2.13, $p=0.02$), N+ status (HR 3.51, $p<0.001$), while high (>5%) TILs infiltration levels (HR 0.54, $p=0.03$) and adjuvant chemotherapy use (HR 0.49, $p=0.007$) were associated with improved RFS. Conclusions: Trop2 is expressed in nearly all early TNBC cases, and Trop2 levels of expression, while associated with T stage, did not impact survival in this population. These results are consistent with the ones reported in the metastatic setting in the ASCENT trial. Trop2 level of expression appearing homogeneous distributed in all the clinicopathological subtypes of TNBC, advocating for the evaluation of combined treatments with anti-Trop2 ADCs and dedicated targeted therapies in specific TNBC subgroups.

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Serum methylmalonic acid concentrations at breast cancer diagnosis are not associated with distant metastases

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Introduction: Methylmalonic acid (MMA), a metabolite and by-product of propionate metabolism, promotes breast cancer (BC) progression in mice via the transforming growth factor-beta (TGF β) signaling pathway (Gomes et al, Nature 2020). It is currently unknown if this effect also exists in patients with BC. **Objectives:** To investigate the association between baseline serum MMA concentrations in patients at BC diagnosis and development of distant metastases via a matched case-control study. **Methods:** We included 32 patients with early Luminal B-like BC (Lumb, median age 62.4y) and 52 patients with early triple-negative BC (TNBC, median age 50.5y) who developed distant metastases within 5 years. They were matched to an equal number of early BC patients with at least 5 years of follow-up (median age 62.2y for Lumb and 50.5y for TNBC) who did not develop distant metastases with at least 5 years of follow-up. Matching was performed based on age at diagnosis date (\pm 5y), tumor stage, and treatment received ((neo)adjuvant chemotherapy and radiotherapy, yes/no). Serum MMA concentrations were determined by liquid chromatography with tandem mass spectrometry (LC-MS-MS). **Summary statistics, paired analyses, and multiple conditional logistic regression analyses** were performed with and without adjusting for potential covariates (age, kidney function, and tumor stage). **Results:** Baseline serum MMA at BC diagnosis significantly correlated with age ($r_s=0.35$, $p=.005$ in Lumb; $r_s=0.35$, $p=.0003$ in TNBC), and negatively correlated with kidney function assessed by estimated glomerular filtration rate (eGFR, $r_s= -0.42$, $p=.0005$ in Lumb; $r_s= -0.32$, $p=.0009$ in TNBC). MMA concentrations at diagnosis were not associated with distant metastases in either subtype, after adjusting for kidney function, age, and tumor stage (all $p>.05$). Next, we categorized BC cases in the public TCGA ($n=174$ for Lumb; $n=140$ for TNBC), METABRIC ($n=461$ for Lumb; $n=199$ for TNBC), and GSE25066 ($n=78$ for Lumb; $n=182$ for TNBC) database according to their 5-year metastatic status, and analyzed the TGF β signaling pathway activity of primary BC. Like MMA concentrations, a gene expression signature of TGF β signaling was not associated with distant metastases in patients with BC. **Conclusion:** Baseline serum MMA concentrations and a gene signature for TGF β signaling at BC diagnosis are not associated with distant metastases among patients with Lumb and TNBC subtypes.

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P2-11-19

Inflammatory indexes as prognostic biomarkers in advanced triple negative breast cancer patients

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Background The identification of treatment selection biomarkers for advanced triple negative breast cancer (aTNBC) patients remains an unmet need. The immune system is known to be involved in the microenvironment of triple negative breast cancer (TNBC). Immune ratios like the neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR), the monocyte-lymphocyte ratio (MLR) and the systemic immune-inflammation index (SII) may reflect the immune system functional status in these patients and the involvement of circulating immune cells in cancer progression. In particular MLR showed to predict overall survival (OS) in aTNBC and to contribute to migration of circulating tumor cells [1]. **Methods** A retrospective-prospective, observational multicenter study from the GIM-14 experience was performed to investigate the association between inflammatory indexes (NLR, MLR, PLR and SII), as measured at baseline and at progression, and clinical and survival aspects in patients with aTNBC in first line setting. The optimal cutoff values between low and high expression of inflammatory indexes were established on the basis of cut-off values determined in a previously conducted study in order to validate them[1], and was used to predict progression-free survival (PFS) and OS. Time-to-event variables (PFS; OS) were calculated using Kaplan-Meier method, while Cox regression model was used to estimate HRs and their 95% CI. **Results** 105 consecutive patients with a diagnosis of aTNBC were fully evaluated for the final analysis. The median age at diagnosis was 55 years (33-86). Of them, 80 patients received a neo/adjuvant treatment after diagnosis. At first progression the majority of patients (n= 97) received chemotherapy, while only 8 patients were treated with chemo-immunotherapy due to the programmed death ligand 1 (PD-L1) expression in the immunohistochemical analyses. At a median follow-up of 54 months, median PFS in the whole patients population was 13 months (95% CI 9,4-16,5), while median OS was 17.3 OS (95% CI 13-22,2). All high inflammation based scores evaluated at diagnosis of metastatic disease were significantly associated with lower PFS, in particular high NLR (≥ 3) and high MLR (≥ 0.34) ($p = 0.0006$ and $p = 0.011$, respectively). Similarly, all high indexes appeared significantly associated with a lower OS, especially NLR (>3), SII (≥ 836) and MLR (≥ 0.34) ($p < 0.0001$, $p = 0.0005$, $p=0.001$ respectively). In particular also NLR and SII evaluated at disease progression after first line treatment were significantly associated with a worse OS ($p=0.0006$ and $p=0.001$ respectively). In multivariable analysis for predictors of overall survival, the number of metastatic sites, NLR, SII and MLR remained significant ($p < 0.0001$, $p=0.006$, $p=0.005$ respectively). **Conclusions** NLR, SII and MLR are predictors of OS in aTNBC. Although our results need validation with larger studies, we suggest that inflammatory ratios could be used as feasible biomarkers of prognosis and treatment efficacy in aTNBC. Further research about HER-2 low categorized patients will be updated and presented at the final meeting. 1. De Giorgi U, Mego M, Scarpi E, Giordano A, Giuliano M, Valero V, Alvarez RH, Ueno NT, Cristofanilli M, Reuben JM. Association between circulating tumor cells and peripheral blood monocytes in metastatic breast cancer. *Ther Adv Med Oncol.* 2019 Aug 14;11:1758835919866065. doi: 10.1177/1758835919866065. PMID: 31452692; PMCID: PMC6696837.

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Challenging the current 1-10% cut-off for defining Estrogen Receptor Low Positive grade 2-3 Estrogen Receptor positive, Human Epidermal growth factor Receptor 2 negative early breast cancer

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Background: The 2020 ASCO-CAP guidelines (Allison KH, JCO 2020; 38: 1346–66) recommended estrogen receptor (ER) Low Positive as new reporting category for breast cancers with 1-10% of cells staining ER positive to acknowledge their distinct clinical behaviour compared to breast cancers with >10% to 100% of tumor nuclei positive for ER. We evaluated the prognostic impact of low ER positivity with both 10% and 33% as cut-off. Patients and methods: A retrospective study was performed of consecutively treated patients in UZ Leuven between 2000-2017 with ER-positive/HER2-negative early, primary, unilateral and unifocal grade 2-3 invasive breast cancers. Patients treated with neo-adjuvant therapy were excluded. ER-positivity was defined as >1% ER-staining on immunohistochemistry (IHC). Patients were allocated to ER-low or ER-high groups for both the 10% and 33% thresholds according to their ER-status on IHC as derived from the Allred PS or from the H-score. Descriptive analyses and Cox regression analyses were performed for both thresholds ($\leq 10\%$ vs. $\leq 33\%$) with $\alpha=0.05$. Primary endpoints were overall survival (OS) and invasive disease-free survival (iDFS). Secondary endpoints were time to local (TTLR), locoregional (TTLRR) and distant metastatic relapse (TTM). Results: This study included 3629 patients (median age: 60.0 years; median follow-up: 12.3 years), with their tumors classified as low (39) versus high (3590) with 10% threshold and as low (92) versus high (3537) with 33% threshold. According to both cut-offs, grade 3 and PR negativity was more frequent in ER Low Positive breast cancer. These patients also received significantly more adjuvant chemotherapy and less adjuvant endocrine therapy. When looking at iDFS, OS, TTLR and TTLRR, both cut-offs generated groups with similar outcome. However, we observed a significant increased risk for distant metastatic relapse in ER Low Positive disease using the cut-off of 33% (univariate HR 2.0, 95%CI 1.3-3.2; $p=0.009$), which was not present for the cut-off of 10% (univariate HR 0.5, 95%CI 0.1-1.8; $p=0.2$). Nevertheless, when correcting this effect for age, grade, PR, tumor size, nodal status, adjuvant chemotherapy and endocrine therapy in multivariate analysis, ER Low Positive according to the cut-off of 33% did not remain significant to predict risk for metastatic relapse (HR 1.3, 95%CI: 0.8-2.3; $p=0.3$). Conclusion: In our series, patients with tumors expressing low ER, defined as 1-33% had a significantly higher univariate risk for metastatic relapse. ER Low Positive tumors are more frequently grade 3, which greatly determines the prognosis. ER Low Positivity did not remain independently significant after multivariate analysis. However, patients with tumors expressing low ER only constituted small fractions of the investigated population.

Disclosure(s):

Bernard Roobroeck, n/a: No financial relationships to disclose

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Giuseppe Floris, PhD, MD: No financial relationships to disclose

Christine Desmedt, PhD, Prof.: No financial relationships to disclose

Kevin Punie, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), travel support (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); FocusPatient: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or

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Sileny Han, PhD, MD: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-11-21

Outcomes and Treatment Pattern in Women With 1 cm or Smaller, Node-Negative Hormone Receptor-negative Breast Cancer in Fudan University Shanghai Cancer Center

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Background: To evaluate the outcome the treatment pattern in women diagnosed with T1mic, T1a and T1b, node-negative, hormone receptor (HR) –negative breast cancer.

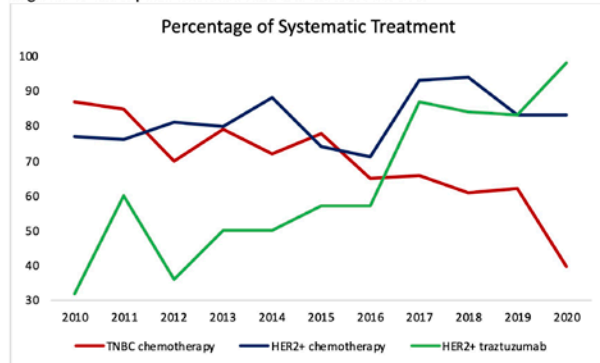
Methods: This was a retrospective cohort study within the Fudan University Shanghai Cancer Center (FUSCC) that included 605 women with T1mic,a,bN0M0 breast cancer treated between 2010 and 2020. Tumors were grouped by size (T1mic, T1a, T1b), biologic subtype defined by hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) status, and receipt of chemotherapy with or without trastuzumab. Kaplan-Meier product was used to calculate invasive disease-free survival (iDFS), breast cancer-specific survival (BCSS) and overall survival (OS).

Results: Median follow-up time was 5.0 years. Seventy-three percent of patients with triple-negative breast cancer (TNBC) were treated with chemotherapy. For those with HER2- positive breast cancers, 82% received chemotherapy, and 71% received trastuzumab. The treatment pattern varied over the years, with a downward trend of chemotherapy in TNBC and an upward trend of trastuzumab in HER2-positive breast cancer. Survival outcomes diverged by subtype and size. In this retrospective cohort study, the 5-year DFS for treated patients with T1mic,a tumors ranged from 96.2% to 97.7%, and for patients with T1b tumors, it ranged from 92.1% to 95.0%. The 5-year DFS for patients with T1mic,a tumors untreated with chemotherapy or trastuzumab was 100%. The 5-year DFS for TNBC patients with T1b tumors untreated with chemotherapy was 90.5%, while for HER2-positive patients with T1b tumors untreated with chemotherapy or trastuzumab it was 87.5%.

Conclusion: Women with T1mic,a tumors have an excellent prognosis without chemotherapy or trastuzumab, representing an optimal group for evaluating less toxic adjuvant regimens to maintain efficacy while minimizing short- and long-term risks.

Figure 1

Figure 1. Systematic Treatment Pattern of Patients With T1mic, a, b N0 Patients With Triple-negative or HER2-positive Breast Cancer from 2010 to 2020



TNBC chemotherapy: percentage of patients who received chemotherapy in triple-negative breast cancer
 HER2+ chemotherapy: percentage of patients who received chemotherapy in HER2-positive breast cancer
 HER2+ trastuzumab: percentage of patients who received trastuzumab in HER2-positive breast cancer

Systematic Treatment Pattern of Patients With T1mic, a, b N0 Patients With Triple-negative or HER2-positive Breast Cancer from 2010 to 2020

Table 1

Table 1. Patient Demographics and Clinicopathologic Characteristics for T1mic, a, b N0 Patients With Triple-negative or HER2-positive Breast Cancer, FUSCC 2010-2020

		TNBC		HER2-positive		Total		P
		N=244	%	N=361	%	N=605	%	
Age	Median (95% CI)	50 (32-68)		50 (32-65)		50 (32-66)		
	<=50	127	52.05	193	53.46	320	52.89	0.733
	>50	117	47.95	168	46.54	285	47.11	
pT	pT1mic	47	19.26	125	34.63	172	28.43	<0.001
	pT1a	22	9.02	82	22.71	104	17.19	
	pT1b	175	71.72	154	42.66	329	54.38	
Histology	Ductal	166	68.03	282	78.12	448	74.05	0.006
	Other	78	31.97	79	21.88	157	25.95	
Grade	I-II	66	27.05	117	32.41	183	30.25	0.002
	III	104	42.62	103	28.53	207	34.21	
	NA	74	30.33	141	39.06	215	35.54	
Ki67	<10	23	9.43	12	3.32	35	5.79	<0.001
	10-30	69	28.28	152	42.11	221	36.53	
	30-50	28	11.48	123	34.07	151	24.96	
	>=50	96	39.34	49	13.57	145	23.97	
	NA	28	11.48	25	6.93	53	8.76	
HR status	Positive	0	0.00	149	41.27	149	24.63	<0.001
	Negative	244	100.00	212	58.73	456	75.37	
Breast surgery	BCS	109	44.67	89	24.65	198	32.73	<0.001
	Mastectomy	135	55.33	272	75.35	407	67.27	
Axillary Surgery	SLNB	188	77.05	294	81.44	482	79.67	0.188
	ALND	56	22.95	67	18.56	123	20.33	
Chemotherapy	No	67	27.46	66	18.28	133	21.98	0.008
	Yes	177	72.54	295	81.72	472	78.02	
Trastuzumab	No	244	100.00	104	28.81	348	57.52	<0.001
	Yes	0	0	257	71.19	257	42.48	

Abbreviations: FUSCC, Fudan University Shanghai Cancer Center; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer

Patient Demographics and Clinicopathologic Characteristics for T1mic, a, b N0 Patients With Triple-negative or HER2-positive Breast Cancer, FUSCC 2010-2020

Table 2

Table 2. Systematic Treatment of Patients With T1mic, a, b N0 Patients With Triple-negative or HER2-positive Breast Cancer, FUSCC 2010-2020

Chemotherapy Regimen		TNBC								HER2-positive			
		pT1micN0 (N=47)		pT1aN0 (N=22)		pT1bN0 (N=175)		pT1micN0 (N=125)		pT1aN0 (N=82)		pT1bN0 (N=154)	
		N	%	N	%	N	%	N	%	N	%	N	%
Chemotherapy Regimen	Anthracycline-included	9	19.15	5	22.72	98	56.00	11	8.80	12	14.63	63	40.91
	Taxol-included	8	17.02	5	22.72	126	72.00	22	17.60	26	31.71	87	56.49
	Carboplatin-included	0	0.00	0	0.00	24	13.71	0	0.00	2	2.44	9	5.84
	Capecitabine	0	0.00	0	0.00	4	2.29	69	55.20	34	41.46	12	7.79
Chemotherapy Cycles	No	28	59.57	13	59.09	26	14.86	25	20.00	14	17.07	27	17.53
	0	28	59.57	13	59.09	26	14.86	25	20.00	14	17.07	27	17.53
	4	10	21.28	6	27.27	19	10.86	22	17.60	21	25.61	35	22.73
	6	8	17.02	2	9.09	89	50.86	77	61.60	43	52.44	50	32.47
	8	1	2.13	1	4.55	41	23.43	1	0.80	4	4.88	42	27.27
Trastuzumab	Yes	0	0.00	0	0.00	0	0.00	90	72.00	63	76.83	104	67.53
	No	47	100.00	22	100.00	275	100.00	35	28.00	19	23.17	50	32.47

Abbreviations: FUSCC, Fudan University Shanghai Cancer Center; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer

Systematic Treatment of Patients With T1mic, a, b N0 Patients With Triple-negative or HER2-positive Breast Cancer, FUSCC 2010-2020

Disclosure(s):

Xiyu Liu, M.D.: No financial relationships to disclose

Min He, n/a: No financial relationships to disclose

12/7/2022

7:00 AM - 8:15 AM

P2-11-22

Expression of milk whey protein genes in human breast carcinoma cells isolated by LCM impacts prediction of clinical outcomes

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Background: Milk whey protein consumption has been associated with breast cancer prevention, therapy and treatment tolerance, and other studies detected these proteins or their mRNAs in breast cancer models or tissues. Our objectives are to ascertain expression of certain whey protein genes in human breast carcinoma cells isolated by Laser Capture Microdissection (LCM) and to determine if gene expression is related to risk of recurrence and overall survival in lesions with various ER/PR status. Genes selected were: LALBA (alpha-lactalbumin), LPO (lactoperoxidase), LTF (lactotransferrin), PAEP (progesterone associated endometrial protein or glycodelin) and SSP1 (secreted phosphoprotein 1 or osteopontin). This retrospective investigation is unique in that highly quantified ER and PR protein levels and ESR1 and PGR relative expression from pure populations of carcinoma cells were employed to stratify cancers into ER/PR subcategories to assess relationships of expression of candidate genes with clinical outcomes. Methods: This investigation of primary breast carcinomas from 170 postmenopausal and 77 premenopausal patients used a matchless deidentified dataset of quantified estrogen receptor (ER) and progesterone receptor (PR) protein results with clinical follow-up. ER/PR protein levels, expressed as fmol/mg cytosol protein, were quantified earlier from each breast carcinoma with FDA-approved kits, either Radioligand-Binding Assay (LBA, NEN/DuPont) and/or enzyme immunoassay (EIA, Abbott Labs). Patients were treated with the standard of care at the time of diagnosis. The PixCell Ite™ (ThermoFisher, Arcturus) LCM instrument was used to procure only carcinoma cells from tissue sections of de-identified, frozen biopsies, using protocols we employed earlier. Total RNA of each fixed specimen was extracted, purified and amplified to obtain relative expression levels of approximately 22,000 genes by microarray, providing an assessment of mRNA in carcinoma cells only. Relationships of relative gene expression, quantified ER/PR and other features of primary breast cancers were analyzed with clinical results using R software v4.2.0 (Vigorous Calisthenics) by Univariable Cox Regression, Kaplan Meier plots and various tests (i.e., Wilcoxon, Log Ranked, Spearman and/or Chi Square tests). Bidirectional elimination stepwise regression was also used to derive best predictors of patient outcomes. Results: Violin plots of expression distribution of each milk protein gene of 247 biopsies regardless of patient menopausal status revealed that LALBA and SSP1 were highly elevated ($p < 0.001$) in ER+ ($n = 146$) or PR+ ($n = 146$) breast cancer cells while PAEP was quite diminished ($p < 0.001$). No difference was observed in LPO expression in ER+ or PR+ cells and LTF was only elevated slightly ($p < 0.05$) in ER+ cells. Regardless of ER/PR status of breast cancer, LTF, LALBA, SSP1, AR and ESR1 gene expression levels were increased significantly in postmenopausal versus premenopausal

patients while PAEP was decreased ($p < 0.001$). No difference was observed in LPO or PGR expression. Correlation matrices examined gene to gene and receptor protein to gene relationships. Using Kaplan Meier analyses of each gene alone with Log Ranked Tests of outcomes, only SSP1 expression was associated with clinical outcome, i.e., overexpression was associated with lower PFS and OS ($p = < 0.05$). Conclusions: Application of bidirectional elimination stepwise regression of gene expression of the five milk proteins collectively with ER/PR protein status of each carcinoma revealed that LALBA gene expression enhanced prediction of PFS in ER+ cancer while PAEP expression was associated with improved prediction of OS in ER+ carcinomas. We report that expression of LALBA and PAEP genes, largely associated with milk production in normal breast tissue, are also expressed in certain breast carcinomas and influence prediction of patient survival.

Disclosure(s):

James L. Wittliff, Ph. D., M. D. hc: No financial relationships to disclose

Michael W. Daniels, M. S.: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-11-23

Evaluation of T-cell infiltrating lymphocytes vs. Th2 in triple negative breast cancers (TNBC)

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Purpose. Triple-negative breast cancers (TNBC) are defined as negative for hormonal receptors and human epidermal growth factor receptors 2 and account for 15% of breast cancers. TNBC carry the worst prognosis mainly because of their high proliferation index and the absence of efficient targeted therapies due to their molecular heterogeneity, even though some promising options are emerging. Besides, they do share a very high and distinct tumor-infiltrating lymphocytes (TILs) infiltration. Amongst TILs, CD8+ cytotoxic and CD4+ helper T-cells (TC) proved to be markers of a good outcome. However, pathologists routinely quantify overall TILs density only. Anti-PD-1/PD-L1 immunotherapies recently became available for immunosuppressive TNBC. Unfortunately, neither PD-1/PD-L1 expression nor TILs quantification is able to predict patients' responses accurately. Thus, we aimed at precisely characterizing TILs sub-populations and evaluating their prognostic significance before their predictive one. **Methods.** We selected 91 patients at the time of surgery before any adjuvant

therapy from January 2013 to December 2018 in Rennes, France. TNBC tumors went through TILs quantification on hematoxylin and eosin slides by a trained pathologist and immune microenvironment characterization using flow cytometry. We then compared the prognostic value of immune microenvironment subpopulations vs total TILs count. Results. TNBCs contained a mean of $22.8 \pm 25.9\%$ TILs, including CD4+ TC (14.1%) mainly made of Th2 (11.7%), CD8+ TC (11.1%), and myeloid cells (8.4%) such as antigen presenting cells (APC). TILs groups and percentages were correlated with the abundance of these cellular subpopulations ($p \leq 0.004$). TILs percentage was predictive of overall survival (OS), while high APC infiltration was of relapse-free survival (RFS) in univariate analyses ($p = 0.044$ & $p \leq 0.030$ respectively). Only Th2 infiltration was predictive of both RFS and OS in univariate ($p = 0.009$ & $p = 0.008$ respectively) and multivariate analyses ($p = 0.002$ & $p = 0.010$ respectively). When considering the different Th populations, only Th2 was a better predictive factor of survival than total leukocytes. Discussion. The development of immune therapies aiming at unlocking the anti-tumor immune response has revealed the desperate need to better characterize the tumor immune infiltrate. TILs quantification by pathologists is the only parameter routinely measured so far but it must be standardized since variability can affect their correlation with pCR. In our study, and contrary to most previous ones, stromal TILs were not significantly associated with RFS and OS. Thus, the characterization of TILs subtypes is critical since they can have either a pro- or an anti-tumorigenic function. Thus, we counteracted the limitations of TILs pathological quantification by finely characterizing the immune infiltrate using flow cytometry. Th2 infiltrate was the most frequent, as previously reported, and counterintuitively, was associated with a favorable prognostic value. This is rarely shown as Th2 infiltration is frequently reported to favor pro-tumorigenic immune tolerance. This proves that a more refined characterization of the intra-tumoral immune landscape is essential to derive interesting therapeutic perspectives, either by recapacitating Th2 response or by targeting their interaction with other immune subsets, like fibroblasts, macrophages, dendritic cells, or eosinophils and IgE. Finally, immunotherapies modulating Th2 response could also be used around the time of surgery that has been proved to induce immunomodulation. Conclusion. The characterization of TILs composition is essential to better understand the potential antitumoral functions of these cells and to substantially improve the associated prognostic and predictive values.

Disclosure(s):

Susie Brousse, n/a: No financial relationships to disclose

Florence Godey, n/a: No financial relationships to disclose

Elodie Laffont, n/a: No financial relationships to disclose

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Matthieu Le Gallo, n/a: No financial relationships to disclose

12/7/2022

7:00 AM - 8:15 AM

P2-11-24

A Novel, Rapid and Economical Prognostic Tool For Adjuvant therapy Decisions in Hormone Positive Breast Cancer

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Several multigene-based, risk scoring methods are available and their use is recommended to support treatment decision making in breast cancer. Although the value of these tests is established, critical challenges remain that limit their use, especially regarding turnaround time for fast decision making and the associated costs. We have developed DigiStain - a novel technology that uses mid-infrared imaging to precisely measure a surrogate of tumour aneuploidy, across unstained biopsy sections. Considering that genomic context shapes the pattern and consequences of aneuploidy during cancer development and progression, aneuploidy may have valuable prognostic or predictive value. Using bespoke software, DigiStain allows a quantitative score 'DigiStain index' (DI) to be reproducibly extracted from an objective physical measurement of a cancer i.e., aneuploidy. This information is generated within minutes and is available at the same time as routine H&E staining. We previously showed that DI significantly correlates with tumour grade and survival. To further validate the technology, we have investigated the ability of the DI to predict 5-year survival in a retrospective analysis of patients with oestrogen receptor (ER) positive breast cancer. Methods: Clinical samples were obtained from patients (N=944) treated at the University Hospital of Nottingham UK. Using the DigiStain imager, H&E images were registered before acquiring the DI score for the section. Statistical methodology followed the recommended approach of Royston et al. 2009, The BMJ. A multivariate logistic model modelling the 'event' of death by 5 years was generated. The predictive performance of the logistic regression model was assessed using Area Under the receiver operating characteristic Curve (AUC) plots. The predicted vs observed event probability was determined at various cut-offs and the accuracy of the classification was measured by its sensitivity and specificity. Results: Of 944 ER+ patients with follow up information, 77 (8.2%) died in the first 5 years. The age distribution was approximately normal, ranging from 26 to 70 (mean = 54.8 years). Tumour size ranged from 0.2 to 7.5 mm (mean = 1.90 mm and median = 1.70 mm) and had normal distribution when the natural log of size was considered. DI contributed to the prognostic model with (p=0.0018). Odds ratios showed increased odds of death by 5 years with higher DI. The AUC obtained for the model was 0.7722. Due to the number of events the sample was not split into training and validation sets. Instead bootstrapping (n=500) was used to assess performance. When adjusted by bootstrapping the AUC was reduced only slightly to 0.76. Classification tables for sensitivity and specificity across different risk cut-offs and distribution of 5-year predicted probabilities showed the best distinction between groups at low levels of predicted probabilities. As expected, there was a trade-off between sensitivity and specificity when choosing an appropriate cut-off point to define high risk of death by 5 years. Conclusions: The risk score obtained using the DI is a significant prognostic factor for 5-year survival in ER+ breast cancer

($p=0.0018$) with good diagnostic accuracy. Analysis of 10-year survival data is ongoing and plans to expand the sample collection to include patients from other sites are underway.

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7:00 AM - 8:15 AM

P2-11-25

A 10-gene signature to predict the prognosis of early-stage triple-negative breast cancer

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Background: Triple-negative breast cancer (TNBC) is highly heterogeneous cancer and the most challenging subtype of breast cancer. And its prognosis is poor compared to the other subtypes. Unlike luminal type cancers, there is no valid biomarker to predict the prognosis of patients with early TNBC. To establish an elaborate therapeutic strategy for TNBC, biomarkers that accurately predict the prognosis and response to treatment are needed. Method: 184 patients with early stage TNBC (training cohort, n = 76; validation cohort, n = 108) were enrolled. Median Follow-up period was 51.5 months (range: 4.6-230.8) for training cohort and 58.3 months (range: 6.6-99.8) for validation cohort. Of the patients in training cohort, 13 patients had recurrence or metastasis. Of the patients in validation cohort, 23 patients had recurrence or metastasis. Using a HiSeq sequencer, RNA sequencing was conducted to analyze the gene expression profiles of tumor samples from TNBC patients. Gene signature was analyzed by combination of DEGs which found in gene expression profiles. Cross

validation and meta-analysis were conducted as pre-validation. Meta-analysis was conducted using CBS probePINGS. To compare gene signature and other methods, PAM 50 call and TCR diversity analysis were investigated. Statistical analyses were conducted using R language (v.3.4.3). Result: To predict prognosis of recurrence or metastasis for TNBC patients, we identified the 10-gene signature (DGKH, GADD45B, KLF7, LYST, NR6A1, PYCARD, ROBO1, SLC22A20P, SLC24A3 and SLC45A4) that stratified patients with TNBC by risk score (sensitivity = 92.31%; specificity = 92.06%; accuracy = 92.11%) and validated in a cohort of separate institutions. Meta-analysis supported the biological relevance of the 10-gene signature to well-known driving pathways in TNBC. When compared with other potential biomarkers like PAM 50 call and T-cell receptor β diversity, the 10-gene signature was the only independent factor that can predict prognosis for invasive disease-free survival in multivariate analysis. Conclusion: Our novel findings can contribute to solving the diagnostic challenges in TNBC and the 10-gene signature may serve as a novel biomarker for risk-based patient care.

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The prognostic role of circulating tumor DNA after neoadjuvant chemotherapy in triple negative breast cancer with residual tumor

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Background The presence of residual tumour at surgery (non-pathological complete response or non-pCR) occurs in about half of TNBCs treated with neoadjuvant chemotherapy (NAC) and signals chemoresistance and poor prognosis. Although further adjuvant chemotherapy (Capecitabine/Xeloda) results in improved survival in patients with non-pCR, only about 15% of such patients do benefit. Circulating tumor DNA (ctDNA) is a plasma-based biomarker that can be used to reveal real-time data about the disease and treatment progression. We have previously shown that detection of ctDNA after NAC signals poor prognosis. To validate and extend our previous results using an academic hospital-based tumor bespoke assay, we

performed ctDNA measurements in non-pCR TNBC patients at the pre-operative, post-operative, 3 and 6-month time points. Methods Whole exome sequencing (WES) was performed on residual tumors from 34 TNBC patients to identify tumour-specific mutations (5/patient). Digital droplet PCR (ddPCR) assays were developed for these mutations and performed as per our previous work. Patients with at least one detectable mutation were considered ctDNA positive for a given time point. The detection of ctDNA was correlated with relapse-free survival (RFS). Results The overall RFS was 44%, with 56 % of patients received adjuvant Xeloda. Detection of ctDNA at the end of NAC (T1) correlated with poor prognosis of RFS (n = 33, p-value = 0.009, HR = 0.29 (95% CI = 0.12 to 0.74)). Detection of ctDNA after surgery (T2) and while on Xeloda (T3) showed no significant prognostic value for RFS. However, ctDNA detection at the 6-month time point, after Xeloda treatment (T4), showed stronger prognostic value for RFS (n = 17, p-value = 0.004, HR = 0.12 (95% CI = 0.03 to 0.51)). When measuring changes in ctDNA detectability from T1 to T4, 4 patients initially positive became ctDNA negative after the 6-month interval, and only 1 of these 4 had a relapse, compared with 10 of 11 that remained positive at the 6-month time point (p = 0.01, Chi-squared test). 3 of the 4 patients that cleared their ctDNA had received Xeloda. In addition, 2 patients initially negative became ctDNA positive at the 6-month time point (T4) and both relapsed, compared with only 1 of 5 that remained negative at 6 months (p = 0.035, Chi-squared test). For patients who received adjuvant Xeloda ctDNA positivity at T1 was associated with a worse RFS (p-value = 0.028, HR = 3.3884 (95% CI = 1.160 to 13.00)). Conclusion ctDNA testing using ddPCR in an academic hospital-based context at the post-NAC time point as well as at 6 months after surgery identifies an excellent prognostic group in TNBC patients with non-pCR and changes in ctDNA during the adjuvant period have prognostic value. This personalized approach to treatment management is ready for prospective testing in patients who have undergone NAC and require additional chemotherapy.

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7:00 AM - 8:15 AM

P2-11-27

Peritumoral desmoplasia in breast cancer – does it matter?

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Background: The peritumoral deposition of collagen is termed desmoplasia. It is characterized by the formation of new extracellular matrix, resulting from activation of tumor-associated fibroblasts. In other cancer entities (e.g. pancreatic and thyroid cancer), the presence of desmoplasia has significant prognostic impact. Furthermore, in preclinical models, targeting desmoplasia therapeutically to normalize the microenvironment has shown promising results. Yet, the role of desmoplasia in breast cancer is still unclear and data regarding this topic is rare. The aim of this study is to investigate whether desmoplasia is present in breast cancer and whether it is associated with other prognostic factors. Methods: We retrospectively analyzed 361 patients with breast cancer who had oncologic surgery at the University Hospital Leipzig, Germany between 2015 and 2018. Patients underwent operation without any preoperative therapy, after neoadjuvant chemotherapy, or after neoadjuvant endocrine treatment. One patient had had radiation in the past. Information regarding desmoplastic tumor reaction and other pathologic characteristics were retrospectively retrieved from the pathology reports. Results: Overall, data regarding desmoplasia was available for 197 patients. Median patient age was 61 years [IQR 50-73] with the most frequent tumor entity (62.9%) being invasive carcinoma of no special type (NST). 184 (93.4%) patients had either a T1 or T2 stadium. Patients had no preoperative therapy, neoadjuvant chemotherapy, or neoadjuvant endocrine treatment in 131 (66.5%), 36 (18.3%) and 29 (14.7%) cases, respectively. Desmoplasia was present in 151 cases. 46 cases showed no evidence for desmoplasia. Median age was almost similar in both groups (60.5 years vs. 61 years). Presence of desmoplasia was not associated with lymph node metastasis (pN1: 26.1% in patients with desmoplasia vs. 31.1% in patients without desmoplasia). Furthermore, there were only small differences in tumor grade between the two groups (G1: 45.7%, G2: 37.8%, G3: 15.9% [patients with desmoplasia] vs. G1: 39.1%, G2: 43.5%, G3: 17.4% [patients with no desmoplasia]). Tumor stages pT1 and pT2 were approximately equal in the two groups (pT1: 66.2% vs. 65.2%, pT2: 29.1% vs. 21.7%). There was a slight trend towards a higher (pT3) tumor stage in patients with desmoplasia (13%) compared to the patients with no desmoplasia (2.7%). Interestingly, the presence of desmoplasia was significantly associated with a higher number of Luminal A subtypes (64.2% vs. 47.8%, p-value: 0.047) and a lower number of triple negative carcinoma (10.6% vs. 17.4%, p-value: 0.22). Conclusions: In our analysis, the presence of desmoplasia is not associated with a more aggressive phenotype of breast cancer. There are hints for an association with a favorable subtype. Larger studies are necessary to validate these data and gain further information.

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Copy number alteration is an independent prognostic biomarker in triple-negative breast cancer patients

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Background: Triple-negative breast cancer (TNBC) is the most fatal breast cancer subtype, which often shows aggressive progression, a high potential to metastasize, and resistance to chemotherapy. Comprehensive genomic profiling using next-generation sequencing (NGS) has been expected to identify gene alterations that are targetable by drugs. However, the significance of these genomic alterations in the cancer biology of TNBC patients has not yet been fully understood due to the lack of accurate clinical outcome data to compare with the genomic data. The aim of this study was to clarify the clinical impact of genomic profiling data, including copy number alterations (CNAs), in TNBC by comparing comprehensive genomic data with clinical outcomes. Methods: A total of 47 patients diagnosed with stage I-III TNBC (from the cohort reported in JCO Precis Oncol. 2018;2:PO.17.00211) were enrolled in this study. The genomic profiling of 435 known cancer genes by NGS with clinical outcomes were analyzed. Overall survival (OS) was evaluated for its association to gene alterations and distinctively CNAs. The cut-off values of CNA for OS were determined from the receiver operating characteristic curve using the Youden index for area under the curve (AUC). Kaplan-Meier plots and log-rank tests of OS were applied for each group. Univariate and multivariate analyses for OS were performed using a Cox proportional-hazards model to obtain the hazard

ratio (HR) and 95% confidence intervals. Results: Utilizing NGS-based genomic profiling, at least one alteration was found in 82 of the 435 cancer-associated genes, and a total of 162 alterations were found in the 47 patients. Among the 82 genes with alterations, the presence or absence of TP53 and PTEN alterations was significantly associated with OS of TNBC patients; patients with TP53 alterations (n = 31) showed significantly shorter OS than those without TP53 alterations (n = 16, p = 0.023), and patients with PTEN alterations (n = 9) showed significantly shorter OS than those without PTEN alterations (n = 38, p = 0.023). The cut-off value of CNA for OS was set at 25 (AUC, 0.788; sensitivity, 0.727; specificity, 0.900). Interestingly, CNA-high patients (n = 20) showed significantly shorter OS than CNA-low patients (n = 27, p = 0.014). Univariate analysis revealed that TP53 alterations and CNAs were significant prognostic factors for OS (HR, 8.81; p = 0.008; and HR, 8.00; p = 0.014, respectively). Finally, multivariate analysis using background clinical data revealed that CNA was an independent prognostic factor for OS in TNBC patients (HR, 7.15; p = 0.044). Conclusion: Our data suggest that CNA is an independent prognostic marker in TNBC, and that can be estimated from comprehensive genomic profiling data by NGS. Further investigation is needed to clarify the mechanisms of how CNAs are associated with this lethal disease.

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The Expression of Claudin-10 in relationship with Her family members in patients with breast cancer

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Introduction. Claudin-10 (CLDN10), a member of the Claudin tight junction (TJ) protein family, was initially known as Oligodendrocyte-Specific Protein-Like (OSP-L). The distribution of CLDN10 in the body is not ubiquitous and is seen more abundantly in kidney and brain and at modest levels in mammary tissues. Limited information suggests that in cells where CLDN10 is expressed, it interacts with other family members including CLDN-11, 12, 16, 17 and the subcoat zonula occludens (ZO-1 and ZO-3) to regulate TJ functions. The role played by CLDN10 in cancer is not clear but there are suggestions that it is a favourable indicator for disease progression in kidney and gastric cancers but an adverse indicator in hormone related cancers such as thyroid cancer. The role of CLDN10 in breast cancer is otherwise not known. We have investigated the expression profile and in particular in its relationship with hormone receptor status. Methods. We carried out CLDN10 transcript and protein analyses by way of quantitative PCR and immunohistochemistry on an established cohort of fresh frozen mammary tissues and breast cancer tissues. Expression was analysed via QPCR against the staging, histology, clinical outcome, hormone status including ER and Her family members, and also its known interactive TJ molecules available to our database. Results. Compared with its interactive TL partner molecules, CLDN10 was expressed at relatively low levels in mammary tissues. There was no significant difference in CLDN10 transcript levels between normal tissues and tumour tissues. Patients with high levels of CLDN10 in breast tumours had significantly shorter overall survival (OS) ($p=0.041$) and disease free survival (DFS) ($p=0.026$). In our cohort, we found a significant correlation between levels of CLDN10 and Her-1/EGFR ($r=0.201$, $p=0.026$) and Her3 ($r=0.935$, $p< 0.0001$), but not with Her-2 nor with Her-4. It was also surprised to find that CLDN10 did not correlated with the ZO-1, ZO-3, CLDN11, 12, 14, and 17. We then identified a subgroup of patients with low levels of CLDN10 and their overall survival

(OS) and disease free survival (DFS) which were significantly correlated with Her-1/Her-3 expression status ($p < 0.0001$ for both OS and DFS). CLDN10, amongst the clinical, pathological and hormone receptor status, is an independent prognostic factor for DFS ($p=0.008$, Hazard Ratio (HR) =4.228 (95% CI 1.449-12.342)) and for OS ($p=0.025$, HR=3.917 (95% CI 1.187-12.924)). The predictive power for triple negative breast cancer (TNBC) and non-TNBC by CLDN10 otherwise remained similar and not statistically significant. It was noted that stratification by ER and Her-2 did not contribute to the value of independency. Conclusion. CLDN10, although expressed at relative lower levels in breast cancer, is a contributing factor to the survival of the patients. Together with the status of EGFR and Her-3, it makes an independent prognostic factor for both the overall survival and disease free survival of the patients.

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7:00 AM - 8:15 AM

P2-11-30

Performance of tumor vascularity as a biomarker is correlated with the change of tumor vascularity after preoperative systemic treatment in patients with breast cancer.

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Background) Breast cancer is a leading cause of death worldwide. Tumor vascularity is a hallmark of cancer including breast cancer. However, targeting tumor vascularity did not show consistent benefit when applied in clinic. This study aimed to investigate in which group of patients can tumor vascularity be a prognostic factor and how does change of tumor vascularity play in this situation. Materials and methods) Female patients with breast cancer who received preoperative chemotherapy due to breast cancer between 2003 and 2018 at Wonju Severance Hospital, Korea, were included. Clinicopathological characteristics were collected. Hounsfield units(HU) on contrast-enhanced computed tomography(CT) was used as a marker indicating tumor vascularity. Tumor to aortic arch ratio(TAR) of HU on contrast enhanced CT was applied to enhance objectivity of measurement. Patients were categorized according to the cut-off values retrieved from the receiver operating characteristic curve. Kaplan-Meier curves were generated to compare recurrence-free interval (RFI) and overall survival (OS). Results) The final cohort included 162 patients with a mean age of 48.63 ± 7.9 (30-69) years. Initial TAR was 0.38 ± 0.103 (range, 0.184-0.946) and TAR after completion of preoperative systemic treatment was 0.29 ± 0.094 (0.677-0.298). Difference between TAR of immediate before surgery and first clinical presentation was -0.086 ± 0.094 (-0.386 – 0.176). TAR was decreased in 122 (75.3%) patients. Initial TAR was significantly correlated with recurrence free survival(RFS)($p=0.002$). However, TAR after preoperative systemic treatment ($p=0.221$) or delta TAR (area under receiver operating characteristics = 0.498) were not significant. Interestingly, initial TAR was significant only in patients with decreased TAR after preoperative systemic treatment($p=0.005$). Conclusion) Tumor vascularity represented with HU was significantly related with patients' survival only when tumor vascularity was decreased in response to systemic treatment. Considering no antiangiogenic agents were applied as preoperative systemic treatment and still capacity of tumor vascularity as a biomarker was influenced by the change of itself,

antiangiogenic agents could be used as a complimentary agent for the other agents which also impact tumor vascularity.

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P2-11-31

FAVORABLE LOCOREGIONAL CONTROL IN CLINICALLY NODE-NEGATIVE HORMONE-RECEPTOR POSITIVE BREAST CANCER WITH LOW 21-GENE RECURRENCE SCORES: A SINGLE INSTITUTIONAL STUDY WITH 10-YEAR FOLLOW-UP

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Background: Recent studies have shown a lower likelihood of locoregional recurrences in patients with low 21-gene recurrence score (RS). In this single institutional study, we investigated any associations between different cut-off values of 21-gene RS and histopathological factors and outcome in patients with long-term follow-up.

Methods: Between February 2010 to February 2013, 61 patients with early stage clinically node-negative hormone receptor-positive and HER2-negative breast cancer tested for the 21-gene RS assay, were included into the study. The clinicopathological, treatment and outcome

characteristics were analyzed.

Results: Median age was 48 (range, 29-72). Of those, 53 patients were diagnosed with Stage 1 (86.9%) and 8 patients were Stage 2 (13.1%) following surgery. Patients with high histologic grade (HG), or with Ki-67 $\geq 25\%$ were significantly more likely to have intermediate/high RS based on RS >11 and >18 (Table 1). Based on the 21-gene RS assay, only 19 patients (31%) received adjuvant chemotherapy. At a median follow-up of 112 months, 3 patients developed local recurrences (4.9%) treated with endocrine therapy alone. Among patients treated with endocrine treatment alone (n=42), the clinicopathological characteristics including age < 40 , age < 50 , high histologic or nuclear grade, high Ki67-scores ($\geq 20\%$, $\geq 25\%$, $\geq 30\%$), presence of lymphovascular invasion, luminal-A type tumor, multifocality, lymph node positivity, tumor size more than 2 cm, RS ≥ 18 or RS >11 were not significantly found to be associated with 10-year locoregional recurrence free survival (LRRFS). However, patients with a RS ≥ 16 have significantly shown a poorer 10-year LRRFS compared to those with RS < 16 (RS < 16 ; 100% vs RS ≥ 16 ; 75%, $p=0.039$, Table 2).

Conclusions: These results suggest that Oncotype DX assay may be of little value in patients with high histologic grade or high Ki67 scores ($\geq 25\%$) as treatment decision criteria to determine any benefit from chemotherapy. Furthermore, patients with a RS ≥ 16 are more likely to benefit from adjuvant chemotherapies, whereas those with a RS < 16 have an excellent outcome and local control on long term follow-up with endocrine treatment alone. Further prospective studies should be performed to validate these findings in future.

Table 1. Correlation of 21-gene Recurrence Score (RS) including different cut-off values with Ki-67 scores and histopathological factors

Characteristics	RS>11	<i>p</i> - <i>value</i>	RS ≥18	<i>p</i> - <i>value</i>	RS >25	<i>p</i> - <i>value</i>	RS >31	<i>p</i> - <i>value</i>
HG low&intermediate (n=51) vs high HG (n=10)	36/51(71%) vs 10/10 (100%)	0.05	16/51(31%) vs 9/10 (90%)	0.001	3/51 (5.9%) vs 4/10 (40%)	0.011	2/51 (3.9%) vs 2/10 (20%)	0.122
Ki67<25% (n=50) vs ≥25% (n=11)	37/50 (74%) vs 9/11 (81.8%)	0.716	17/50 (34%) vs 8/11 (72.7%)	0.038	3/50(6%) vs 4/11 (36.4%)	0.016	2/50 (4%) vs 2/11 (18.2%)	0.146

Table 2. Clinicopathologic factors and 21-gene Recurrence Score (=RS) associated with disease free survival (DFS) and locoregional recurrence free survival free survival (=LRRFS). (DFS is equal to LRRFS since none of the patients developed distant metastases)

Factors	10- year LRRFS=10-year DFS	p-value
Total (N=61)		
RS \leq 11 vs RS>11	100% vs 90.2%	0.292
RS<16 vs RS \geq 16	100% vs 88%	0.149
RS< 18 vs RS \geq 18	91.6% vs 94.1%	0.808
Without Adjuvant Chemotherapy (n=42)		
RS \leq 11 vs RS>11	100% vs 83%	0.180
RS<16 vs RS \geq 16	100% vs 75%	0.039
RS< 18 vs RS \geq 18	91.3% vs 75%	0.274

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7:00 AM - 8:15 AM

P2-11-33

Striatin and its interactive proteins Protein Phosphatase-2 (PP2) and PP2 regulatory elements in breast cancer

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Introduction. The striatin protein family are calmodulin binding scaffolding proteins. Striatins have been involved in cell signalling and recently found also acting as cell adhesion molecules and adhesion regulators in adherens junctions and tight junctions. Striatins, particularly striatin-2 forms a recently discovered protein complex, STRIPAK, with other complex members including Protein Phosphatase-2 (PP2), STRIP, SIKE1 and certain PP2 regulatory proteins. The STRIPAK regulates multiple cell functions including gene transcription, endo- and exocytosis and cell adhesion, and several other important cell functions in cancer development and progression. The constitute members of the striatin protein complex may thus have important clinical bearings. In the present study, we investigated the expression profile of the striatin family members and key members of their interacting proteins, and discerned the relationship between the expression and disease progression and clinical outcome. Methods. Using an established fresh frozen breast cancer tissues cohort that included both normal mammary tissues and cancer tissues, we quantitatively evaluated the transcript expression of striatin-1 (STRN), striatin-3 (STRN3), striatin-4 (STRN4), its key regulator calmodulin (CALM) and the protein complex regulators protein phosphatase-2A (PPP2A), -2B (PPP2B) and the PPP2 regulatory elements PPP2R4 and PPP2R1A. The expression of each molecule was assessed against the clinical, pathological and prognostic factors of the patients. The integrated pattern of the complex members were also tested against the clinical outcome. Results. All three striatin members were expressed at good levels in mammary tissues and cancer tissues. STRN had little significant value against clinical and pathological factors. STRN3 and STRN4 were seen at high levels in tumours of high grade, with node positivity and with breast cancer

related incidence. It was high level expressions of STRN3, STRN4 and CALM that were respectively associated with shorter overall survival (OS) of the patients and together they formed a poor prognostic indicator ($p=0.034$, $HR=1.7$). STRN had little impact on clinical outcomes. In a clear contrast, high levels of PPP2A, PPP2B and PPPR1A, but not PPP2R4, were seen in patients with significantly longer OS and together form a favourable prognostic indicator ($p=0.034$, $HR=0.685$). Integration of both STRN group and PPP2 group indicators constitutes a highly significant prognostic indicator for OS ($p < 0.00001$, $HR=2.1$ (95%CI 1.36-3.07)) and DFS ($p=0.003$, $HR=1.402$ (95%CI 1.12-1.75)). The predictive value of the integrated profile is independent of other clinical, pathological and hormone receptor status in multivariate analyses with OS ($p < 0.0001$, $HR=3.861$) and for DFS ($p < 0.001$, $HR=2.055$ (95%CI 1.36-3.07)). The same value stands when applied for the subtypes including triple negative breast cancers. Discussion. The STRIPAK complexes including Striatins play important regulatory roles in various cell functions and cancer development. Consistently, we found that high level expressions of STRN3, STRN4 and CALM, as a poor prognostic indicator were associated with shorter overall survival (OS) of the patients, while high levels of PPP2A, PPP2B and PPPR1A, as a favourable prognostic indicator, were seen in patients with significantly longer OS. Combination of both STRN group and PPP2 group indicators constitutes a greater significant prognostic indicator for OS and DFS. Future studies should focus on investigating the exact roles of the STRIPAK in cancer development and progression.

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P2-11-34

Mitotic spindle hotspot counting using deep learning networks is highly associated with clinical outcomes in patients with early-stage triple-negative breast cancer who did not receive systemic therapy

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Background: Triple-negative breast cancers (TNBC) exhibit high rates of recurrence and mortality. However, recent studies suggest that a subset of patients (pts) with early-stage TNBC enriched in tumor-infiltrating lymphocytes (TILs) have excellent clinical outcomes even in the absence of systemic therapy. Additional histological biomarkers that could identify pts for future systemic therapy escalation/de-escalation strategies are of great interest. TNBC are frequently highly proliferative with abundant mitoses. However, classic markers of proliferation (manual mitosis counting and Ki-67) appear to offer no prognostic value. Here, we evaluated the prognostic effects of automated mitotic spindle hotspot (AMSH) counting on RFS in independent cohorts of systemically untreated early-stage TNBC.

Methods: AMSH counting was conducted with a state-of-the-art deep learning algorithm trained on the detection of mitoses within 2 mm² areas with the highest mitotic density (i.e. hotspots) in digital H&E images. Details of the development, training and validation of the algorithm were published previously [1] in a cohort of unselected TNBC. We obtained AMSH counts in a centrally confirmed TNBC cohort from Mayo Clinic [2] and focused our analysis on pts who received locoregional therapy but no systemic therapy. Using a fractional polynomial analysis with a multivariable proportional hazards regression model, we confirmed the assumption of linearity in the log hazard for the continuous variable AMSH and evaluated whether AMSH counts were prognostic of RFS. We corroborated our findings in an independent cohort of systemically untreated TNBC pts from the Radboud University Medical Center in the Netherlands (Radboud Cohort). Results are reported at a median follow-up of 8.1 and 6.7 years for the Mayo and Netherlands cohorts, respectively.

Results: Among 182 pts with who did not receive systemic therapy in the Mayo Cohort, 140 (77%) with available AMSH counts were included. The mean age was 61 (range: 31-94), 71% were postmenopausal, 67% had tumors \leq 2cm, and 83% were node-negative. As expected, most tumors were Nottingham grade 3 (84%) and had a high Ki-67 proliferation index (54% with Ki-67 $>$ 30%). Most tumors (73%) had stromal TILs \leq 30%. The median AMSH count was 18 (IQR: 8, 42). AMSH counts were linearly associated with grade and tumor size, with the proportion of pts with grade 3 tumors and size $>$ 2 cm increasing as the AMSH counts increased ($p=0.007$ and $p=0.059$, respectively). In a multivariate model controlling for nodal

status, tumor size, and stromal TILs, AMSH counts were independently associated with RFS ($p < 0.0001$). For every 10-point increase in the AMSH count, we observed a 17% increase in the risk of experiencing an RFS event (HR 1.17, 95% CI 1.08-1.26). We corroborated our findings in the Radboud Cohort ($n=126$). The mean age was 68 (range: 40-96), and 81% were node-negative. While the median AMSH count was 36 (IQR: 16-63), higher than in the Mayo Cohort ($p=0.004$), the prognostic impact was similar, with a significant association between AMSH count and RFS ($p=0.028$) in a multivariate model corrected for nodal status, tumor size, and stromal TILs. For every 10-point increase in the AMSH count in the Netherlands cohort, we observed a 9% increase in the risk of experiencing an RFS event (HR 1.09, 95% CI 1.01-1.17). RFS rates according to AMSH counts for both cohorts are shown in the Table.

Conclusions: AMSH counting is a new proliferation biomarker that provides prognostic value independent of nodal status, tumor size, and stromal TILs in systemically untreated early-stage TNBC. Plans are underway to evaluate AMSH counts in additional cohorts of systemically untreated TNBC, and in other disease settings such as prior to neoadjuvant systemic therapy. If validated, this biomarker should be prospectively evaluated as a potential selection biomarker in clinical trials of systemic therapy de-escalation.

References:

1. PMID: 29994086
2. PMID: 28913760

Table

Outcome	Mayo Cohort			Radboud Cohort		
	AMSH counts <30	AMSH counts 31-75	AMSH counts >75	AMSH counts <30	AMSH counts 31-75	AMSH counts >75
3-year RFS (95% CI)	85% (77-94)	66% (52-86)	43% (24-79)	85% (0.75-0.96)	77% (65-90)	55% (37-82)
5-year RFS (95% CI)	82% (74-92)	62% (46-83)	27% (11-66)	77% (65-91)	51% (38-70)	50% (33-78)

RFS according to AMSH counts in the Mayo and Radboud Cohorts

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7:00 AM - 8:15 AM

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A tight junctional scaffold protein MUPP1/MPDZ and its docking proteins, angiomotins in breast cancer

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A tight junctional scaffold protein MUPP1/MPDZ and its docking proteins, angiomotins in breast cancer Han Gao¹, Fiona Ruge¹, Lin Ye¹, Jane Lane¹, Eleri Davies², Wen G. Jiang¹, Tracey A. Martin¹ ¹Cardiff University School of Medicine, Heath Park, Cardiff CF14 4XN, UK ²Wales Breast Centre, University Llandough Hospital, Cardiff CF64 2XX, UK Introduction. MUPP1 (Multiple PDZ Domain Crumbs Cell Polarity Complex Component) or MPDZ is a scaffold protein with multiple PDZ domains, critical for multiple protein docking and protein-protein interactions in cells. MUPP1 is particularly interesting as it offers docking sites for a number of tight junction (TJ) proteins and proteins known to regulate cell junction and motility, including angiomin (AMOT) and angiomin-like proteins, the latter being important in regulating cell migration of endothelial cells and an important member in TJ protein complexes. The MUPP1 protein complex at cell junctions also includes CAR/CXADR (coxsackie adenovirus receptor) and members of the ERM (Moesin-Ezrin-Radixin) protein family. It was proposed that the junctional-related MUPP1 docking protein complex may collectively have a role in the development and progression of cancer including breast cancer. The present study examined the profile and integrated expression of these MUPP1 docking molecules in relationship with the outcome, clinical and pathological factors of breast cancer. Methods. Using the datasets of an existing breast cancer cohort at Cardiff, we visited the expression profile of the MUPP1/MPDZ docking molecules including MUPP1, four members of the ERM family, including ezrin, moesin, radixin and EHM2 (also known as NF2) and CAR/CXADR (coxsackie adenovirus receptor). The profile and integrated expression of the profile were analysed against clinical, pathological and outcome factors and also the hormone receptor status of breast cancers. Results. MUPP1 is a weakly linked to the disease progression, so as angiomin, angiomin-like¹ and angiomin-like². Alone, only EHM2 showed significance in linking with

the survival of the patient's OS ($p=0.38$), neither of the remaining MUPP1 complex molecules, including MUPP1, AMOT, AMOTL1, AMOTL2, ezrin, moesin and radixin was able to offer a significant predictive value for the survival of the patients. However, it was found that MUPP1 has a significant correlation with AMOTs, EHM2 and ezrin. When these significantly correlated molecules were integrated in the analysis, the integrated expression pattern showed a highly significant value in evaluating the overall survival ($p=0.003$) and disease-free survival ($p=0.007$). Both of these predictive powers are independent in a multivariate analyses including the clinical and hormone receptors for OS ($p=0.022$, Hazard Ratio (HR)=1.352 95%CI (1.044-1.752)) and RFS ($p=0.023$, HR=1.241 (95% CI. 1.031-1.498)). It was interesting to note that the link between the expression pattern and OS was more prominent in ER negative ($p=0.018$) than in ER positive tumours ($p=0.177$). The same was observed with disease free survival for ER negative ($p=0.011$) compared with ER positive ($p=0.462$) tumours. Non-triple negative breast cancer had shown a similar sensitivity compared with triple negative breast cancer. Discussion. MUPP1, a PDZ domain containing docking protein closed linked with TJ structure, forms an interesting expression profile with its docking molecules including angiomotins and EHM2 that allows evaluation of disease progress and clinical outcome of the patients with breast cancer.

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Osteopontin splice variants indicate prognosis in premalignant breast lesions

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BACKGROUND: Premalignant breast lesions pose variable risks for transformation, raising the question who should receive treatment to counteract the potential progression to breast cancer. Prognostic indicators will spare low-risk patients the burden of substantial treatment side effects and will enable high-risk patients to comfortably take preemptive action. Osteopontin (OPN) is a secreted mediator of breast cancer progression, which is subject to alternative splicing in transformed tissues and has been known to be a marker for breast cancer aggressiveness. Here, we test the variants OPN-a and OPN-c as potential prognosticators for the transformation of premalignant breast lesions. The presence of spliced Osteopontin-c in these lesions does reflect the risk for cancer development within 5 years. **METHODS:** By immunohistochemistry, we analyze the association of Osteopontin variant expression in healthy breasts, hyperplasias, radial scars, lobular and ductal carcinomas in situ from 434 women as well as papillomas from 114 women to assess a) staining for OPN exon 4 (present in OPN-a and OPN-b) and OPN-c in low-risk to high-risk lesions b) correlations between staining and progression to cancer or survival. **RESULTS:** The staining intensity for OPN-c correlates with risk, and it is prognostic for ensuing invasive disease and survival. About 10% of OPN-c pathology score 0–1 (intensity), vs. 40% of score 3 experience cancer over 5 years. More than 90% of women, who progress, had pathology scores of 2–3 for OPN-c intensity at the time of initial diagnosis. When combining OPN-c and OPN exon 4 staining, all of the low intensity patients are alive after 5 years, whereas women in the high category have a close to 30% chance to die within 5 years. Of patients who succumb, close to 80% had a high combined score at the time of initial diagnosis. In the papilloma patients, fewer than 5% of OPN-c pathology score 0-1 (intensity), versus almost 18% of score 2-3 experienced cancer in follow-up. 9 of 12 women, who progressed, had pathology scores of 2-3 for OPN-c intensity at the time of initial diagnosis, none had a score of 0. When developing a combined risk score from intensity plus percent positivity for OPN-c, the progression risk for patients with low score was 3.2%, for intermediate score was 5.7%, and for high score was 18.8%. Papillomas in patients, who were later diagnosed with cancer in the contralateral breast, displayed stronger staining positivity than non-progressors. **CONCLUSION:** The information of OPN-c immunohistochemistry can provide a foundation for very reliable prognostication and has the potential to aid decision making in the treatment or watchful waiting of early breast lesions. The addition of OPN-a refines the prognostication of survival. The staining intensity for OPN variants may also inform on the cancer risk in the unaffected breast, which may reflect a genetic predisposition for Osteopontin expression and splicing. OPN splice variant immunohistochemistry on breast biopsies will allow counseling of the patients on their risk to develop breast cancer at a later time.

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A comprehensive assessment of researcher needs to increase biospecimen donations for breast cancer research: A Patients and Researchers Together (PART) Program

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A comprehensive assessment of researcher needs to increase biospecimen donations for breast cancer research: A Patients and Researchers Together (PART) Program Introduction: Tissue-based breast cancer research can help translate scientific discoveries to improve treatments or reduce cancer risk. Tissue donation programs require a partnership between patients being asked to donate tissue and researchers using tissue for translational investigation. Lineberger Comprehensive Cancer Center (LCCC) has established a program called Patients and Researchers Together (PART) to increase the number of patients that donate tissue for research. PART believes patients will be more willing to donate tissue if they are informed about the research process and its impact and are valued as partners of LCCC. The PART program is evaluating the tissue donation process to positively impact efficiencies.

Methods: PART leaders conducted interviews to assess current and future needs of LCCC cancer care providers involved in tissue-based research. A total of 13 breast cancer care providers at LCCC with different lengths of research experience were interviewed. These included 4 surgeons, 4 clinical study coordinators, 2 pathologists, 2 medical oncologists and 1 member of the Tissue Procurement Facility (TPF) staff. Interviewees identified key themes, provided insight into barriers and facilitators, and recommended resources to enhance the tissue-based research process. Results: Interviewees noted the high need for fresh tissue, which requires real-time coordination between clinicians, clinical study coordinators, surgeons, pathologists and researchers. Interviewees identified numerous barriers to the tissue donation process that hinder patient recruitment. These included: lack of knowledge about tissue-based research, time commitment required by an additional procedure, loss of privacy, lack of trust and knowledge about how the tissue will be used and access to cancer care (transportation). Interviewees also identified facilitators for recruiting patients to donate tissue for research, including: tailored communication between the patient and their cancer care team, a high interest in medical research, plain language and understandable educational materials and input of a trusted care team member at the appropriate time. Interviewees identified the need for additional tissue collection support and provided recommendations to improve the tissue donation process. Recommendations included: 1) increase the quantity of tissue available for research, 2) increase the racial and treatment history diversity of patients involved in tissue donation research, 3) increase diversity in the biological types of tissue donations (i.e., blood, stool, tumor), and 4) ensure that the available tissue is optimal for use in research. In addition, interviewees identified resources to enhance the tissue-based research process. One suggested resource is a team of coordinators tasked with managing the day-to-day operations of the tissue collection process and serving as a point of contact throughout. Ideally, the designated team would facilitate communication throughout the tissue collection process from the identification of a patient to the tissue's use in research. Other recommendations included plain language patient educational materials, internal website improvements to enhance communication between researchers, and a written standard operating procedure guide shared with clinical and research team members. Finally, interviewees noted the importance of communication between tissue collection process stakeholders, highlighting the disparity in knowledge regarding best practices between new and more experienced researchers. Findings can inform the development of educational materials and other strategies to increase patient participation in tissue-based breast cancer research.

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ClinicalomicsDB - Bridging the gap between clinical omics data and machine learning

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BACKGROUND

Clinical trials are controlled patient studies aiming to objectively assess the effectiveness of treatment interventions. However, the average effectiveness observed at the group level does not directly apply to individual patients. Cancer clinical trials that include molecular profiling on the baseline tumor samples enable the discovery of treatment response-associated molecular features and the development of prediction models that help discriminate responders from non-responders in each treatment arm. Despite potential opportunities, there are many challenges associated with the predictive modeling of such data, as exemplified by the small sample size and large feature space. Advances in machine learning and artificial intelligence (AI) may provide new solutions to address these challenges. However, for machine learning and AI to have an impact, data needs to be carefully curated, high-quality, standardized, and easily accessible and understood by data scientists, who may not have the domain knowledge.

METHODS

Here, we created a python package "ClinicalOmicsDB" to address the challenges of data accessibility and promote development and application of machine learning methods to omics data from clinical trial samples with treatment response information. The package makes data readily analyzable by data scientists so that they can develop, utilize, and optimize their algorithms for predicting treatment responses and discovering novel biomarkers. To promote a two-way dialogue, we have also developed several Jupyter Notebook tutorials for biologists or clinicians who wish to gain expertise in machine learning. Omics data from clinical studies are downloaded from Gene Expression Omnibus (GEO) and responses were determined based on clinical trial primary endpoints. Currently, the package has datasets from 22 breast cancer clinical trials, including a total of 5050 patients (Table 1). It will be continuously expanded to include additional trials for breast cancer and other cancer types.

RESULTS

To evaluate package utility, we built machine learning models to predict neoadjuvant chemotherapy with four cycles of 5-fluorouracil/epirubicin/cyclophosphamide (FEC) followed by four cycles of docetaxel/capecitabine on US Oncology clinical trial 02-103 [GSE42822]. The best performing model was the Random Forest Classifier model, which had an AUC of 0.817.

To determine the generalizability of machine learning models established from the package, we trained a Random Forest Classifier model using the GSE25055 breast cancer dataset and apply the model to a different breast cancer dataset, GSE20194, which yielded an AUC of 0.648. These results suggest utilizing machine learning on clinical omics datasets can provide predictive and generalizable models that could be implemented in clinical settings for future breast cancer patients.

CONCLUSION

We are expanding the database for data scientists, biologists, and clinicians to practice novel biotechnology-derived therapies to facilitate the implementation of precision medicine approaches for future patients. As more people add new data to the package, we will work towards improving pharmaceutical and private companies' clinical trial data sharing policies and practices to promote data sharing.

Table1. Available breast cancer datasets in ClinicalOmicsDB

Datasets	Therapy	Cancer types	Sample (n)	Criteria for R	Criteria for NR	Treatment types	Platform
GSE194040	[Veliparib/Carboplatin], [Neratinib], [MK2206], [Ganitumab], [Gadoterate meglumine] Doxorubicin + Cyclophosphamide	Breast	988	pCR	RD	Cytotoxic	microarray
GSE196093	[Veliparib/carboplatin], [neratinib], [MK2206], [Ganitumab], [Gadoterate meglumine] Doxorubicin + Cyclophosphamide	Breast	736	pCR	RD	Cytotoxic	Protein
GSE164458	Veliparib/Carboplatin/Paclitaxel/Doxorubicin/Cyclophosphamide	Breast	482	pCR	RD	Cytotoxic	RNA-Seq
GSE25055	Taxane/Anthracycline	Breast	310	pCR	RD	Cytotoxic	microarray
GSE41998	Doxorubicin/Cyclophosphamide/Ixabepilone/Paclitaxel	Breast	279	pCR	RD	Cytotoxic	microarray
GSE20194	Paclitaxel/5-FU/Doxorubicin	Breast	278	pCR	RD	Cytotoxic	microarray
GSE32603	Taxane/Anthracycline	Breast	248	pCR	RD	Cytotoxic	microarray
GSE163882	Taxane/Anthracycline/Cyclophosphamide	Breast	222	pCR	RD	Cytotoxic	RNA-Seq
GSE20271	Taxane/5-FU anthracycline cyclophosphamide	Breast	178	pCR	RD	Cytotoxic	microarray
GSE6861	5-FU epirubicin cyclophosphamide/ Docetaxel	Breast	161	pCR	npCR	Cytotoxic	microarray
GSE123845	Taxane/Anthracycline Cyclophosphamide	Breast	146	pCR	RD	Cytotoxic	RNA-Seq
GSE106977	Taxane/Anthracycline Cyclophosphamide/Carboplatin	Breast	119	pCR	RD	Cytotoxic	Microarray
GSE87411	Aromatase	Breast	109	Endocrine Sensitive	Endocrine Resistant	Targeted	Microarray
GSE41994	Anastrozole	Breast	107	No Disease Progression	Disease Progression	Targeted	microarray
GSE22093	5-Fluorouracil/Doxorubicin/ Cyclophosphamide	Breast	103	pCR	RD	Cytotoxic	microarray
GSE4779	Anthracycline/ 5-FU epirubicin cyclophosphamide	Breast	102	pCR	npCR	Cytotoxic	microarray
GSE42822	5-FU epirubicin cyclophosphamide/ Taxane	Breast	91	pCR	RD	Cytotoxic	microarray
GSE140494	Docetaxel/5-FU/Epirubicin/Cyclophosphamide	Breast	91	pCR	pPR	Cytotoxic	microarray
GSE119262	Everolimus	Breast	88	delta-ki67<to p tertile	delta-ki67>to p tertile	Targeted	microarray
GSE66305	Lapatinib	Breast	88	pCR	RD	Targeted	microarray
GSE66999	Docetaxel/Epirubicin	Breast	76	CR	PR	Cytotoxic	microarray
GSE19697	Epirubicin/Docetaxel	Breast	24	No Recurrence	Recurrence	Cytotoxic	microarray
GSE28796	Docetaxel	Breast	24	pCR	RD	Cytotoxic	microarray

The current database has 22 breast cancer clinical trials with 5050 total patients. Therapy shows various cytotoxic and/or targeted treatments utilized in a clinical trial. The database will be continuously expanded to include additional trials for breast cancer and other cancer types.

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Enrollment Trends Among Patients With Breast Central Nervous System Metastasis in Active Clinical Trials

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Background: Breast cancer is the second leading cause of solid tumor brain metastasis. Up to 16% of patients with metastatic breast cancer (mBC), and 50% patients with HER2+ metastatic breast cancer will develop central nervous system (CNS) metastasis overtime. Prognosis in these patients is dismal with a median overall survival of 2-15 months. Despite advances in systemic therapy of mBC, treatment options for patients with breast cancer brain metastasis (BCBM) remain limited. Although newer approaches to treat BCBM are imminently needed, BCBM patients have traditionally been excluded from clinical trials. We aimed to examine the current state of BCBM-related enrollment in ongoing prospective systemic therapy clinical trials for mBC. Methods: We performed a systematic search of the clinicaltrials.gov website on May 1, 2022 to characterize current trends in clinical trial enrollment for BCBM patients in ongoing interventional trials using the key search term "Breast Cancer". Trial search was further limited to "open" and "interventional studies". Data was abstracted and verified by two independent researchers. Trials were excluded if they were specific for other disease types, did not include a systemic anticancer pharmaceutical, or excluded advanced/metastatic disease. Inclusion of active CNS disease [BCMB and leptomeningeal disease (LMD)] and exclusion of CNS disease were the co-primary end points. Covariates of interest were gender, location (US, international or both), disease site (breast cancer specific vs multi-disease trials), therapy category (immunotherapy (IO), targeted therapy, endocrine therapy, chemotherapy, or combination) and sponsor type. Logistic regression was used to model inclusion of active CNS disease. Results: A total of 1720 trials were identified, and 576 trials met the inclusion criteria. 179 (31.6%) were phase I, 129 (22.4%) were phase I/II, 196 (34.0%) were phase II, 60 (10.4%) were phase III and 9 (1.6%) were phase IV. 347 (60.4%) were breast cancer specific and 229 (39.6%) were multi-site trials. 66 (11.5%) trials were specific for HER-2+ cancer and 70 (12.1%) were triple negative breast cancer specific. 238 (41.3%) trials were US only and 290 (50.3%) were pharmaceutical industry sponsored. Overall, only 29 trials (5%) included patients with any form of BCBM and only 11 trials (1.9%) allowed patients with LMD. 12 (2.1%) trials allowed patients with treated BCBMs only. In univariate models, breast cancer only trials (OR 4.07, 95% CI 1.77-9.36, p=0.0009), trials excluding men (OR 1.97, 95% CI 1.03-3.77, p=0.0412), non-IO therapy trials (non-IO vs IO OR 3.57, 95% CI 1.08-11.82, p=0.369), and non-pharmaceutical industry sponsored trials (OR 2.65, 95% CI 1.34-5.22, p=0.0049) were more likely to include patients with active CNS disease. Additionally, inclusion of LMD (OR 7.85, 95% CI 2.19-28.17, p =

0.0016) was a significant predictor of inclusion of active CNS disease. In a combined model, disease site remained significant (breast only vs multi-site OR 4.07, 95% CI 1.77-9.36, p = 0.0009). Conclusion: The vast majority of the ongoing breast cancer clinical trials continue to exclude patients with breast cancer brain metastasis. With an increasing prevalence of breast cancer brain metastasis, evaluating intracranial efficacy of novel therapies early on in drug development remains an area of urgent unmet need.

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COBRA: Characteristics and Outcomes of patients with BReast cancer in phAse I trials at Gustave Roussy Cancer center

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Background: Breast cancer (BC) is the most frequent cancer and the second leading cause of cancer death for women. Although there is a need of new treatments to improve BC outcome, patients with BC are still under-represented in early phase trials, possibly because of the availability of numerous approved treatments and widely recruiting phase II and III trials. We aim to characterize the molecular profile, outcome and prognostic factors of patients with BC treated in a phase I trial at our institution. Methods: We retrospectively analyzed medical records of every BC patients treated consecutively in a phase I trial in the Early Drug Development Department (DITEP) at Gustave Roussy Cancer Center. Multivariate logistic regression models were used to determine the association between known prognostic factors such as ECOG, LDH or albumin levels, number of previous lines of treatment, metastatic sites and duration of treatment. When available, molecular profile was also reviewed. Results: Between April 1st 2008 and December 31st 2021, 4682 patients were enrolled and treated in a phase I trial in our department. Among them, 272 were treated for BC (5.8%): 271 women and 1 man, in 74 different trials. The median number of BC patients treated per year was 16.5 (min 1; max 33). Median time between consented date and C1D1 was 14 days (min 1; max 63). Median age at C1D1 was 50 years old (min 24; max 82). 5 patients (1.8%) were treated in an adjuvant setting (therapeutic vaccine) while all the others were metastatic. 12 patients (4.5%) had brain metastases and 127 patients (47.6%) had liver metastases. 186 patients (70%) had

only 1 or 2 metastatic sites, and 81 (30%) had three or more sites. Triple negative was the most common subtype, representing 132 patients (48.5%), 125 (46%) were ER+ and 15 (5.5%) Her2+. Patients received a median number of 3 prior lines before enrollment (min 0; max 19). Overall, only 78 patients (28%) had a genetic testing: 30.7% had a germline BRCA1/2 mutation. 146 patients (54%) had a molecular profile (liquid biopsy or tissue sample) before their enrollment and among them 32,9% were oriented in a trial according to their specific profile. Regarding the type of treatments received: 21.7% were immunotherapy, 73.6% were targeted therapies (46.7% in monotherapy, 26.9% in different combinations with immunotherapy, chemotherapy, radiotherapy or endocrine treatments), 2.9% were chemotherapy and 1.8% endocrine therapy. The overall response rate was 11.1% (0.4% complete response, 10.7% partial response, 37.5% stable disease, 43.8% progressive disease and 7.6% not evaluable). Main reasons for discontinuation of treatment were: progressive disease (80.5%), toxicity (9.6%) and end of trial (6.6%). Median duration of treatment was 2 months (min 0; max 44), only 28.6% of patients were still treated after 3 months of trial and 10% at 6 months. At data cut off (June 21st 2022) median overall survival was 11 months. All patients had discontinued the trial by the time of the analysis: median number of lines of subsequent treatment was 2 (min 0; max 10) and 31 patients (11%) were enrolled in another phase I trial in our center. In a multivariate analysis, there was no prognostic factor associated with duration of treatment whether it was albumin ($p=0.76$) or LDH levels ($p=0.68$), ECOG ($p=0.67$), number of prior lines of treatment ($p=0.79$) or number of metastatic site ($p=0.05$). Conclusion: These results are consistent with prior published data as only few patients with BC are addressed for inclusion in a phase I trial, despite response rates and survival rates similar to other phase I patients. We did not find any specific factor associated with duration of treatment. It is likely that a thorough molecular profile could open more treatment options and access to phase I trials.

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Feasibility of generating an external control comparator using RWD by matching with previously conducted RCTs: CDK4/6 Inhibitors for the treatment of Metastatic Breast Cancer

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Objectives: Real-world data (RWD) from the clinical care of patients captured through Electronic Health Records (EHRs) is a valuable resource for research. Understanding the relationship between characteristics and outcomes of patients treated in the real world and in oncology clinical trials by producing evaluable trial-like populations from RWD can advance clinical and regulatory knowledge.

Methods: RWD from the Flatiron Health EHR-derived, de-identified, longitudinal database were compared with pooled patient-level data from the three randomized controlled trials (RCTs) supporting regular approval of CDK4/6 inhibitors for patients with previously untreated hormone receptor-positive, HER- metastatic breast cancer (mBC). The RCT group included patients who received aromatase inhibitor (AI) monotherapy (RCT-control), and an experimental group (RCT-experimental) that received a cyclin dependent kinase 4/6 (CDK4/6) inhibitor + AI. The real-world control group (rwCG) of patients initiating AI monotherapy was selected using the key eligibility criteria across the RCTs. Patients from the rwCG were matched to the RCT-control and the RCT-experimental patients, respectively. Matching (1:1) was performed through the propensity score (PS) method adjusting for baseline covariates of age, race, site of disease, ECOG PS, and metastatic disease (recurrent, De novo). Multiple imputation (MI) was adopted to impute missing ECOG PS in the rwCG due to the high percentage of missingness.

Progression-free survival (PFS) and overall survival (OS) were analyzed for the following groups: A) rwCG and RCT- control B) rwCG and RCT-experimental and C) RCT-control and RCT-experimental. To assess the feasibility of RCT control arm replication, we assessed whether the trial replication hazard ratio (HR) estimates from analysis B were within the published trial estimates' 95% confidence intervals (CIs). HR and their 95% CIs were estimated using Cox proportional hazard model.

Results: A total of 1292 patients were selected from the EHR-derived database to comprise the rwCG and 1827 patients were pooled across the RCTs (1106 for RCT-experimental and 721 patients for RCT-control). With MI, 520 rwCG patients were matched to the RCT-control for analysis A, and 658 rwCG patients were matched to the RCT-experimental for analysis B. The results are summarized in Table 1. The point estimate of the PFS HR comparing the rwCG to the RCT-experimental was within the 95% CIs for three RCTs. For OS, the point estimate of the HR was within the 95% CI for MONALESSA-2 but not for PALOMA-2.

Conclusion: PFS and OS appeared longer in the RCT-control than in the rwCG, and the difference was more pronounced in OS. While it appears that there is greater similarity for PFS than for OS based on the results of the matched analysis of RCT- experimental vs. rwCG, evaluation of PFS results are limited by substantial differences in assessment and outcome definitions for progression between RCT-control (RECIST) and rwCG. Despite PS matching, there are apparent differences between patients treated in RCTs and routine practice, highlighting the importance of clinical setting, trial selection, study design, and use of

randomization. There are still outstanding feasibility questions on the evaluation of OS and further research is required to understand factors potentially impacting the outcomes between RCTs and RWD.

Table 1: Estimated Treatment Effects in PFS and OS, rwCG vs RCT-control vs RCT-experimental

	HR (95% CI)
PFS per Investigator¹	
A) RCT-control (N=520) vs. <u>rwCG</u> (N=520)	0.83 (0.67, 1.04)
B) RCT-experimental (N=658) vs. <u>rwCG</u> (N=658)	0.48 (0.39, 0.60)
C) RCT-experimental (N=1106) vs. RCT-control (N=721)	0.56 (0.49, 0.65)
Published PFS Results	
<i>MONARCH-3: Abemaciclib (N=328) vs. Control (N=165)</i>	<i>0.54 (0.42, 0.70)</i>
<i>PALOMA-2: Palbociclib (N=444) vs. Control (N=222)</i>	<i>0.58 (0.46, 0.72)</i>
<i>MONALESSA-2: Ribociclib (N=334) vs. Control (N=334)</i>	<i>0.56 (0.43, 0.72)</i>
OS	
A) RCT-control (N=520) vs. <u>rwCG</u> (N=520)	0.78 (0.66, 0.93)
B) RCT-experimental (N=658) vs. <u>rwCG</u> (N=658)	0.64 (0.53, 0.77)
C) RCT-experimental (N=1106) vs. RCT-control (N=721)	0.84 (0.72, 0.98)
Published OS Results	
<i>MONARCH-3: Abemaciclib (N=328) vs. Control (N=165)</i>	<i>NR²</i>
<i>PALOMA-2: Palbociclib (N=444) vs. Control (N=222)</i>	<i>0.96 (0.78, 1.18)</i>
<i>MONALESSA-2: Ribociclib (N=334) vs. Control (N=334)</i>	<i>0.76 (0.63, 0.93)</i>

¹ The definition of rw PFS varies from PFS by RECIST (Torres, et al Adv Ther2022)

² Not Reported due to data not reaching maturity

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7:00 AM - 8:15 AM

P2-13-04

Inclusion of Patients with Leptomeningeal Disease in Phase III Randomized Clinical Trials of Patients with Advanced Breast Cancer, Lung Cancer, and Melanoma: A Systematic Review

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Introduction: Leptomeningeal disease (LMD) is a late complication of metastatic cancer that significantly limits patient survival. LMD is most prevalent in patients with melanoma, lung, and breast cancer, with incidence reaching 24.1% among those treated for brain metastases with both surgery and radiotherapy. As systemic treatment advances in oncology continue to improve patient survival, the incidence of LMD is expected to rise. This necessitates increased efforts to identify effective LMD therapies. Further, recent reporting of focal LMD in asymptomatic patients indicates that unique categories of LMD exist which may not necessarily portend a dismal prognosis. Unfortunately, exclusion of these patients from clinical trials has resulted in a paucity of high-quality evidence to guide management in this patient population. We therefore conducted a systematic review to determine the proportion and characteristics of phase III randomized clinical trials in breast cancer, lung cancer, and melanoma that included patients with LMD and/or included LMD-specific outcomes.

Methods: The online ClinicalTrials.gov database was searched on December 22, 2020 for eligible phase III randomized control trials. No time limits were applied. The 1619 search results were screened by two independent reviewers for randomized, multi-arm therapeutic trials in advanced breast cancer, lung cancer, or melanoma.

Results: 245 trials were included in this review, 75/245 (30.6%) of which included LMD-specific enrollment criteria. 67/245 (27.3%) trials explicitly excluded all patients with LMD, while 8 trials (3.3%) allowed conditional enrollment of patients with LMD; these stipulated that LMD must be asymptomatic/stable, and in some cases, treated. All 8 trials which conditionally allowed LMD patients to enroll were lung cancer trials. No temporal trend towards LMD inclusion was noted. CNS-specific outcomes, which did not include specific mention of LMD, were noted in 13/245 (5.4%) trials, 2 (15.4%) of which used standardized response criteria. No trials included LMD-specific outcomes.

Conclusion: In this review, high rates of LMD exclusion and a complete lack of LMD-specific outcomes were noted in phase III trials for advanced breast cancer, lung cancer, and melanoma, despite these cancers carrying the highest risks of LMD. Lung cancer trials were most likely to include patients with LMD; this may be due to differences in tumor biology, drug penetration in the CNS and drug efficacy. Standardized and validated measures should be integrated into clinical trial design to facilitate inclusion of these patients when feasible and allow for meaningful assessment of LMD response to therapy.

Table 1: Trial factors associated with exclusion of patients with leptomeningeal metastases

Trial Characteristic	Categorization	N	N (%) with complete exclusion of patients with leptomeningeal metastases	p-value	N (%) with conditional inclusion of patients with leptomeningeal metastases	p-value
Industry Funding	Yes	225	60 (27)	0.643	6 (3)	0.077
	No	20	7 (35)		2 (10)	
Year	<2000	2	0 (0)	0.053	0 (0)	0.24
	2000-2004	19	5 (26)		0 (0)	
	2005-2009	91	20 (22)		3 (3)	
	2010-2014	90	25 (28)		2 (2)	
	2015-2019	43	17 (40)		3 (7)	
Disease site	Breast	85	29 (34)	0.037	0 (0)	0.027
	Lung	131	27 (21)		8 (6)	
	Melanoma	29	11 (28)		0 (0)	
Systemic therapy	Cytotoxic chemotherapy	37	15 (41)	0.051	0 (0)	0.225
	Targeted therapy +/- chemotherapy	208	52 (25)		8 (4)	
Location	Asia	24	2 (17)	0.559	2 (17)	0.359
	Europe	9	0 (0)		0 (0)	
	North America	22	10 (45)		1 (5)	
	Intercontinental	175	45 (26)		5 (3)	
Stage	III and IV	161	39 (24)	0.13	8 (5)	0.038
	Stage IV only	84	28 (33)		0 (0)	
CNS-specific outcomes	Yes	13	3 (23)	0.72	3 (23)	<0.001
	No	232	64 (28)		5 (2)	

a. based on study start date listed on clinicaltrials.gov, defined as “the actual date on which the first participant was enrolled in a clinical study.”

b. based on studies with known location. Statistical test was between intercontinental versus single continent studies.

Disclosure(s):

Alisha Sharma, BHSc: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-13-05

Triple Negative Breast Cancer (TNBC) patients are more likely to digitally explore clinical trial options and prior to receiving treatment for advanced disease compared to non-TNBC patients

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Introduction: Triple-negative breast cancer (TNBC), an aggressive form of breast cancer (BC) that is associated with poor prognosis, accounts for 10-15% of all BCs. Chemotherapy remains the standard of care (SOC) for advanced disease, with limited clinical benefit. Oncology clinical trials (CTs) are globally recommended and encouraged as the preferred treatment (tx) option for any cancer patient (pt). 'Trialjectory' (TJ) is an artificial intelligence (AI)-based technology that matches pts to oncology CTs. Here, we identified distinct characteristics of TNBC pts who signed up to the TJ platform compared to non-TNBC pts. Methods: Using AI and an unsupervised natural language processing approach, the TJ platform clinically matches pts to CTs. Matching is achieved by pt response to an online dynamic questionnaire (www.trialjectory.com) that collects detailed clinical data including clinico-pathologic characteristics, tx history, general health, and comorbidities. Those are compared to the eligibility criteria of available CTs to yield a high-quality actionable matched-trial list. Results: Between 1/2020 and 12/2021, out of 9796 BC pts that signed up, 2688 were TNBC pts (27%). There was no significant difference in age at sign-up between TNBC and non-TNBC patients (median age of 57 years vs 58 years, respectively). Consistently with Non-hispanic black (NHB) race prevalence in the different molecular subtypes in the general US population, NHB race had higher signup rate in TNBC compared to non-TNBC (9.95% vs 5.76%, respectively). TNBC pts signed up at a later disease stage compared to non-TNBC pts (19% of TNBC reported having a stage 1 disease compared to 27% of non-TNBC pts, $p < 0.001$). A significantly higher percentage of pts with advanced/metastatic TNBC signed up to the TJ platform before starting tx compared to non-TNBC patients (34% vs 22%, respectively, $p < 0.001$). Furthermore, there was a significant difference in the willingness to travel any distance within the US for a matched clinical trial between TNBC and non-TNBC pts (39% vs 34%, respectively, $p < 0.001$).

Conclusions: In this study, we found significant differences in the characteristics of TNBC vs non-TNBC pts that have signed up to the TJ platform. There was an up to 2-fold enrichment of TNBC on the TJ platform pts compared to their frequency in the general population. While previous studies do not show a difference in stage distribution between different subtypes, TNBC patients initiated their search for CTs at a higher stage. In addition, advanced TNBC patients started their search earlier in their journey, before starting chemotherapy. This may reflect the lack of effective SOC and possibly, the motivation to avoid the use of chemotherapy. This is also supported by the willingness of TNBC patients to travel farther in order to identify and enroll in a CT compared to non-TNBC pts. Importantly, the motivation of TNBC pts to travel

any distance has not been reduced despite the COVID-19 pandemic, reflecting a strong drive of this pt population to enroll in CTs. It also demonstrates that with the right access, diverse patient populations are willing to participate in clinical trials. In sum, TNBC pts are more likely to explore CT options, in the advanced stage setting, earlier in their journey. This study demonstrates the power of TJ platform for clinico-pathologic characterization and diverse pt groups, including their drivers and behavioral choices during their battle with cancer.

12/7/2022

7:00 AM - 8:15 AM

P2-14-01

MOLECULAR FLUORESCENCE-GUIDED SURGERY USING BEVA800 FOR THE ASSESSMENT OF TUMOR MARGINS DURING BREAST CONSERVING SURGERY OF PATIENTS WITH PRIMARY BREAST CANCER (MARGIN-II)

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Introduction: The goal of breast conserving surgery (BCS) for early breast cancer (EBC) is to remove the tumor in toto and preserving as much of the normal breast tissue as possible. In 20-50% of cases a re-excision is necessary because of involved margins. Repeat surgeries are not only a burden to patients physically but also psychologically and can delay recommended adjuvant therapies. Accurate determination of tumor margins during surgery is therefore a critical need. Breast cancer tissue produces significantly higher amounts of VEGF-A than healthy tissue. VEGF-A stimulates tumor angiogenesis and is therefore a target for molecular imaging techniques. The fluorescence imaging agent bevacizumab-IRDye800CW (Beva800) is a conjugate of bevacizumab and IRDye800CW and binds specifically to VEGF-A. Beva800 provides a potentially efficacious approach to imaging specimen and cavity margins during BCS. We are presenting a phase II study that combined Beva800 with the SurgVision Explorer Air camera for intraoperative margin assessment during BCS for EBC. Methods: MARGIN II is a multicenter open-label single arm prospective clinical trial aimed at evaluating Beva800 for assessment of tumor margins in women with EBC scheduled for BCS. The study was a within-patient comparison of positive tumor margin rates using BCS standard of care margin assessment compared to intraoperative assessment with 4.5 mg Beva800 and fluorescence imaging with the SurgVision Explorer Air camera. All patients received an i.-v. bolus injection of 4.5 mg of Beva800 three days before surgery. The fluorescent signal was visualized during surgery using NIR fluorescence imaging (700–1000 nm). Standard of care margin assessment

was defined as visual inspection, palpation and, in cases of pre-operative wire marking, specimen sonography or mammography. Beva800 efficacy was determined as the number of patients in which a pathology-confirmed positive margin was identified by fluorescence-guided surgery using Beva800 but not by standard of care BCS. Results: 49 patients were included in 5 centers. 4 training cases were only included in the safety analysis, 45 patients were evaluable for the efficacy analysis. 8 patients (17.8%) had involved margins after standard of care BCS, 4 of which were detected by molecular fluorescence intraoperatively resulting in the reduction of patients with positive margins by 50% (95% CI: 15.7%, 84.3%). 4 patients (8.9%; 95% CI: 2.5%, 21.1%) needed a re-excision because of involved margins. In 27 patients (60.0%) the additional molecular fluorescence guided cavity shaving did not change the resection status from positive to negative (false positive). Adverse events were reported by 16 of 49 patients (32.7%), but only 3 (6.1%) were related to Beva800 (syncope, hot flush, hypertensive crisis). One patient experienced a treatment related SAE (hypertensive crisis). No anti-Beva800 antibodies were detected. Conclusion: In our analysis the rate of necessary second operations was reduced by 50% using Beva800 and the SurgVision Explorer Air camera. The safety analysis confirmed the positive safety profile of Beva800 found in previous studies. Molecular fluorescence-guided surgery may have the potential to change the practice of breast conserving surgery by reducing unnecessary re-excisions. Future studies will have to address the high false positive rates.

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Hans-Christian Kolberg, MD PhD: Agendia: Consulting Fees (e.g., advisory boards) (Ongoing); Amgen: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Carl Zeiss Meditec: Consulting Fees (e.g., advisory boards) (Ongoing); Diichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Genomic Health/Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); GSK: Consulting Fees (e.g., advisory boards) (Ongoing); Janssen-Cilag: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); LIV Pharma: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Onkowissen: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Phaon Scientific GmbH: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Riemser: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Fees for lectures (Ongoing); SeaGen: Consulting Fees (e.g., advisory boards) (Ongoing); SurgVision: Consulting Fees (e.g., advisory boards) (Ongoing); Tesaro: travel expenses (Ongoing); TEVA: Consulting Fees (e.g., advisory boards) (Ongoing); Theraclion: Consulting Fees (e.g., advisory boards) (Ongoing); Theraclion SA: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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7:00 AM - 8:15 AM

P2-14-02

Surgical options of the breast and clinical outcomes in breast cancer patients after neoadjuvant chemotherapy: a single-center retrospective study.

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Background: Neoadjuvant chemotherapy (NAC) has evolved significantly and has been widely accepted for downstaging disease in early-stage and locally advanced breast cancer patients. Since the optimal surgical intervention of the breast for patients receiving NAC remains controversial, we aim to investigate the survival outcome of patients treated with different surgical management.

Methods: Patients with invasive breast cancer that underwent NAC in Fudan University Shanghai Cancer Center from January 2010 to June 2019 were involved in this study. Based on surgical intervention of the breast following NAC, patients were divided into mastectomy and breast conservation groups. To be specific, the mastectomy group involved patients who received mastectomy alone or mastectomy plus immediate breast reconstruction (M+IBR), while the breast conservation group evolved patients who underwent conventional breast-conserving surgery (CBCS) and oncoplastic surgery (OPS). Surgical interventions were performed by breast surgeons. Propensity scores matching was utilized for group matching.

Results: A total of 2080 patients were enrolled in this study. Among them, 1819 (87.5%) patients were categorized as mastectomy group, and 261 (12.5%) patients were classed as breast conservation group. In the mastectomy group, mastectomy alone and M+IBR accounted for 82.5% (1715/2080) and 5% (104/2080) patients respectively. As for breast conservation, 170 (8.2%) and 91 (4.4%) patients were treated with CBCS and OPS after NAC. Over 9-years of research, the proportion of breast conservation steadily increased in patients after NAC. Notably, the percentage of patients undergoing OPS increased from 0.43 % to 7.60 % throughout the 9 years. Moreover, increasing rate of M+IBR was also observed in the study cohort, whereas fewer patients opted for mastectomy alone as surgical intervention after NAC. Compared with mastectomy group, patients underwent BCS showed younger age ($P < 0.001$), as well as higher proportion of normal BMI ($P = 0.022$), pre-menopausal status ($P < 0.001$), and triple-negative breast cancer ($P < 0.008$). Additionally, patients with tumors of advanced clinical T stage ($P < 0.001$) and TNM stage ($P = 0.002$) were more often to be treated with mastectomy (Table 1). After propensity score matching, 460 patients were matched successfully (Table 2). Compared with the mastectomy group, significant benefits in overall survival (Hazard ratio 0.51, [95% confidence interval: 0.27-0.96]; $p=0.044$) and disease-free survival (Hazard ratio 0.62, [95% confidence interval: 0.39-0.99]; $p < 0.05$) were observed in the breast conservation group (Table 3A and 3B). Moreover, there was no statistical difference in locoregional recurrence among the surgical groups (Table 3C).

Conclusions: Tumor biology can significantly impact the surgical decision in patients administrated with NAC. Breast conservation was a safe alternative for mastectomy in the NAC setting without compromising survival outcomes.

Table 1.

Characteristics	Cases	Mastectomy (%)	Breast conservation (%)	P value
No. of patients	2080	1819 (87.5)	261 (12.5)	
Age at diagnosis (years)				< 0.001
	≤40	382 (21.0)	93 (35.6)	
	41-64	1334 (73.3)	160 (61.3)	
	≥65	103 (5.7)	8 (3.1)	
BMI (kg/m²)				0.022
	Underweight (<18.5)	53 (2.9)	4 (1.5)	
	Normal weight (18.5-25)	1207 (66.4)	195 (75.7)	
	Overweight (> 25)	559 (30.7)	62 (23.8)	
Menopausal status				< 0.001
	Pre-menopausal	932 (51.2)	175 (67.0)	
	Post-menopausal	887 (48.8)	86 (33.0)	
cT stage				< 0.001
	T0	9 (0.5)	0	
	T1	156 (8.6)	49 (18.8)	
	T2	1081 (59.4)	176 (67.4)	
	T3	307 (16.9)	26 (10.0)	
	T4	266 (14.6)	10 (3.8)	
cN stage				0.168
	N0	466 (25.6)	81 (31.0)	
	N1/N2	1021 (56.1)	138 (52.9)	
	N3	332 (18.3)	42 (16.1)	
TNM stage				0.002
	I	201 (11.1)	29 (11.1)	
	II	751 (41.3)	137 (52.5)	
	III	867 (47.7)	95 (36.4)	
ER status				0.086
	Positive	1064 (58.5)	138 (52.9)	
	Negative	755 (41.5)	123 (47.1)	
PR status				0.306
	Positive	891 (49.0)	119 (45.6)	
	Negative	928 (51.0)	142 (54.4)	
HER2 status				0.404
	Positive	731 (40.2)	97 (37.2)	
	Negative	1082 (59.5)	164 (62.8)	
	Equivocal	6 (0.3)	0	
Molecular subtypes				0.008
	Luminal-like	760 (41.8)	96 (36.8)	
	HER2-positive	731 (40.2)	97 (37.2)	
	Triple-negative	328 (18.0)	68 (26.0)	
Axillary surgery				< 0.001
	Sentinel lymph node biopsy	144 (7.9)	97 (37.2)	
	Axillary lymph node dissection	1664 (91.5)	162 (62.1)	
	Without surgical intervention	11 (0.6)	2 (0.7)	

BMI, Body Mass Index; cT, clinical tumor; cN, clinical lymph node; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2.

Clinicopathologic characteristics of patients in mastectomy and breast conservation groups.

Table 2.

Variables	Post-matching	
	Mastectomy N = 230 (%)	Breast conservation N = 230 (%)
Age at diagnosis (years)		
	≤40	80 (34.8)
	41-64	148 (64.3)
	≥65	2 (0.9)
Menopausal status		
	Pre-menopausal	140 (60.9)
	Post-menopausal	90 (39.1)
cT stage		
	T0/T1	38 (16.5)
	T2	162 (70.4)
	T3/T4	30 (13.1)
TNM stage		
	I	43 (18.7)
	II	111 (48.3)
	III	76 (33.0)
pCR		
	Yes	95 (41.3)
	No	135 (58.7)
Molecular subtypes		
	Luminal	87 (37.8)
	HER2-positive	91 (39.6)
	Triple-negative	52 (22.6)
Axillary surgery		
	Sentinel lymph node biopsy	74 (32.2)
	Axillary lymph node dissection	155 (67.4)
	Without surgical intervention	1 (0.4)

cT, clinical tumor; pCR, pathological complete response; HER2, human epidermal growth factor receptor 2.

Balanced statistics of patients receiving mastectomy and breast conservation after propensity score matching.

Table 3.

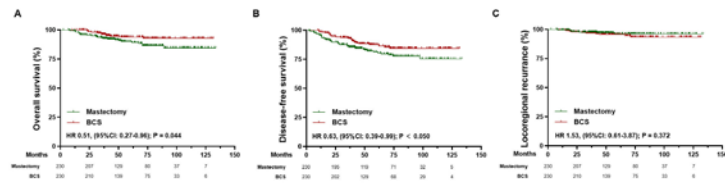


Table 3. Survival analysis between matched cohort of patients receiving mastectomy (n=230), breast-conserving therapy (n=230). A. Kaplan-Meier curves for overall survival analysis in patients of different surgical groups. B. Kaplan-Meier curves for disease-free survival analysis in patients of different surgical groups. C. Kaplan-Meier curves for locoregional recurrence analysis in patients of different surgical groups. BCS, conventional breast-conserving surgery; HR, Hazard ratio; 95% CI, 95% confidence interval.

Survival analysis between matched cohort of patients receiving mastectomy (n=230), breast-conserving therapy (n=230).

Disclosure(s):

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7:00 AM - 8:15 AM

P2-14-03

Learning curve for Robotic assisted nipple sparing mastectomy: a single institution experience

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Backgrounds/Aims: Nipple sparing mastectomy (NSM) is popularly performed as this surgical technique is oncological safety and better cosmetic outcomes. Robot assisted NSM (RANSM) is emerging because of its exceptional advantages: hidden incisions, high resolution, wider visualization and ergonomically moving. Although several studies reported that RANSM has shown a short learning curve, there were few reports about learning curve of this cutting-edge surgical technique. In this study, we reported the learning curve and feasibility of RANSM. **Methods:** A retrospective and prospective study was conducted for women who underwent RANSM with immediate breast reconstruction at Samsung Medical Center from July 2019 to April 2022. All RANSM were performed by a single surgeon. We divided the total cases in half and set up two phases; an early phase (case 1st to 23th) and a late phase (case 24th to 46th). The total operation time, mastectomy time, docking time, pre-console time and console time was defined as the interval between the creation of the skin incision and the end of the reconstructive surgery, the interval between the time of skin incision and the time of the specimen out of the operation field, the interval between the preparation for docking and the end of docking, the interval between the creation of the skin incision and the end of robot docking, and the time spent by a surgeon to operate the console for mastectomy. To evaluate the impact of case experience accumulation on the operation time of RANSM, the cumulative sum (CUSUM) method was used to analyze the learning curve. Clinicopathologic characteristics, perioperative complications, and operation time were collected. **Results:** Overall, 42 women underwent 46 RANSM procedures conducted. The median patient

age was 44.5 years old (26-59 years) and the median breast weight was 338.5 gram (101.4-817 gram). BRCA 1 mutation carriers were 2 patients and BRCA 2 mutation carriers were 3 patients. 5 patients with BRCA 1/2 mutation carriers underwent contralateral risk-reducing RANSM. Clinicopathologic characteristics of patients between the early phase and late phase were summarized in Table 1. There were no significant differences in almost clinicopathologic characteristics. Median time of total operation, mastectomy, docking time, pre-console time, and console time was 344.0 minutes (254.0-480.0 minutes), 238.5 minutes (166-394 minutes), 6.5 minutes (1-25 minutes), 61.5 minutes (29-180 minutes), and 64.5 minutes (33-134 minutes), respectively. Comparing the early phase and the late phase, median total operation time was 357 minutes (273-480 minutes) and 321 minutes (254-459 minutes), ($p = 0.067$); median mastectomy time was 245 minutes (204-394 minutes) and 229 minutes (166-376 minutes), ($p = 0.070$); docking time 7.0 minutes (3-25 minutes) and 5.0 minutes (1-20 minutes), ($p = 0.093$); pre-console time was 70.0 minutes (49-162 minutes) and 54.0 minutes (29-180 minutes), ($p = 0.028$); console time was 71.0 minutes (40-134 minutes) and 60.0 minutes (33-105 minutes), ($p = 0.095$). In the learning curve analysis, it took the 21th procedure in RANSM to decrease the breast operation time. Clavien-Dindo grade III postoperative complication was two cases (8.6%, one case was infection and one case was nipple ischemia) in only early phase and none in the late phase. Clavien-Dindo grade II postoperative complication was absent in all phases. Clavien-Dindo grade I postoperative complications were seven cases (30.4%, all cases were nipple crust) in the early phase and one case (4.3%, one case was nipple crust) in the late phase. Nipple ischemia was found in two cases (8.6%) but only one case required nipple excision given in the early phase.

Conclusions: It has shown that the breast operation time improved from the 21th procedure of RANSM. RANSM is technically feasible and acceptable with a short learning curve.

TABLE 1 Basic characteristics of patients between the early phase and late phase

TABLE 1 Basic characteristics of patients between the early phase and late phase

Variables	Phase I, n = 23 (case 1 to case23)	Phase II, n = 23 (case 24 to case 46)	p value
Age (years) (Median , interquartile range)	45.0 [40.0;49.0]	44.0 [35.5;46.5]	0.461
BMI (kg/m2) (Median , interquartile range)	22.5 [20.7;24.7]	22.4 [21.1;25.5]	0.644
HTN			1
no	22 (95.7%)	23 (100.0%)	
yes	1 (4.3%)	0 (0.0%)	
DM, n (%)			
no	23 (100.0%)	23 (100.0%)	
Smoking history, n (%)			1
no	23 (100.0%)	22 (95.7%)	
yes	0 (0.0%)	1 (4.3%)	
BRCA 1/2 mutation status, n (%)			0.054
no examination or no mutation	19 (82.6%)	18 (78.3%)	
BRCA 1 mutation	0 (0.0%)	4 (17.4%)	
BRCA 2 mutation	4 (17.4%)	1 (4.3%)	
Location			0.554
Rt.	11 (47.8%)	14 (60.9%)	
Lt.	12 (52.2%)	9 (39.1%)	
Breast wt. (gram) (Median , interquartile range)	377.0 [258.5;444.0]	279.0 [227.2;385.0]	0.205
Clinical T stage^a			0.606
0 (carcinoma in situ)	6 (28.6%)	3 (15.0%)	
I	7 (33.3%)	10 (50.0%)	
II	6 (28.6%)	6 (30.0%)	
III	2 (9.5%)	1 (5.0%)	
Clinical N stage^a			0.980
0	21 (100.0%)	19 (95.0%)	
1	0 (0.0%)	1 (5.0%)	
Axillary surgery^a			0.522
SLNB	21 (91.3%)	19 (82.6%)	
ALND	0 (0.0%)	1 (4.3%)	
None	2 (8.7%)	3 (13.0%)	
number of lymph node metastasis^a			0.078
0	19 (90.5%)	17 (85.0%)	
1	2 (9.5%)	0 (0.0%)	
2	0 (0.0%)	3 (15.0%)	
pathologic T stage^a			0.016
Tis	2 (9.5%)	10 (50.0%)	
I	14 (66.7%)	8 (40.0%)	

II	5 (23.8%)	2 (10.0%)	
pathologic N stage^a			0.954
0	19 (90.5%)	17 (85.0%)	
1	2 (9.5%)	3 (15.0%)	
Histology			0.213
DCIS	2 (8.7%)	6 (26.1%)	
IDC	17 (73.9%)	14 (60.9%)	
BRCA carrier	2 (8.7%)	3 (13.0%)	
others	2 (8.7%)	0 (0.0%)	
Subtype (invasive carcinoma)			0.432
HR+/HER2-	15 (65.2%)	10 (43.5%)	
HR+/HER2+	1 (4.3%)	2 (8.7%)	
HR-/HER2+	1 (4.3%)	0 (0.0%)	
HR-/HER2-	1 (4.3%)	2 (8.7%)	
none or unknown(DCIS or BRCA carrier)	5 (21.7%)	9 (39.1%)	
Grade^a			0.098
Well	2 (9.5%)	6 (30.0%)	
Moderate	14 (66.7%)	7 (35.0%)	
Poor or undifferentiated	5 (23.8%)	7 (35.0%)	
Mean follow-up (days) (Median , interquartile range)	392.0 [271.5;635.5]	48.0 [19.5;176.0]	< 0.001

^a patients who underwent risk-reducing mastectomy due to BRCA 1/2 mutation carriers were excluded.

Abbreviations: SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection.

Disclosure(s):

Yeon Jin Kim, M.D: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-14-05

Patient rather than tumor factors predict contralateral prophylactic mastectomy for inflammatory breast cancer

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Introduction: Inflammatory breast cancer (IBC) is an aggressive form of breast cancer with best outcomes result-ing from trimodality therapy: neoadjuvant chemotherapy (NAC), modified radical mastectomy (MRM), and radiation (PMRT). Contralateral prophylactic mastectomy (CPM) is generally discour-aged at the time of MRM due to poor prognosis. Our aim was to identify factors associated with CPM for IBC and determine its relationship with overall survival (OS). Methods: The National Cancer Database was used to identify female patients with AJCC stage IIIC unilateral IBC (cT4d and inflammatory histology code) treated 2004-2018. Patients were stratified by mastec-tomy type: unilateral mastectomy (UM) was defined as MRM or simple mastectomy, and CPM was defined as UM + CPM. Logistic regression identified factors associated with mastectomy type, and multivariable proportional Cox hazards regression identified factors associated with OS. A subset analysis of patients receiving NAC compared complete pathologic response (pCR) between mastec-tomy groups. Results: Of the 2,837 patients with non-metastatic IBC, 2,013 (70.2%) underwent UM and 855 (29.8%) had CPM. The CPM group was significantly younger than the UM group (mean age 52 vs. 56.6 years, $p=0.028$), more frequently identified as Non-Hispanic White (79.7% vs. 70.1%, $p<0.001$), and had private insurance (66.9% vs. 55.6%, $p<0.001$). Nearly all patients received chemotherapy and over 80% were treated with NAC. Receipt of PMRT did not differ by mastectomy type (80% for UM and CPM). On multivariable logistic regression, patients age <40 were more likely to undergo CPM than UM (OR 3.7, 95% CI 1.61-8.5, $p<0.002$). Patients with age >70 , Hispanic ethnicity, and public insur-ance were significantly less likely to receive CPM (all $p\leq0.002$). On

multivariable Cox regression adjusted for patient, tumor, and treatment factors, CPM was not associated with OS benefit (HR 0.86, 95% CI 0.73-1.02, p=0.08). Higher histologic grade, node-positive disease, and greater co-morbidity were associated with poorer OS, while receipt of chemotherapy and PMRT improved OS. In the subset of NAC patients, overall pCR did not differ significantly by mastectomy type (CPM 22.3%, UM 19.4%, p=0.26). When included in multivariable models, pCR rates were not predictive of CPM despite being associated with improved OS. Conclusion: Nearly 30% of IBC patients undergo CPM despite discouragement by guidelines. Demographic characteristics – particularly age < 40 – predicted CPM, suggesting patient preferences and access to care affect surgical decisions. As expected, trimodality therapy and favorable NAC response improved oncologic outcomes, but CPM had no association with OS. While CPM may be chosen for risk reduction and symmetry, patients should be counseled that it does not improve survival for IBC.

Disclosure(s):

Lauren M. Drapalik, MD: No financial relationships to disclose

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P2-14-06

Prospective, multicenter, clinical validation study of the repeatability and accuracy of internal mammary sentinel lymph node biopsy with modified injection technique (CBCSG026/CBCSG027)

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Background

As a first-echelon nodal drainage site of breast cancer, the status of axillary lymph nodes (ALN) and internal mammary lymph nodes (IMLN) is both valuable for regional staging and treatment choice. The internal mammary sentinel lymph node biopsy (IM-SLNB) may provide minimally invasive staging, and guide individual IMLN radiation. Modified technique (periareolar intraparenchymal, high volume and ultrasound guidance) got a high internal mammary sentinel lymph nodes (IM-SLN) visualization rate of 71.1% in single center, and the prospective multicenter study was designed to verify its repeatability (CBCSG026, NCT03541278). High visualization rate and low false negative rate are prerequisites for the widespread of IM-SLNB. The question arises as to whether IM-SLN detected with the modified technique should be considered as "true" IM-SLN. The prospective, multicenter, clinical validation study of IM-SLNB followed by internal mammary lymph node dissection (IM-LND) was designed to verify the accuracy of IM-SLNB in patients with ALN positive breast cancer (CBCSG027, NCT03024463).

Methods

While CBCSG026 trial enrolled patients with both axillary negative and positive breast cancer,

CBCSG027 trial only enrolled axillary positive patients receiving mastectomy (either biopsy proving cN+ disease or cN0 with positive axillary SLN). The 1st to 3rd intercostal IM-LND was performed immediately after IM-SLNB to verify its accuracy in the CBCSG027 trial.

Result

From May 2018 to June 2022, 600 and 264 patients were enrolled in the CBCSG026 and CBCSG027 trial from seven centers in China, respectively.

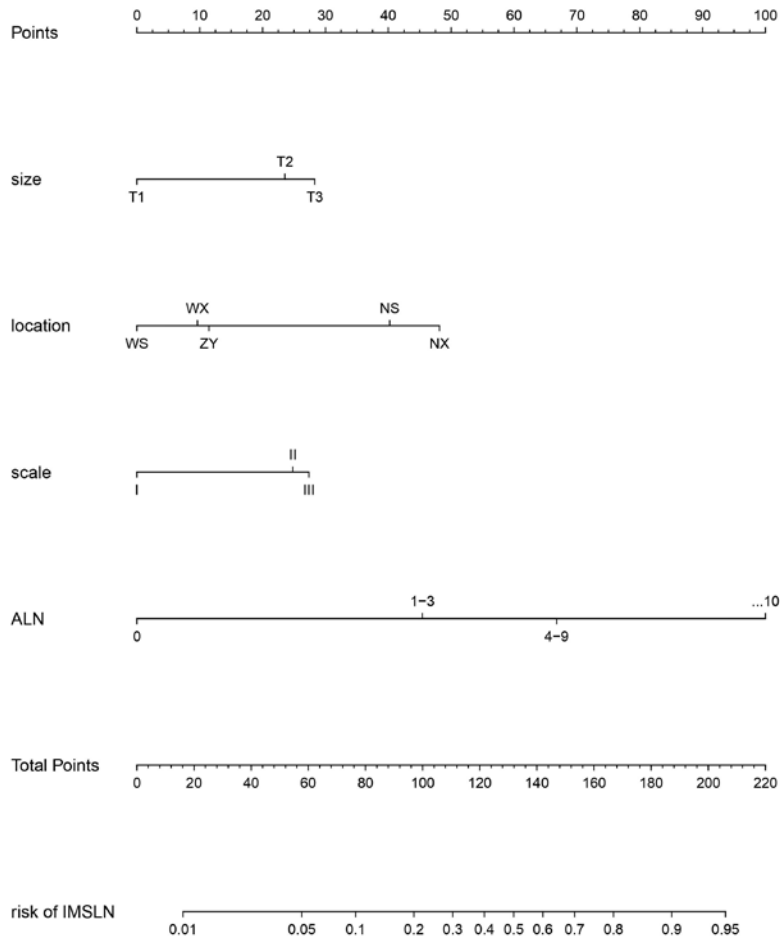
Among the 600 recruited patients in the CBCSG026, the IM-SLN visualization rate was 65.0% (390/600), which was significantly related to patient's age, body mass index, radiotracer intensity and interval time between injection and IM-SLN identification (all $P < 0.05$). The IM-SLNB successful rate was 97.4% (380/390), and the complication was 6.9%. The median number of IM-SLN was 1. The overall IM-SLN metastases rate was 18.9% (72/380), with 33.0% (65/195) and 3.8% (7/185) in ALN positive and negative patients, respectively. Multivariate analysis showed that the tumor size ($P=0.028$), the tumor location ($P < 0.001$) and the number of positive ALNs ($P < 0.001$) were independent predictors of IM-SLN metastasis. Those variables were included in a novel nomogram (Table 1), which was significantly better than the probability based on the number of metastatic ALNs alone according to the current guidelines (area under the curve: 0.860 vs. 0.804, $P < 0.001$).

Of the 264 patients enrolled in the CBCSG027 trial, 185 patients (70.1%) had IM-SLN visualization (included 107 with cN+ disease and 78 with positive axillary SLN). The median number of IM-SLN and IM-nSLN was 2 (1~4) and 3 (1~9), respectively. The positive rate of IMLN and IM-SLN was 37.8% (70/185) and 36.8% (68/185), respectively, yielding the false negative rate of IM-SLNB 2.9% (2/70), the accuracy of 98.9% (183/185) and the sensitivity of 97.1% (68/70). The false negative rate of patients with cN+ disease and patients with positive axillary SLN was 4.8% (2/42) and 0, respectively. The positive IM-SLNs were the only positive IMLNs identified in 51.4% (36/70) patients. IM-SLNB can change the pN stages of 37.2% (68/183) patients. IMLN irradiation could be avoided in 72.7% (80/110) patients with axillary pN1 and 46.7% (35/75) with pN2/N3 disease in the study.

Conclusions

The modified technique of radiotracer injection (periareolar intraparenchymal, high volume, and ultrasound guidance) can significantly improve the detection rate of IM-SLN with very low false-negative rate with the prospective, multicenter validation results, providing minimally invasive staging and guiding individual IMLN radiation. When there is no IM-SLN visualization, the nomogram can predict the risk of IMLN metastasis and guide IMLN radiation.

The nomogram which can predict the risk of IMLN metastasis



size: tumor size; location: tumor location; scale: tumor grade; WS: upper outer quadrant ; WX: lower outer quadrant; ZY: central quadrant; NS: upper inner quadrant; NX: lower inner quadrant; ALN: number of positive ALNs

Disclosure(s):

Yong-Sheng Wang, n/a: No financial relationships to disclose

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P2-14-07

Omission of Sentinel Lymph Node Biopsy in Patients with Early Stage Breast Cancer: Looking Beyond the Choosing Wisely Guidelines for Age < 70

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Background: The Surgical Society of Oncology Choosing Wisely Campaign for breast cancer advocates against the routine use of sentinel lymph node biopsy (SLNB) for women ≥ 70 years with early stage estrogen positive (ER+), clinically node negative (cN0) disease, given the low likelihood of axillary involvement and axillary recurrence risk, absence of survival benefit and greater reliance on genomic testing for therapeutic decisions. We hypothesize that this practice may be extended to a younger cohort of patients. In this proof-of-concept feasibility study, we first sought to determine the incidence of node positive (N+) disease in our health system using natural language understanding (NLU) technology to extract relevant data from the electronic medical record (EMR).

NLU of the clinical narrative has been proven to aid clinical decision support by extracting relevant information and can populate clinical databases to facilitate optimal population management strategies. The advantage of NLU over a cancer registry is the speed and efficiency of data extraction for a large number of patients in real time, plus the capture of data points not conventionally included in a registry.

Methods: All patients with early stage ER+, cN0 breast cancer who had SLNB from January 2015-December 2017 were identified in an integrated academic health network comprised of 15 hospitals in Western Pennsylvania. Patient clinical data were abstracted from the EMR using Realyze Intelligence™ NLU technology. The Realyze NLU pipeline uses a combination of machine learning algorithms and standard terminologies to create a breast cancer patient model that includes genomic, phenotypic, and clinical data. The pipeline gathers information from all data sources – structured and unstructured – and normalizes the information to create a complete model of patient clinical criteria.

Realyze Information Models use clinical data formatting flexible enough to represent clinical disorders on a concept level as well as the encounter, patient, and population levels. A breast cancer model with focus on the lymph node identification, pathological as well as clinical tumor

and node classification were developed and mapped to standard terminology. A Semantic Reasoning layer is provided by different mechanisms including a rule-based layer to render answers to the questions posed in this hypothesis.

NLU performance was validated by manually verifying key clinical variables (i.e., clinical stage, pathologic stage, and nodal positivity) on a subset of patients. Statistical analysis to determine any difference in N+ rates by age was performed using Chi-square testing with significance set at $p < 0.05$.

Results: We identified 602 pts with early stage ER+, cN0 breast cancer over this period who underwent SLNB. Average age was 59.6 years old. As a whole group, there was an increase in N+ rates as the stage increased (Table 1). When comparing incidence of N+ disease stratified by age (< 70 or >70), there was no difference in N+ rates across all stages. In addition, equally low rates of SLN positivity were seen for patients specifically with stage T1a and T1b disease.

Conclusions: These data suggest that the Choosing Wisely recommendation to omit SLNB may be extended to a younger cohort of pts with ER+, cN0 disease, specifically those with stage T1a or T1b tumors. With low rates of N+ disease, and less reliance on axillary stage for treatment decision making, the harms of surgical axillary staging may outweigh the benefits. Future validation is needed with a larger sample size.

Table 1

n = 591 patients who underwent SLNB			
	Rate of SLN Positivity		p-value
	< 70yo	≥ 70yo	
T1a	10.4% (5 / 48)	6.7% (1 / 15)	0.99
T1b	6.8% (5 / 74)	5.9% (1 / 17)	0.99
T1c	17.3% (29 / 168)	13.2% (5 / 38)	0.64
T2	30.4% (45 / 148)	27.8% (10 / 36)	0.84
T3	58.5% (24 / 41)	33% (2 / 6)	0.39

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Trends in neoadjuvant systemic therapy rates in Europe: Pre-planned substudy of TAXIS (OPBC-03, SAKK 23/16, IBCSG 57-18, ABCSG-53, GBG 101)

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Introduction: Even though randomized controlled trials could not show a significant survival benefit for the use of neoadjuvant systemic therapy (NST), it is increasingly recommended for patients with clinically node-positive breast cancer due to its implications on prognosis, locoregional downstaging and response-driven adjuvant systemic therapy. The aim of this study was to assess the need for international standardization of treatment recommendations by evaluating clinical practice heterogeneity in use of NST for patients with clinically node-positive breast cancer in Europe. **Methods:** The study was preplanned in the international multicenter phase-III OPBC-03/TAXIS trial (ClinicalTrials.gov Identifier: NCT03513614) after randomization of the first 500 patients with clinically node-positive breast cancer who underwent axillary lymph node dissection (ALND) or axillary radiation (ART) without ALND after tailored axillary surgery (TAS) in the context of extended regional nodal irradiation. Clinically node-positive breast cancer was defined by confirmed nodal disease at the time of initial diagnosis; in case of neoadjuvant therapy, residual nodal disease was mandatory. Investigators were encouraged to enroll all eligible patients consecutively. However, TAXIS is unique inasmuch as its pragmatic design allows both the neoadjuvant and adjuvant setting according to the preferences of the treating physicians and institutions and thus provides an excellent opportunity to study patterns and trends in use of NST in patients with clinically positive nodes in Europe. **Results:** A total of 500 patients with a median age of 57 years (IQR: 48-69 years) were included at 44 breast centers in 6 European countries from August 2018 to June 2022. Subtype was hormone receptor (HR) positive (+) and human epidermal growth factor receptor 2 (HER2) negative (-) in 393 (80.0%), HR+/HER2+ in 52 (10.6%), HR-/HER2+ in 5 (1.0%) and HR-/HER2- in 34 (6.9%) patients. The rate of patients undergoing NST was 31.4% with a significant upward trend over time during the study period (from 20.0% in 2018 to 38.1% in 2022; $p=0.044$). The use of NST varied significantly by country ($p<0.001$) and by site ($p=0.015$). For patients with clinical AJCC tumor stage II and III, the rates of patients undergoing NST in Switzerland were 26.5% (18 of 68) and 35.9% (92 of 256), in Germany 22.2% (2 of 9) and 30.4% (7 of 23), in Austria 50% (7 of 14) and 60% (9 of 15) and in Hungary 0% (0 of 15) and 20.7% (18 of 87), respectively ($p=0.019$ and 0.004). Large differences by country were found for ER+/HER2- breast cancer, ranging from 13.1% (11 of 84) in Hungary to 47.8% (11 of 23) in Austria ($p=0.007$). Within Switzerland, which was the country with most included patients (328 of 500) and participating sites ($n=25$), the rate of patients undergoing NST for ER+/HER2- breast cancer varied considerably by site, ranging from 10% (2 of 20) to 50% (11 of 22). **Discussion:** This study revealed substantial heterogeneity in clinical practice in Europe, indicating the need for development of and adherence to consistent guidelines to standardize the international use of NST.

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Sensory Evaluation of Nipple-Areolar Complex after Nipple-Sparing Mastectomy: A Comparison of Incision Approaches

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Background:

Since nipple-sparing mastectomy (NSM) has been widely practiced, majority of previous studies have evaluated the effects of Nipple-areolar complex (NAC) preservation on body image adjustment. However, few have evaluated NAC sensation after NSM in a large sample size. This study aims to assess NAC sensation after NSM and compare the results according to different incisional approaches; specifically, inframammary fold (IMF) and peri-areolar.

Methods:

Post NSM patients from Oct 2019 to Nov 2021 have been recruited prospectively. A total of 115 patients (IMF 69 and peri-areolar 36) were evaluated for NAC sensory at various time points during follow up within 1.5 to 4 years after surgery. NAC sensation was scored by pin-prick test in a scale of 0 to 2 (0: no sensation, 1: dull sensation, 2: sharp sensation), divided in 5 areas of the NAC and summed up to a total of 10.

Results:

In all patients, a median of the pin-prick test total score on NAC was 3 (0-10). Pin-prick test of NAC showed numerically higher NAC sensory score in the IMF incision than in the peri-areolar group without a statistical significance (IMF: Median 4 Mean 3.83 ± 3.04 , Peri-areolar Median 2 Mean 2.69 ± 3.64 , $p=0.062$). When sensory scores were evaluated depending on NAC zones (A: Nipple, B: Upper outer, C: Upper inner, D: Lower outer, E: Lower inner) the IMF incision group showed better outcomes in zone B ($p=0.015$) and E ($p=0.043$). Simple linear regression analysis showed the possibility of incisional approach, diabetes mellitus (DM) history, previous radiotherapy of ipsilateral breast, post mastectomy radiotherapy (PMRT), adjuvant chemotherapy, tumor to nipple distance and laterality influencing NAC sensory with $p < 0.2$. When these factors were taken to multiple linear regression analysis, DM history ($p=0.045$), previous radiotherapy ($p=0.001$), postop radiotherapy ($p=0.001$), and adjuvant chemotherapy

(p=0.001).

Conclusion:

NAC sensory deteriorated postoperatively in general. Scores of NAC sensation were numerically higher in the patients with IMF incision, although the difference was not statistically significant. NAC sensation was negatively affected by DM history, previous ipsilateral breast radiotherapy and post-NSM treatments such as chemotherapy and PMRT. While incision type may improve aesthetic outcomes, additional efforts are necessary to ameliorate the post-NSM NAC desensitization.

Table 1. Patient characteristics

Table 1. Patient characteristics

Characteristics	IMF (n=69)	Peri-areolar (n=36)	p
Age (mean, years)	46.96 ± 6.26	44.53 ± 7.54	0.082
NAC sensory total score (mean)	3.83 ± 3.04	2.69 ± 3.64	0.062
Family history of breast cancer, NO. (%)	14 (20.3)	13 (36.1)	0.078
BRCA carrier, NO. (%)	2 (2.9)	2 (5.6)	0.334*
Invasive carcinoma, NO. (%)	56 (81)	28 (77.8)	0.763
BMI (mean, kg/m ²)	22.70 ± 3.26	22.27 ± 3.02	0.522
Smoking history, NO. (%)	1 (1.4)	1 (2.8)	1.00*
Diabetes mellitus, NO. (%)	2 (2.9)	0	0.302
Hypertension, NO. (%)	3 (4.3)	1 (2.8)	0.690
Previous surgery, NO. (%)	12 (17.4)	11 (30.6)	0.122
Radiotherapy, NO. (%)			
Previous radiotherapy	7 (10.1)	6 (16.7)	0.336
Postoperative radiotherapy	12 (17.4)	9 (25)	0.355
Chemotherapy, NO. (%)			
Previous chemotherapy	10 (14.5)	3 (8.3)	0.621
Neoadjuvant chemotherapy	10 (14.5)	7 (19.4)	0.513
Adjuvant chemotherapy	24 (34.8)	14 (38.9)	0.678
Endocrine therapy, NO. (%)	51 (73.9)	27 (75)	0.904
Tumor size ≥ 2cm, NO. (%)	18 (26.1)	10 (27.8)	0.948
Tumor to nipple distance (mean, cm)	2.89 ± 1.64	2.99 ± 1.65	0.767
Tumor location, NO. (%)			0.201*
Upper outer	34 (49.3)	24 (66.7)	
Upper inner	15 (21.7)	5 (13.9)	
Lower outer	13 (18.8)	7 (19.4)	
Lower inner	6 (8.7)	0	
Center or whole breast	1 (1.4)	0	
Complication, NO. (%)			0.363*
Infection	3 (4.3)	0	
Skin necrosis	4 (5.8)	0	
Nipple necrosis	7 (10.1)	2 (5.6)	

* Fisher's exact test

Table 2. Linear regression analysis for clinical factors affecting NAC sensory

Table 2. Simple and multiple linear regression analysis for clinical factors affecting NAC sensory

Determinants	Simple linear regression			Multiple linear regression		
	Unstandardized B	Standardized B	p	Unstandardized B	Standardized B	p
Incision approach	-1.132	-0.183	0.062	-0.853	-0.138	0.130
BMI≥23	0.222	0.590	0.707			
smoking	-1.466	-0.068	0.489			
DM	-3.505	-0.163	0.096	-3.853	-0.179	0.045
HTN	1.624	0.106	0.283			
Previous breast surgery	-0.895	-0.126	0.200			
Previous radiotherapy	-2.519	-0.282	0.004	-3.189	-0.358	0.001
Post-op radiotherapy	-2.155	-0.293	0.002	-2.1878	-0.298	0.001
Neoadjuvant chemotherapy	-0.803	-0.101	0.306			
Adjuvant chemotherapy	-1.635	-0.268	0.006	-1.695	-0.277	0.001
Post-op endocrine therapy	0.091	0.014	0.891			
Lymphovascular invasion	0.031	0.003	0.960			
Tumor size (≥2cm)	-0.286	-0.044	0.686			
Tumor to nipple distance	-0.242	-0.135	0.171	-0.065	-0.036	0.673
Unilateral vs Bilateral	2.690	0.195	0.046	0.057	0.025	0.715
Breast specimen weight	0.000	-0.019	0.849			
Complication	0.060	0.026	0.790			

Disclosure(s):

Yoonwon Kook, M.D.: No financial relationships to disclose

Ji Soo Jang, M.D.: No financial relationships to disclose

Seung Ho Baek, M.D.: No financial relationships to disclose
Soong June Bae, MD: No financial relationships to disclose
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7:00 AM - 8:15 AM

P2-14-10

Axillary Reverse Mapping Aids in Reducing the Rates of BCRL in Underserved Ethnically Diverse Population

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Background: Breast Cancer Related Lymphedema (BCRL), is a long-term side effect affecting the patient's quality of life after lymph node surgery. Historically BCRL is seen in 5-7% and 15-40% of patients undergoing sentinel lymph node biopsy (SLNB) and axillary lymph node dissection (ALND) respectively; with the risk increasing two-fold in low-income and ethnic minority groups. Axillary Reverse Mapping (ARM) is a novel technique to distinguish drainage pathways of the arm and breast, and prior studies have reported significantly lower rates of BCRL with ARM. Lymphatic re-approximation can prevent and/or reduce lymphedema rates in cases where crossover nodes are encountered. Furthermore, blue nodes can be preserved during ALND; however, if resected during ALND, lymphatic venous (LYMPHA) procedure can help to restore lymphatic flow. However, there is a paucity of literature looking at the utility of ARM in ethnically minority groups. Therefore, we aimed to evaluate the prevalence of lymphedema in our patient population with breast cancer undergoing SLNB and ALND using ARM and in turn compare these findings to historical controls.

Materials & Methods: A retrospective study was carried out on patients who underwent axillary surgery with ARM from January 2019 to July 2021. Patient demographics such as age, BMI, gender, and ethnicity were recorded. Patients undergoing mastectomy vs breast conservation with SLNB ± ALND associated with ARM were monitored for lymphedema for a year at 3-month intervals using SOZO® scores, and then for another 2 years clinically. At each follow-up, SOZO® scores were computed using bioimpedance spectroscopy and compared to preoperative baseline scores.

Results: A total of 142 patients' data was evaluated, of which 83.8% belonged to the minority group (African American = 46, Hispanic = 63, Asian = 10). Mean BMI accounted for 29.1±5.31. Breast conservation surgery and mastectomy were performed in 71.8% (n=102) and 28.1% (n=40) of patients respectively. SLNB was performed on 88.7% (n=126) of the patients and ALND was carried out on 11.3% (n=16). Furthermore, 73.9% (n=105) of the patients underwent radiation therapy. Positive lymph nodes were identified in 24.6% (n=35) of patients. Blue nodes and blue lymphatics were encountered in 17.6% (n=25) and 32.4% (n=46) of patients respectively. Out of the blue nodes identified (n=25), 44% (n=11) were excised and 32% (n=8) were diagnosed as crossover nodes. All the crossover nodes were resected but none of them contributed to the development of lymphedema. Moreover, 90.9% of the patients with blue

lymphatics underwent lymphatic re-approximation after excision of the blue nodes. Of the 142 patients, 59 had a three-month follow-up of which 2 patients (3.4%) developed clinical lymphedema diagnosed via SOZO® who had undergone SLNB which resolved by 6-month follow-up. Additionally, compared to the historical incidence of BCRL which accounts for up to 40.4% in ethnic minorities, we found a significantly lower incidence of lymphedema ($p < 0.001$) in our patient population. Moreover, in our study, ALND and radiation therapy did not contribute to lymphedema rates.

Conclusion: ARM procedure can significantly lower BCRL even in ethnically minority groups. 3.4% of patients undergoing SLNB developed BCRL, which was significantly lower than historically reported data. Furthermore, in our study, no patients who underwent ALND developed lymphedema. Also, crossover nodes or radiation therapy did not contribute to the development of lymphedema after surgery demonstrating the effectiveness of ARM technique. Further studies with larger sample size and longer follow-up duration are necessary to better understand the utility of ARM technique in this population.

Table 1

Table 1: Baseline characteristics and follow-up data of the patients included in the study

Total Patients	142
Age, y, mean (SD)	58.9 (12.24)
Race/ethnicity	
White	23 (16.2%)
Black	46 (32.4%)
Hispanic	63 (44.3%)
Asian/ Pacific Islander	10 (7%)
Body Mass Index (BMI), mean (SD)	29.1 (5.31)
Laterality	
Left	64 (45%)
Right	78 (55%)
Breast Conservation (Lumpectomy)	102 (71.8%)
Mastectomy	40 (28.2%)
Without reconstruction	26 (65%)
With reconstruction	14 (35%)
SLNB	126 (88.7%)
SLNB + Blue Node	19 (13.3%)
ALND	16 (11.3%)
ALND + Blue Node	6 (4.22%)
Intraoperative Radiotherapy (IORT)	32 (22.5%)
Stage	
0	11 (7.74%)
1	81 (57%)
2	41 (28.8%)
3	8 (5.63%)
4	2 (1.4%)
Positive nodes (Total)	24.6% (35)
0	107 (75.4%)
1-4	31 (21.8%)
5-9	3 (2.1%)
10+	1 (0.7%)
Blue nodes identified	25 (17.6%)
Blue nodes excised	11 (44%)
Lymphatic Re-approximation following blue nodes excision	10 (90.9%)
Elevated SOZO [®] after Lymphatic Re-approximation	0 (0%)
Crossover rate	8 (32%)
Blue lymphatics present	46 (32.4%)
Adjuvant radiation	73 (51.4%)
SOZO [®] Measurements (Total)	59
Patients with increased Measurement at 3-month (Lymphedema)	2 (3.4%)
Patients with increased Measurement at 6-month (Lymphedema)	0
Follow-up time (days)	
Mean (SD)	744 (18.4)
Median	733
Range	368 - 1280

Baseline characteristics and follow-up data of the patients undergoing Axillary Reverse Mapping with SLNB ± ALND

Disclosure(s):

Fardeen Bhimani, M.D.: No financial relationships to disclose

Maureen McEvoy, M.D.: No financial relationships to disclose

Kelly Johnson, D.O.: No financial relationships to disclose

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P2-14-11

Oncological outcomes in patients undergoing targeted axillary dissection with carbon marker

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Background: The use of axillary marking before neoadjuvant systemic therapy (NST) is the standard of care in patients with positive lymph nodes (LN). Several methods have been tested leading to reduced false negative rate compared to sentinel lymph node biopsy (SLNB). With the increase in therapies in patients with residual disease, it is necessary to improve the accuracy of the axillary assessment. The aim of this study was to evaluate oncological

outcomes in patients undergoing targeted axillary dissection with positive LN pre-NST marked with 4% carbon marker, the secondary objective was to evaluate the association between SLNB and pre-NST marked lymph node. Methods: A prospective study was performed in patients with cT1-T4, cN1-N2 breast cancer who underwent NST. An ultrasound-guided 4% carbon marking was performed before proposed treatment. After NST, the carbon marked lymph node (CMLN) was identified and resected associated with SLNB. When at least one lymph node was positive, axillary dissection was performed. The oncological outcomes registered were overall survival (OS), specific survival (SS), disease-free survival (DFS), axillary recurrence (AR) and local recurrence (LR). Results: 176 patients operated between July 2014 and January 2019 were included in the analysis. The CMLN were identified in 168/176 (95.4%) and the SLNB 145/176 (82.3%) operations. SLNB and CMLN were coincident in 93/176 (52.8%) cases. The LNs were not coincident in 44/176 (25%) cases and at least one of the methods were not identified in 39/176 (22.1%). When condensing the lymph nodes not found as positive lymph node, the sample agreement was 148/176 (81.4%) [Kappa = 0.67 (95%CI: 0.56 – 0.78)], when separating the positive lymph nodes from the lymph nodes not found, the agreement was 133/176 (75.6%) [Kappa = 0.56 (95%CI: 0.46 – 0.66)] (Table 1). With a mean follow-up of 49 months, 168 patients were included in the analysis of oncologic outcomes. Among the patients analyzed, 7/168 (4,1%) had LR, 5/168 (2,9%) had AR, 28/168 (16.6%) had distant recurrences [DFS = 83.3%]. There were 10/168 (5,9%) deaths [OS = 94%], with 5 confirmed by breast cancer and 4 of undetermined cause. There was a significant association between axillary dissection and axillary recurrence (0 versus 6% p = 0.012). OS for clinical stages 2B, 3A and 3B were 97, 88 and 87.5% respectively. Conclusions: The use of 4% carbon marker is a feasible and cheap method for targeted axillary dissection. The oncological outcomes are compatible with the survival curves of the American Joint Committee on Cancer 8th edition, therefore, a safe tool to spare women cN+ from axillary dissection when there is a complete axillary response to NST. The concordance rate between the CMLN and the SLNB was moderate when we took into account the failure of some method, noting the need for a supplementary method to the SLNB after NST.

Frequency and percentages of anatomopathological results and methods of lymph node identification.

Positive SLNB	Positive CMLN			Total
	No	Yes	Not found	
No	91 51.7%	5 2.8%	5 2.8%	101
Yes	5 2.8%	39 22.2%	0 0.0%	44
Not found	13 7.4%	15 8.5%	3 1.7%	31
Total	109	59	8	176

SLNB = sentinel lymph node biopsy; CMLN = carbon marked lymph node

Occurrence of oncological outcomes

Oncological Outcome	No.	Outcome	No. (%)
Local Recurrence	168	No	161 (95.8)
		Yes	7 (4.1)
Axillary Recurrence	168	No	163 (97)
		Yes	5 (2.9)
Distant Recurrence	168	No	140 (83.3)
		Yes	28 (16.6)
Specific Death	164	No	159 (97)
		Yes	5 (3)
Death	168	No	158 (94)
		Yes	10 (6)

Disclosure(s):

Lucas R. Budel, MD: No financial relationships to disclose

Cleverton C. Spautz, MSc: No financial relationships to disclose

Maria Helena Louveira, PhD: No financial relationships to disclose

Teresa Cristina S. Cavalcanti, PhD: No financial relationships to disclose

Alessandra C. Fornazari, MD: No financial relationships to disclose

Plinio Gasperin, PhD, Jr.: No financial relationships to disclose

Leonardo P. Nissen, MD: No financial relationships to disclose

Vinicius M. Budel, PhD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-14-12

Endoscopic Nipple-Sparing Mastectomy : A single Institutional Experience of 50 Consecutive Cases

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Purpose : The purpose of this study is to introduce an early experience of endoscopic nipple-sparing mastectomy (NSM) combined with immediate breast reconstruction through simple single-port access that placed in axillary incision. **Methods and Materials :** Between November 2018 and June 2022, 48 female patients with breast cancer, total 50 cases of breast cancer (bilateral breast cancer in 2 patients) were treated with endoscopic NSM combined with immediate breast reconstruction through simple single-port access that placed in axillary incision. Forty-six patients, total forty-eight cases, underwent breast reconstruction with silicone implant, two patient underwent TRAM reconstruction. **Surgical procedures of endoscopic NSM :** Patients were placed in a supine position with both upper limbs on arm boards abducted 90 degree. An incision of 5 cm was made along the anterior axillary line from the inferior mammary fold. The sentinel lymph node was excised through the incision. A workspace for the insertion of a Glove Port (Nelis, Republic of Korea) was created within a radius of 3 cm from the incision, and the subcutaneous tissue flaps were raised. The Glove Port was inserted first into the retromammary space, carbon dioxide (CO₂) gas was insufflated, and the pressure was maintained at approximately 7 mmHg. The retromammary space dissection was performed with caution to avoid dissecting the interpectoral space, using an energy device and an endoscopic grasper guided by a flexible endoscope (ENDO EYE FLEX 10 mm, OLYMPUS, Japan). The breast was elevated to the edge of the latissimus dorsi muscle laterally, to the thoracoabdominal aponeurosis inferiorly, to the level of the clavicle superiorly, and to the edge of the sternum medially. After dissecting the retromammary fat plane, the Glove Port was relocated into the subcutaneous space. Skin flap was dissected using an energy device, and the duct beneath the nipple was cut off using endoscopic scissors. The subcutaneous flap was dissected completely along the boundaries of the breast, and the entire breast was removed. **Results :** The patients were 30-55 years old (mean, 43 years). The tumor located at the left breast in 26 cases and at the right breast in 23 cases. The diameter of tumor ranged from 1.5 to 5.2 cm (mean, 3.4 cm). Median operation time was 153 minutes. After operation, nipple necrosis or skin flap necrosis was not observed. No subcutaneous emphysema occurred. There is one tumor involvement to nipple in postoperative pathological examination. So, excision of nipple-areolar-complex was performed 2 weeks after first operation. All patients were followed up 1-43 months (median, 19 months). According to the Harris assessment criteria for appearance of reconstructed breast, there were 43 cases of excellent and 7 cases of good. No tumor recurrence or metastasis occurred during follow-up. **Conclusion :** It is a safe and feasible method of endoscopic NSM combined with immediate breast reconstruction

through simple single-port access that placed in axillary incision, and can obtain good cosmetic results. It is a new option to breast reconstruction.

Disclosure(s):

HYEYOON LEE, n/a: No financial relationships to disclose

Kyusang Cho, n/a: No financial relationships to disclose

YOUNGWOON CHANG, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-14-13

Propensity score matching for survival outcomes in breast cancer patients with nipple sparing mastectomy versus total mastectomy and breast-conserving surgery: a single-center retrospective study

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Objective: With the development of the diagnosis and treatment of breast cancer, the pattern of multidisciplinary treatment has resulted a new tendency of breast conserving surgery and reconstruction. Nipple sparing mastectomy (NSM) preserves the aesthetically important nipple-areolar complex, improved appearance satisfaction and quality of life of patients after mastectomy , and had similar oncologic outcomes compared with traditional mastectomy techniques. The primary guiding principles of NSM are oncologic safety. Some studies have demonstrated its oncologic safety while others have demonstrated recurrent risk increasing because of the nipple-areolar complex. We sought to assess the overall survival and disease-free survival of NSM compared with breast-conserving surgery (BCS) and total mastectomy (TM). **Key words:** nipple sparing mastectomy, breast-conserving surgery, total mastectomy, the overall survival, the disease-free survival **Methods:** This retrospective matched-cohort study was conducted patients accepted breast surgery between January 2007 and December 2017 in the Department of Breast Surgery of Fudan University Shanghai Cancer Center. Cancer stages were identified depending on the American Joint Committee on Cancer [AJCC] TNM staging system. The inclusion criteria included (1) female breast cancer, (2) histopathology confirmed

invasive breast cancer without distant metastasis or local relapses, (3) had complete clinical and pathological T&N stages. The exclusion criteria included in situ carcinoma, phylloides tumor, recurrent or metastatic breast cancer and pregnancy. The primary outcome was the overall survival (OS), the secondary outcome was the disease-free survival (DFS). Statistical methods included Kaplan-Meier survival analysis and COX regression analysis, all of which were completed by SPSS 20.0. Results: A total of 2757 patients were evaluated for eligibility, of which 430 were included (86 NSM vs 172 BCS vs 172 TM) · the median follow-up is 61.57 months. Clinical T&N stage and other factors of the above three operations were balanced and comparable after matching. COX regression analysis reported that pT (pT3 vs pT1, P=0.00, HR 16.051, 95%CI:3.822-67.409) and pN (pN2 vs pN0, P=0.00, HR 16.626, 95%CI:4.581-60.337) were related factors for OS, and pT (pT3 vs pT1, P=0.021, HR 6.619, 95%CI:1.331-32.927) and pN (pN2 vs pN0, P=0.000; HR 13.320, 95%CI:3.250-54.591) are independent predictive factor of OS. In addition, pN (pN2 vs pN0, P=0.013; HR 3.448, 95%CI:1.304-9.118) was a related factor for DFS. Among 94.19% patients of the NSM group underwent breast reconstruction, 70 underwent implant-based breast reconstruction, 8 underwent autogenous flaps reconstruction, and 3 patients chose latissimus dorsi flap combined with prosthesis immediate breast reconstruction. Only 4 of 172 patients underwent autogenous flaps reconstruction in TM, and 1 chose implant-based breast reconstruction. Kaplan-Meier survival analysis found that the 5-year OS of NSM group, TM group and BCS group were respectively 100%, 95.8% and 99.2%. The 5-year DFS of three operations were respectively 95.2%, 92.1%, 93.5%. Patients who underwent NSM had no difference compared with BCS or TM regarding the OS (P=0.875, HR 0.938, 95%CI:0.421-2.090) and the DFS (P=0.882, HR 0.967, 95%CI:0.623-1.502). Conclusions: Patients undergoing NSM are not disadvantaged in terms of the OS and the DFS compared with patients who underwent BCS or TM. Patients with NSM tend to opt for breast reconstruction to keep good shape and it has the same prognostic outcome as patients with TM or BCS.

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Min Xiong, n/a: No financial relationships to disclose

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P2-14-14

Effect Of Intra-operative And Post-operative Topical Tranexamic Acid On early post-operative complications In Patients Undergoing Axillary Lymph Node Dissection For Breast Cancer- A randomized controlled study.

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TITLE: Effect of intra-operative and post-operative topical tranexamic acid on early post-operative complications in patients undergoing axillary lymph node dissection for breast cancer. **Authors:** PACHIMATLA AKHIL GOUD¹, ISHITHA LAROIYA², SIDDHANT KHARE³, R N NAGA SANTHOSH IRRINKI², GURPREET SINGH⁴. **Affiliation:** 1. Junior Resident, Department of General Surgery, Post Graduate Institute of Medical Education & Research (P.G.I.M.E.R.), Chandigarh. 2. Assistant professor, Department of General Surgery, Post Graduate Institute of Medical Education & Research (P.G.I.M.E.R.), Chandigarh. 3. Associate professor, Department of General Surgery, Post Graduate Institute of Medical Education & Research (P.G.I.M.E.R.), Chandigarh. 4. Professor and Head (retired), Department of General Surgery, Post Graduate Institute of Medical Education & Research (P.G.I.M.E.R.), Chandigarh. **BACKGROUND:** Seroma formation after breast surgery has been a consistent problem with no established causes or risk factors. The role of topical tranexamic acid in reducing the incidence of seroma after axillary clearance in breast cancer is controversial. **AIMS & OBJECTIVES:** To study the effect of intra-operative and post-operative topical Tranexamic acid on the duration of drain and volume of seroma in patients undergoing axillary lymph node dissection (ALND) for breast cancer. **MATERIALS AND METHODS:** In this prospective, non-blinded, triple-arm randomized controlled trial conducted at the Department of General Surgery, PGIMER, 154 breast cancer patients were enrolled and studied from July 2020-July 2021. They were randomized into three

groups. Group A (n=51) received a single dose of diluted topical tranexamic acid intra-operatively, Group B (n=52) received intra-operative dose and daily post-operative doses till day-5 through the suction drain placed intra-operatively, and Group C(n=51) did not receive any topical tranexamic acid. The study groups were primarily compared for the total drain duration and total drainage volume. Daily drain volume for the first five days, complications like seroma, wound infection and severity of surgical site infections using Southampton score, and adverse reactions of the drug were compared. RESULTS Out of the 154 patients, four have failed to maintain appropriate records and analysis was done with 150 patients. The mean age of the study population was 52.17 ± 8.69 yrs, with a mean BMI of 26.20 ± 4.14 . The final analysis showed no significant difference in total drain volume across the three groups, but patients receiving multiple doses of topical tranexamic acid had the lowest total volume drained compared to patients receiving a single dose or no dose (1763ml Vs 1597 Vs 1773ml: $p=0.269$). There was no significant change in the duration of the post-operative drain (21.6 Vs 19.2 Vs 19.55 days: $p=0.54$). There was no statistically significant difference in complications between the groups. Seroma was seen in 6 vs 7 vs 4% ($p=0.629$) patients in groups A, B and C respectively. Wound site infection was noted in 11 vs 13 vs 10% of patients ($p= 0.766$). None of the patient characteristics like age, BMI, co-morbidities, previous lumpectomy, menopause, and length of history significantly correlated with seroma formation in the study population. CONCLUSION There was no significant reduction in drain volume or duration with either single or multiple doses of topical tranexamic acid after the axillary clearance for breast cancer. Even though not significant, an increasing trend in wound site infections was noted among the patients who received multiple doses of tranexamic acid was noted.

Disclosure(s):

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P2-14-15

Comparison of recurrence-free survival according to axillary surgery extent for clinical N0, sentinel node(s) positive, primary breast cancer patients who underwent total mastectomy.

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Purpose We investigated the recurrence-free survival difference between limited axillary node surgery and axillary node dissection (ALND) in clinical N0 primary breast cancer patients with one to three sentinel node metastasis who underwent total mastectomy. **Method** We retrospectively analyzed clinical data of 579 primary breast cancer patients who underwent total mastectomy between 2014 and 2018 from Seoul National University Hospital and Asan Medical Center. All included patients had clinical T1-2, N0 disease at the time of diagnosis based on physical exam, radiologic evaluation, and pathologic assessment if needed. The patients had one to three metastatic sentinel node(s) at the time of surgery. The patients received sentinel lymph node biopsy (SLNB) with result of one to three metastatic node(s) and either proceeded to ALND or not. We performed propensity score matching between the SLNB and ALND group with baseline clinical factors including clinical T stage and number of metastatic sentinel node(s). Finally, 208 patients were matched 1:1 for each group respectively for further analysis. Also, we stratified the eligible patients based on radiation therapy for subgroup analysis. We examined disease-free survival, regional recurrence-free survival, distant metastasis-free survival and compared the results between the groups. **Result** The median follow-up period was 64.7 months. Among matched cohorts, mean number of metastatic nodes on final pathology result was 1.2 for SLNB group and 1.7 for ALND group. Also, mean number of total removed nodes was 8.3 for SLNB group and 17.4 for ALND group. The disease-free survival [DFS] at 7 years was 89.7% for SLNB group and 91.1% for ALND group with no statistically significant difference. (hazard ratio [HR] 1.43, 95% confidence interval [CI] 0.70 to 2.92, p=0.32) Among patients who were treated with radiation, the DFS was 94.1% in the SLNB group and 94.4% in the ALND group. (HR, 0.82, 95% CI 0.17 to 4.0, p=0.81) For the subgroup without radiation, the DFS was 87.7% in the SLNB group and 89.4% in the ALND group. (HR, 1.68,

95% CI 0.75 to 3.75, $p=0.19$) We observed no statistically significant differences in the regional recurrence-free survival at 7 years (95.8% in the SLNB vs. 95% in the ALND, HR 0.62, 95% CI 0.53-4.95, $p=0.39$), and in the distant metastasis-free survival at 7 years (95.8% in the SLNB vs. 95% in the ALND, HR 1.28, 95% CI 0.59 to 2.73, $p=0.52$) Conclusion Our results suggest that limited axillary surgery with sentinel node biopsy may be as effective as axillary node dissection in terms of recurrence-free survival, for clinically node negative, primary breast cancer patients with limited metastatic sentinel node(s) who are candidates for total mastectomy. Key words: Breast cancer, Total mastectomy, Axillary lymph node dissection, Sentinel lymph node biopsy.

Disclosure(s):

Jung Whan Chun, MD: No financial relationships to disclose

Hong-Kyu Kim, MD,PhD: Bertic.inc: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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7:00 AM - 8:15 AM

P2-14-16

Breast surgery for metastatic breast cancer: a Cochrane systematic review.

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Background Breast surgery is not standard treatment for metastatic disease, however several recent retrospective studies have suggested that breast surgery could increase survival. These studies have methodological limitations including selection bias. A systematic review mapping all randomized controlled trials addressing the benefits and potential harms of breast surgery is ideal to answer this question. **Objectives** To assess the effects of breast surgery on long term outcomes of women with metastatic breast cancer. **Search methods** We conducted searches using the MeSH terms 'breast neoplasms', 'mastectomy', and 'analysis, survival' in the following databases: the Cochrane Breast Cancer Specialised Register, CENTRAL, MEDLINE (by PubMed) and Embase (by OvidSP) on 08 December 2021. **Selection criteria** The inclusion criteria were randomized controlled trials of women with metastatic breast cancer at initial diagnosis comparing breast surgery plus systemic therapy versus systemic therapy alone. The primary outcomes were overall survival and quality of life. Secondary outcomes were progression-free survival (local and distant control), breast cancer-specific survival, and toxicity from local therapy. **Data collection and analysis** Two review authors independently conducted trial selection, data extraction, and 'Risk of bias' assessment (using Cochrane's 'Risk of bias'

tool), which a third review author checked. We used the GRADE tool to assess the quality of the body of evidence. We used the risk ratio (RR) to measure the effect of treatment for dichotomous outcomes and the hazard ratio (HR) for time-to-event outcomes. We calculated 95% confidence intervals (CI) for these measures. We used the random-effects model, as we expected clinical or methodological heterogeneity, or both, among the included studies. Main results We included four trials enrolling women with metastatic breast cancer in the review. These studies included 961 participants, 477 in the surgery group, and 485 in the control group. The evidence suggests that surgery does not improve overall survival as the quality of the evidence has been assessed as very low (HR 0.92, 95% CI 0.72 to 1.18; 4 studies; 961 women). The evidence suggests that surgery does not improve overall survival subgroup analysis according to the number of metastasis sites (HR 1.08, 95% CI 0.74 to 1.58; 3 studies, 320 women); bone metastasis only (HR 0.86, 95% CI 0.67 to 1.11; 3 studies, 253 women). According to the tumor subtype surgery seems not improve the overall survival in triple-negative (HR 1.10, 95% CI 0.53 to 2.28; 3 studies, 132 women) and HER 2 positive profile (HR 0.83, 95% CI 0.63 to 1.11; 3 studies, 262 women). However, for patients with luminal tumors surgery can significantly or marginally increase the survival (HR 0.81, 95% CI 0.67 to 0.98; 3 studies, 547 women). Breast surgery may improve local progression-free survival (HR 0.48, 95% CI 0.27 to 0.84; 3 studies; 686 women; low-quality evidence), while it does not change distant progression-free survival (HR 1.03, 95% CI 0.77 to 1.36; 3 studies; very low-quality evidence). Two studies reported quality of life outcomes, however it was not possible to perform a meta-analysis due to different tools used by these trials. Authors' conclusions Based on existing evidence from four randomized clinical trials, breast surgery does not to improve overall survival for women with metastatic breast cancer. However, in subgroup analysis, women with luminal tumors present increase in survival. The quality of evidence was very low and the decision to perform breast surgery on these women should be individualized and discussed by a multidisciplinary team considering the potential risks, benefits, and costs of each intervention.

Disclosure(s):

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7:00 AM - 8:15 AM

P2-14-18

Oncological Outcomes of Nipple-Sparing Mastectomy after Neoadjuvant Chemotherapy

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Introduction:

Surgery is the mainstay treatment of breast cancer and has been improving in aesthetic outcomes even in locally advanced disease. Radical mastectomies are being replaced by less aggressive surgeries with immediate breast reconstruction. Nipple-Sparing Mastectomy (NSM) preserves Nipple Areolar Complex (NAC) along with the entire breast skin envelope and is associated with better aesthetic results and quality of life, improving patient satisfaction. Since NSM is a relatively recent technique and few studies have shown the feasibility of NSM after neoadjuvant chemotherapy (NACT), there are some concerns and controversies about its oncological safety, especially, with regard to the NAC recurrence due to the remaining tissue in the retroareolar area. This study compares the long-term oncological outcomes and correlated factors of NSM and skin-sparing mastectomy (SSM) after NACT.

Methods:

After approval by the institution's ethics committee a retrospective review was conducted to identify all patients who underwent NSM and SSM with immediate breast reconstruction after NACT between January 2011 and December 2018 at Centro de Doenças da Mama- Breast Unit Hospital Nossa Senhora das Graças. Metastatic disease, recurrent breast cancer, and other types of mastectomies were excluded. Clinicopathological and survival data, as well as recurrence events were collected from the electronic medical records. NSM was offered to the patients without involvement of the NAC and skin clinically and on imaging. All patients underwent ultrasonography, mammography and breast MRI in the preoperative period, as well as breast MRI after NACT. The decision to undergo adjuvant radiotherapy was determined by the treating radiation oncologists according to NCCN and ASTRO recommendation. A propensity score match was used to reduce the effect of selection bias on type of surgery and create well-balanced groups. The covariates included for matching were: anatomical stage, radiotherapy and molecular subtype.

Results:

A total of 188 patients underwent mastectomy in this period, 134 NSM and 54 SSM. After propensity score matching, 92 patients in the NSM group were matched to the 54 patients in the SSM group. The median follow up time was 44,7 months to NSM and 40,3 months to SSM. The characteristics of patients included in both groups after propensity score matching are described in Table 1. NAC recurrence was observed in 5 (5.4%) of 92 NSM patients, and median time of recurrence was 24.2 (11.7- 40.1) months. Ki67 showed a significant relationship with relapse in the NAC. The distance from the tumor to the NAC and other clinicopathologic variables were not correlated with NAC recurrence (Table 2). There were no significant differences between the groups in locoregional recurrence ($p=0.102$), distant metastasis ($p=0.223$) and death ($p=0.610$) (Table 3).

Conclusion:

In this matched control study, there was no difference in oncological outcomes in patients submitted to NSM and SSM after NACT, suggesting NSM with immediate breast reconstruction is a feasible option in this setting.

Table 1. Characteristics of patients treated with NSM and SSM after propensity score matching

Variable		Group		p*
		NSM (n=92)	SSM (n=54)	
Age (years)	Average ± SD	41.6 ± 10 (23 - 68)	46.7 ± 11.6 (25-79)	0.009
Menopausal status	Pre	77 (83.7%)	36 (66.7%)	0.024
	Post	15 (16.3%)	18 (33.3%)	
Histologic Type	Ductal	76 (82.6%)	45 (83.3%)	
	Lobular	5 (5.4%)	4 (7.4%)	
	Pleomorphic Lobular	3 (3.3%)	1 (1.9%)	
	Ductal+ Lobular	4 (4.35%)	1 (1.9%)	
	Other	4 (4.35%)	3 (5.5%)	
Histologic grade	1	7 (7.6%)	1 (1.9%)	0.282
	2	51 (55.4%)	29 (53.7%)	
	3	34 (37%)	24 (44.4%)	
Tumor size classification (clinical)	T1	11 (12%)	6 (11.1%)	0.210
	T2	55 (59.8%)	26 (48.2%)	
	T3	23 (25%)	16 (29.6%)	
	T4	3 (3.3%)	6 (11.1%)	
Lymph node involvement (clinical)	N0	39 (42.4%)	12 (22.2%)	0.022
	N1	44 (47.8%)	37 (68.5%)	
	N2	5 (5.4%)	5 (9.3%)	
	N3	4 (4.4%)	0 (0%)	
Anatomic clinical stage	I	4 (4.4%)	2 (3.7%)	0.343
	II	66 (71.7%)	33 (61.1%)	
	III	22 (23.9%)	19 (35.2%)	
Estrogen Receptor	Negative	37 (40.2%)	14 (25.9%)	0.106
	Positive	55 (59.8%)	40 (74.1%)	
Progesterone Receptor	Negative	39 (42.4%)	17 (31.5%)	0.220
	Positive	53 (57.6%)	37 (68.5%)	
HER2	Negative	70 (76.1%)	39 (72.2%)	0.694
	Positive	22 (23.9%)	15 (27.8%)	
Ki67	Average± SD(min-max)	49.0 ± 25.5 (7 - 95)	42.6 ± 23.8 (10 - 97)	0.140
Molecular subtype Immunohistochemical classification St Gallen 2013	Luminal A	7 (7.6%)	7 (13%)	0.515
	Luminal B	37 (40.2%)	24 (44.4%)	
	Luminal B - HER2 +	12 (13%)	9 (16.7%)	
	HER 2	9 (9.8%)	4 (7.4%)	
Radiotherapy	TNBC	27 (29.4%)	10 (18.5%)	0.307
	No	44 (47.8%)	21 (38.9%)	
Multifocality/Multicentricity	Yes	48 (52.2%)	33 (61.1%)	0.734
	No	43 (46.7%)	27 (50%)	
	Yes	49 (53.3%)	27 (50%)	

*Student's t test for independent samples or non-parametric Mann-Whitney test (quantitative variables); Fisher's exact test or chi square test (categorical variables); p<0.05

Table 2. Correlation between clinicopathologic variables and recurrence in the NAC

Clinicopathologic variable		n	NAC Relapse		p*	SHR	IC95%
			No recurrence n(%)	With recurrence n(%)			
Age (years)	Average ± SD	92	41.5 ± 10.0	42.6 ± 10.4	0.826	1.01	0.93 – 1.09
Pathologic multifocality/ multicentricity	No (ref)	43	2 (4.7%)		0.779	1.29	0.22 – 7.74
	Yes	49	3 (6.1%)				
Tumor size (mm) - ultrasonography before NACT	Average ± SD	92	25 (6 - 82)	20 (11 - 24)	0.056	0.93	0.86 – 1.00
Tumor size (mm) MRI before NACT	Median (min-max)	92	30 (8 - 94)	32.5 (16 - 64)	0.833	1.00	0.95 – 1.05
MRI distance from the tumor to NAC before NACT	Average ± SD (mm)	92	30 (0 - 95)	19 (4 - 84)	0.915	1.00	0.92 – 1.08
MRI distance from the tumor to NAC after NACT	Average ± SD (mm)	92	43.5 (0 - 101)	65.5 (12 - 90)	0.266	1.03	0.98 – 1.08
Estrogen Receptor	Negative (ref)	37	2 (5.4%)		0.887	0.88	0.15 – 5.24
	Positive	55	3 (5.5%)				
Progesterone Receptor	Negative (ref)	39	2 (5.1%)		0.982	1.02	0.17 – 6.06
	Positive	53	3 (5.7%)				
HER2	Negative (ref)	70	3 (4.3%)		0.413	2.09	0.36 – 12.2
	Positive	22	2 (9.1%)				
Ki67	Average ± SD	92	47.7 ± 25.3	71.6 ± 18.8	0.020	1.04	1.01 – 1.08

*Fine and Gray Regression Model including death as a competitive risk and Wald test, p<0.05

Table 3. Oncological outcomes in NSM and SSM groups

	n	Locoregional Recurrence		p*	SHR	CI 95%
		n (%)	median time (months)			
NSM	92	12 (13.0%)	19.1 (3.5 – 40.1)	0.102	3.50	0.78 -15.7
SSM	54	2 (3.7%)	12.2 (3 – 21.5)			
	n	Distant Metastasis		p**	HR	CI 95%
	n (%)	median time (months)				
NSM	92	15 (16.3%)	21 (2.7 – 130.2)	0.223	1.64	0.74 – 3.64
SSM	54	11 (20.4%)	21,3 (7.7 – 91.9)			
	n	Death		p***	HR	CI 95%
	n (%)	median time (months)				
NSM	92	11 (12.0%)	39 (4.6 – 98.4)	0.610	1.30	0.48 – 3.55
SSM	54	6 (11.1%)	38.2 (2.2 – 100.5)			

*Model Fine & Gray and Wald test, p<0,05

**Cox Regression Model and Wald test, p<0.05

*** Log-rank test, p<0,05

Disclosure(s):

IRIS RABINOVICH, MD PhD: No financial relationships to disclose

Leonardo P. Nissen, MD: No financial relationships to disclose

Isabela C. Soares, MD: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-14-19

Targeted Axillary Lymph Node Dissections Using Radar Reflector Localization Can Reduce Unnecessary Axillary Lymph Node Dissections in Node Positive Patients Treated with Neoadjuvant Chemotherapy

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Background Targeted axillary dissection (TAD) is a surgical strategy that involves staging the axilla through sentinel lymph node biopsy (SLNB) combined with the removal of a biopsy-proven positive lymph node identified by a clip. TAD reduces the false negative rate of SLNB alone in patients with clinically detected nodal metastasis who receive neoadjuvant chemotherapy (NAC) while avoiding axillary lymph node dissections (ALND). Radar reflector-localization (RRL) can be used to identify previously positive nodes and safely and effectively guide dissection. **Methods** We performed an institutional retrospective chart review of breast cancer patients with clinical stage T1-3 and N1-3 disease treated with NAC from 2015 to 2020 who had a biopsy proven positive node and underwent TAD using RRL. The primary outcome was the retrieval of clipped node as documented by gross visualization or specimen radiography. Secondary outcomes included pathologic complete response rates and completion axillary lymph node dissections (cALND). **Results** 79 patients were identified who fulfilled inclusion criteria. 32 (40.5%) had RRL markers placed prior to chemotherapy (mean 187 days prior to surgery) and 47 (59.5%) had RRL markers placed following the completion of chemotherapy (mean 7 days prior to surgery). The clipped node was retrieved in 77 patients (97.5%). 32 of the 34 ypN0 (i+) patients avoided an ALND; 1 patient had a cALND for failure to localize the RRL and 1 patient had a cALND for a false-positive on frozen section. There was no significant difference in clip recovery rates in the pre vs post NAC RRL groups ($p=1.00$). **Conclusion** RRL systems are an effective way to guide TAD with a high success rate in identifying and removing previously biopsied nodes. These markers can be placed prior to NAC without migration or deactivation. This strategy allows surgeons to avoid unnecessary cALND.

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Lilia Lunt, MD: No financial relationships to disclose

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Andrea Madrigano, MD: Merit Oncology: Consulting Fees (e.g., advisory boards) (Ongoing)

Cristina O'Donoghue, MD, MPH: No financial relationships to disclose

12/7/2022

7:00 AM - 8:15 AM

P2-14-20

Comparison of robot-assisted nipple sparing mastectomy with conventional nipple sparing mastectomy: a single-center experience.

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Purpose: Robot-assisted nipple-sparing mastectomy (RANSM) improves cosmetic outcomes compared to conventional nipple-sparing mastectomy (CNSM) since RANSM is performed with minimal incisions. However, there are few studies on the feasibility and surgical outcome of RANSM. The aim of this study was to compare the surgical outcomes of RANSM and CNSM in breast cancer patients. Method: A retrospective observational study was conducted at our institution between January 2021 and December 2021. A total of 54 patients diagnosed with breast malignancy that underwent either a robotic-assisted or conventional nipple-sparing mastectomy were included. The demographics of the patient's sex, age, body mass index (BMI), breast weight, and preoperative diagnosis were investigated. The surgical method, operation time (including docking time and console time in the case of robotic surgery), postoperative complications, length of hospital stay, pain score, and adjuvant therapy were analyzed. Result: A total of 57 breasts in 54 female patients were included in the study: 36 invasive ductal carcinoma patients, 11 ductal carcinoma cases, 6 invasive lobular carcinoma, 2 mucinous carcinoma, one solid papillary carcinoma and one lobular carcinoma in situ. A median age of 49(27-66), mean BMI of 22 (18.89-26.28), and mean breast weight was 246 g (120-305g). The mean operation time was 122 minutes (robotic 140 vs. conventional 118), and the average docking time was five minutes and console time 60 minutes in the robot-assisted surgery. There was only one postoperative complication in the robot group and ten cases in the conventional group. The mean hospital stay was 12.6 days (RANSM 10.75 vs. CNSM 12.92), and the average pain score was 3.53 (RANSM 3.50 vs. CNSM 3.54). None needed adjuvant therapy in the robot group. In the conventional surgical group, four patients underwent adjuvant radiotherapy and sixteen patients underwent chemotherapy including six neoadjuvant cases. Conclusion: Our results showed that RANSM had advantages of shorter hospitalization and lower pain scores although it had slightly longer operation time and could not be applicable in relatively large breasts. In the near future, RANSM may be considered as the surgery of choice over CNSM in breast cancer patients.

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Ji Young You, MD, PhD: No financial relationships to disclose

Haemin Lee, MD: No financial relationships to disclose

Eun-Shin Lee, MD: No financial relationships to disclose

Seung Pil Jung, MD, PhD: No financial relationships to disclose

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P2-14-21

NiToNo Study. Evaluation in terms of quality of life and upper extremity functionality after Targeted Axillary Dissection versus lymphadenectomy

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Introduction:

Targeted Axillary Dissection (TAD) is the combination of the sentinel lymph node biopsy

(SLNB) and retrieval of the clipped node that was proved positive before neoadjuvant treatment (NAT). Previous studies have demonstrated that this approach has a low false-negative rate in patients with cN+ before NAT. Current guidelines recommend axillary radiotherapy in cN+ despite a complete pathological response reported after NAT.

Aim:

To evaluate if TAD improves the quality of life and arm functionality compared to axillary lymph node dissection (ALND) in patients with cN+ before NAT.

Methods:

Prospective observational study. The study started in 2017 and ended in 2021. We included patients with one to three suspected lymph nodes and at least one confirmed by fine-needle aspiration. Suspicious lymph nodes were clipped before NAT. After NAT if a complete radiological response was achieved by axillary ultrasound, TAD was performed. During surgery, we used ultrasound-guided marked lymph node dissection and dual tracer SLNB. Clipped and SLN were assessed with intraoperative frozen section H&E, standard H&E, and IHC with CKAE1/AE3. After surgery, the breast tumor board analyzes the pathological findings and the surgical performance. When ITC, micro-metastases, or macro-metastases were found in the nodes, or when surgical performance is considered suboptimal, we proceed to ALND. We assessed QoL with standard forms and upper extremity mobility and lymphedema by physical examination.

Results:

We analyzed 44 women. Median age 53.9 years old. ALND was performed on 28 patients and TAD on 16 patients. Age and other confounding factors such as (BMI, type of surgery, and type of NAT) were similar in both groups. Median follow-up time: 24 months (5-60). No regional relapse in both groups. The axillary staging is shown in table 1. The surgical procedure and indications for ALND are shown in Table 2. Any patient with a Luminal-A-like profile had an axillary response to NAT and subsequent ALND was performed in all 4 patients. By contrast, patients with HER2 overexpression or triple negatives had better axillary responsiveness and 12/21 were stratified only with TAD. Two patients had a false positive finding on the post-NAT axillary ultrasound (one patient with LuminalB-Her2 positive tumor and one patient with HER2 positive not luminal) and ALND was performed, complete pathological response with only fibrosis was observed. Indications of ALND are shown in table 1. On the questionnaires, health status perception (84.9 TAD vs 65.77 ALND, $p=0.02$), QoL (83.33 TAD vs 64.29 ALND $p=0.03$), upper extremity symptoms (8.33% TAD vs 30.16% ALND, $p< 0.01$) and breast symptoms (14.06% TAD vs 31.25% ALND, $p=0.03$) are better on TAD than in ALND patients. On physical examination, 11 patients of the ALND group had some alteration in functionality (8 patients had limitation of abduction and 7 patients had lymphedema). By contrast, any alteration was found in the patients staged only with TAD.

Conclusions:

Targeted axillary dissection reduces posttreatment symptomatology and allows a better quality of life with no axillary relapses though follow-up is short. Patients with Luminal-A-like cancer probably are not good candidates for TAD because of a lack of responsiveness and perhaps another approach must be considered.

Table 1

	Total	ypN0	yPN+	Axillary cPR rate
Luminal-A-like	9	0	9	0%
Luminal-B-HER2 neg	14	4	6	29%
Luminal-B-HER2 positive	9	6	3	67%
HER2 positive not luminal	4	3	1	75%
Triple negative	8	6	2	75%

Table 1: Axillary staging after NAT

Table 2

	Axillary staging				Indications ALND			
	Total	TAD only	ALND	Conservative rate	Positive US	Positive TAD	Surgical issues	US false positive
Luminal-A-like	9	0	9	0%	4	4	0	
Luminal-B-HER2 neg	14	4	10	29%	5	4	1	
Luminal-B-HER2 positive	9	4	5	44%	1	3	0	1
HER2 positive not luminal	4	2	2	50%	2	0	0	
Triple negative	8	5	3	63%	2	0	0	1

Table 2: Surgical procedure and indications for lymphadenectomy

Disclosure(s):

Laia Vila Homs, Hospital Universitari Son Espases: No financial relationships to disclose

MARIA Lourdes Carrillo-Guivernau, LCG: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-14-22

Evaluation of male breast cancer and the application of sentinel lymph node biopsy: A multi-center retrospective study

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Objective :

Sentinel lymph node biopsy (SLNB) is currently used as a routine treatment for breast cancer patients. Many clinical studies, such as the NSABP B-32, have demonstrated that SLNB can safely replace axillary lymph node dissection (ALND) for patients with clinically node-negative breast cancer. However, it may not be applicable for male breast cancer (MBC) patients because they have notably different clinicopathological features from those occurring in females. There is a lack of evidence of SLNB application and safe exemption from ALND in MBC patients. This study aimed to evaluate the application of SLNB to provide information for the standardized treatment of MBC patients.

Methods :

The MBC patient records from four institutions ranging from January 2001 to November 2020 were retrospectively reviewed. Patients undergoing surgery as a primary treatment were included. Patients with stage IV and non-primary breast cancer were excluded. Patients were followed up postoperatively for survival analysis. The primary outcome was disease-free survival (DFS), and the secondary outcome was overall survival (OS).

Results :

There were 220 MBC patients with a median age of 60 (range 24-88) years and an average tumor size of 2.3 cm (range 0.5 cm - 6.5 cm). MBC patients were characterized by old age, advanced stage, and higher pathological grade. The median follow-up time was 5.0 (range, 1.0-17.3) years. Survival analysis showed the 5-year DFS and OS were 73.5% and 83.3%, respectively. 66 patients (30%) underwent SLNB and 39% of them showed positive results. 157 patients (71%) underwent ALND, while only half of them had positive nodes, causing unnecessary complications. For 92 patients at clinical early-stage (stage I or IIA), 28 patients only had SLNB as axillary treatment, 26 patients only had ALND and 38 patients underwent

SLNB and ALND. From Kaplan-Meier survival analysis, we found that the SLNB showed a non-inferiority to the ALND treatment in DFS ($p=0.18$) and OS ($p=0.055$).

Conclusion :

MBC patients are older at the time of diagnosis and present a higher pathological grade. There are certain obstacles to the broad application of SLNB due to the lower proportion of clinically-negative lymph node patients. However, it is undeniable that SLNB can safely and effectively exempt MBC patients at early-stage with clinically-negative nodes from ALND to reduce subsequent complications. It's still an ideal criterion for the axillary staging of MBC patients.

Clinicopathologic characteristics of MBC patients

[Table 1.tif](#)

All denominators refer to number of patients with available clinical information for that specific parameter.

Disclosure(s):

Qingyao Shang, n/a: No financial relationships to disclose

Ya Wei, n/a: No financial relationships to disclose

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Jingruo Li, n/a: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-15-02

Omentum-Lipoaspirate Free-Flap Breast Reconstruction in Women with BMI <25

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The Omental Fat-Augmented Free-flap (O-FAFF) is being offered at our institution as an alternative method of breast reconstruction. This novel free-flap construct is ideal for underweight and normal weight women who lack abdominal or other donor tissue, desire to avoid donor site morbidity and/or are averse to implant-based reconstruction. We analyze omentum, mastectomy and final construct weights in women with BMI < 25 kg/m² who underwent nipple-sparing mastectomies and O-FAFF reconstruction. Methods Operative technical features of women undergoing nipple-sparing mastectomies with immediate O-FAFF breast reconstruction over a 34 month period are included. Steps of the operative procedure are as follows : laparoscopic omentectomy, liposuction and unilateral or bilateral mastectomy is performed. An acellular dermal matrix (ADM) shell is fashioned around a tissue expander. This mold is filled with the omentum and then engrafted with lipoaspirate followed by microsurgical anastomoses of gastroepiploic artery and vein to internal mammary artery and vein. Weight of biological construct is compared to native breast weight. Results 26 women with average BMI 21.2 kg/m² underwent unilateral (15) or bilateral (11) nipple-sparing mastectomies and O-FAFF reconstruction. Average omentum weight for 37 breasts was 149 gm (82- 262) and average mastectomy weighed 212.4 gm (85 – 396). The ratio of engrafted fat to omentum weight was 0.73 for unilateral versus 0.91 for bilateral cases. The ratio of omentum-fat graft construct to mastectomy weight was 1.24 for unilateral and 0.96 for bilateral cases. Conclusion O-FAFF is a novel procedure for autologous tissue breast reconstruction after nipple-sparing mastectomy in underweight and normal weight women. Comparable weight replacement for extirpated native breast is achieved.

Disclosure(s):

Irene L. Wapnir, MD: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-15-03

Impact of radiotherapy on the long-term patient-reported outcomes of immediate breast reconstruction: The UK Brighter

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Introduction: Post-mastectomy radiotherapy (PMRT) is an important component of breast cancer treatment and has been shown to improve overall survival for women with large cancers or node positive disease. The long-term effects of radiotherapy on the outcomes of immediate breast reconstruction (IBR) and how these are perceived from the patients' perspective, however, are largely unknown. The UK Brighter study aimed to evaluate the long-term impact of PMRT on the patient-reported outcomes of IBR to support informed decision-making.

Methods: Women who underwent unilateral mastectomy and/or breast reconstruction for invasive breast cancer or ductal carcinoma in situ (DCIS) in England between 1/4/2008 and 31/3/2009 were identified from National Health Service (NHS) Hospital Episode Statistics

(HES), and current contact information for the surviving cohort provided by the NHS Personal Demographic Service. Women were sent a letter inviting them to complete three validated patient-reported outcome questionnaires, the BREAST Q, EQ-5D-5L and ICECAP-A, electronically or by post at a minimum of 12 years following their index surgery. Questionnaires were scored according to developers' instructions and scores for women who had received PMRT following IBR compared with those who underwent IBR without radiotherapy, in the cohort as a whole and by reconstruction type. Results: 11,977 women were invited to participate of whom 4,207 (35.1%) completed the questionnaires. Some 1,236 (29.4%) underwent IBR with 343 (27.8%) expander/implant (EI) reconstructions, 629 (50.9%) latissimus dorsi (LD) flaps with or without (+/-) an implant, and 264 (21.4%) abdominal flap (AF) reconstructions. Of these, 388 (31.4%) (EI n=79 (20.4%); LD+/--implant n=222 (57.2%); AF n=87 (22.4%)) received PMRT. In the cohort overall, women who received PMRT following IBR reported significantly lower 'Satisfaction with Breasts' scores at 12 years compared with those who did not receive radiotherapy (PMRT mean 56.4, standard deviation (SD) 21.5 vs. no PMRT mean 61.3, SD 20.5), $p < 0.001$). However, this difference varied across procedure types. Specifically, the 'Satisfaction with Breasts' scores of women receiving PMRT following AF reconstruction were 10.5 points lower than those not receiving PMRT (PMRT mean 60.9, SD 20.2; no PMRT mean 71.4, SD 19.6, $p < 0.001$). This difference was lower in women undergoing LD reconstruction (mean with PMRT 54.3, SD 21.1; mean without PMRT 61.6, SD 20.7; $p < 0.001$). There were no significant differences in women undergoing EI reconstruction (PMRT mean 57.5, SD 23.6, no PMRT mean 53.9, SD 17.7). 'Physical Well-being' (chest) scores were also significantly lower in women receiving PMRT following IBR in the cohort overall (PMRT mean 78.7, SD 20.1, no PMRT 83.6, SD 18.6, $p < 0.001$) but women undergoing AF reconstruction showed the greatest difference in scores (PMRT mean 83.2, SD 17.0 vs No PMRT mean 90.1, SD 15.0, $p < 0.001$). There were no significant differences in 'Physical Well-being' scores for women who underwent EI reconstruction with or without PMRT. 'Psychosocial Well-being' scores were lower in women receiving PMRT after IBR (PMRT mean 70.8, SD 22.0, No PMRT 75.4, SD 21.0), but again, differential effects were seen by procedure type with no significant differences seen in the EI group but significant differences in scores seen in women receiving PMRT after flap-based procedures. Conclusions: Women undergoing PMRT report significantly lower long-term patient-reported outcomes of flap-based reconstruction, in particular 'Satisfaction with Breasts' and 'Physical Well-being' scores. This difference was not apparent in women undergoing EI procedures. This information should be shared with patients to help them make fully informed decisions about the type and timing of their reconstructive surgery.

Disclosure(s):

Leigh Johnson, BSc: No financial relationships to disclose

Paul White, BSc, MSc, PhD: No financial relationships to disclose

Ranjeet Jeevan, PhD FRCS: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-15-04

Surgical outcomes of ambulatory mastectomy with immediate alloplastic reconstruction for breast cancer or risk reduction.

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Purpose: Since 2015, mastectomy with immediate implant-based reconstruction at our institution is an ambulatory "day surgery" procedure. Ambulatory criteria for surgery including ASA level, BMI and major comorbidities were used to screen patients. We aim to evaluate surgical outcomes for women who undergo ambulatory mastectomy with immediate alloplastic reconstruction for breast cancer or risk reduction. Our primary objective was to determine the impact of mastectomy type (nipple- or skin-sparing mastectomy) and device location (subpectoral versus prepectoral plane) on complication rates.

Methods: We performed a retrospective cohort study of women receiving immediate alloplastic reconstruction following mastectomy for either breast cancer or risk reduction at Women's College Hospital in Toronto, Ontario, Canada between 2015 and 2021. We collected demographic data on age, ethnicity, smoking status, and menopausal status. Clinical data collected included breast size, ptosis, surgical indications, laterality, location and type of implant, type of mesh used, and overall complication rate. We used a multivariable logistic regression model to determine the impact of mastectomy type and implant location on complication rates, with age, smoking status, breast size, ptosis, surgical indication, and use of mesh as covariates. Statistical analysis was performed using SAS® OnDemand for Academics and P values < 0.05 were considered statistically significant.

Results: 284 women underwent mastectomy with immediate alloplastic reconstruction for risk

reduction (130, 45.8%) and breast cancer (154, 54.2%). 134 (47%) underwent skin-sparing mastectomy (SSM) and 149 (53%) underwent nipple-sparing mastectomy (NSM). Demographic and clinical data are presented in Table 1. There was an overall complication rate of 19.4%; women having NSM had a higher crude complication rate compared with SSM (25.5% vs 12.6%, $P = 0.006$). In our multivariable logistic regression model, there was no interaction between mastectomy type and device location on complication rate ($P = 0.5$). There was also no difference in complication rates associated with SSM compared with NSM (OR 2.9, 95% CI 0.95 – 9.0, $P = .06$) or implant location ($P = 0.1$). Younger age (OR 0.93/year increase in age, 95% CI 0.89-0.98, $P = 0.005$) and having surgery for breast cancer (OR 3.4, 95% CI 1.1 – 10.2, $P = 0.03$) were associated with an increased likelihood of complications.

Conclusion: In women undergoing ambulatory mastectomy with immediate alloplastic reconstruction for breast cancer or risk reduction, there was no impact of mastectomy type (SSM vs NSM) or implant location (subpectoral vs prepectoral) on complication rates. Non-modifiable factors such as age and having surgery for breast cancer predicted having a complication. Our data suggest that with appropriate patient selection, there is no difference in surgical outcomes between mastectomy types and implant location in the ambulatory surgery setting.

Table 1.1 Total Cohort Demographic and Clinical Data

	Total (n=284)	Skin Sparing Mastectomy (n=135)	Nipple Sparing Mastectomy (n=149)	P value
Operative Date (n, %)				
2015	37 (13)	21 (16)	16 (11)	0.02
2016	35 (12)	15 (11)	20 (13)	
2017	46 (16)	31 (23)	15 (10)	
2018	42 (15)	22 (16)	20 (13)	
2019	50 (18)	17 (13)	33 (22)	
2020	45 (16)	17 (13)	28 (19)	
2021	29 (10)	12 (9)	17 (11)	
Age (mean, SD)	44.8 (11.2)	48.9 (11.1)	41.0 (9.9)	≤ 0001
Ethnicity (n, %)				
White	97 (34.2)	44 (86.3)	53 (82.8)	0.6
Asian	18 (6.3)	7 (13.7)	11 (17.2)	
Missing	169 (59.5)	84	85	
Smoking Status (n, %)				
Active	23 (8.1)	10 (8.4)	13 (10.0)	0.005
Former	48 (16.9)	33 (27.7)	15 (11.5)	
Never	178 (62.7)	76 (63.9)	102 (78.5)	
Missing	35 (12.3)	16	19	
Menopausal Status (n, %)				
Premenopausal	138 (48.6)	49 (72.1)	89 (93.7)	0.0002
Postmenopausal	25 (8.8)	19 (27.9)	6 (6.3)	
Missing	121 (42.6)	67	54	
Breast Size				
A Cup	27 (9.5)	5 (5.4)	22 (20.8)	0.02
B Cup	58 (20.4)	28 (30.4)	30 (28.3)	
C Cup	67 (23.6)	33 (35.9)	34 (32.1)	
D Cup	21 (7.4)	10 (10.9)	11 (10.4)	
DD/E Cup & Above	25 (8.8)	16 (17.4)	9 (8.5)	
Missing	86 (30.3)	43	43	
Breast Ptosis				
Grade 1*	44* (15.5)	13 (20.0)	31* (39.7)	0.0004
Grade 2	36 (12.7)	19 (29.2)	17 (21.8)	
Grade 3	29 (10.2)	22 (33.9)	7 (9.0)	
None	34 (12.0)	11 (16.9)	23 (29.5)	
Missing	141 (49.7)	70	71	
* Includes 2 pseudoptosis (NSM)				
Surgical Indications (n, %)				
Gene Mutation	105(37.0)	34 (25.2)	71 (47.7)	≤ 0.001
Family History	25 (8.8)	6 (4.4)	19 (12.8)	
Breast Cancer	154 (54.2)	95 (70.94)	59 (39.6)	
Laterality (n, %)				
Unilateral	67 (23.6)	47 (34.8)	20 (13.4)	≤ 0.001
Bilateral	217 (76.4)	88 (65.2)	129 (86.6)	

Table 1.2 Total Cohort Demographic and Clinical Data

Implant Placement (n, %)				
Subpectoral	207 (72.9)	111 (82.2)	96 (64.4)	≤ 0.001
Prepectoral	77 (27.1)	24 (17.8)	53 (35.6)	
Implant Type (n, %)				
Tissue Expander	112 (39.4)	79 (58.5)	33 (22.1)	≤ 0.001
Direct to Implant	172 (60.6)	56 (41.5)	116 (77.9)	
Type of Mesh (n, %)				
Alloderm	182 (64.1)	88 (65.2)	94 (63.1)	0.2
Vicryl Mesh	29 (10.2)	11 (8.1)	18 (12.1)	
Both	9 (3.2)	2 (1.5)	7 (4.7)	
None	64 (22.5)	34 (25.2)	30 (20.1)	
Overall Complication Rate (n, %)				
No	229 (80.6)	118 (87.4)	111(74.5)	0.006
Yes	55 (19.4)	17 (12.6)	38 (25.5)	
Complications				
Hematoma managed conservatively	2	0	2	
Nipple necrosis managed conservatively	1	0	1	
Return to OR	7	4	3	
Hematoma/infection/return to OR/implant loss	1	0	1	
Hematoma with return to OR	1	0	1	
Infection/skin necrosis/return to OR/implant loss	3	1	2	
Infection with return to OR	1	0	1	
Infection, return to OR, implant loss	6	4	2	
Nipple necrosis	1	N/A	1	
Nipple necrosis with return to OR	3	N/A	3	
Nipple necrosis, return to OR, and implant loss	3	N/A	3	
Skin necrosis with return to OR	3	2	1	
Skin necrosis, return to OR, implant loss	3	1	2	
Return to OR and implant loss	20	4	16	
No complication	229	118	111	

Disclosure(s):

Simran Sandhu, BSc.: No financial relationships to disclose

Tulin D. Cil, MD, MEd: No financial relationships to disclose

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David Lim, MDCM MEd PhD FRCSC: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Merck & Co., Inc.: Consulting Fees (e.g., advisory boards) (Ongoing)

12/7/2022

7:00 AM - 8:15 AM

P2-15-05

Prepectoral versus subpectoral implant-based breast reconstruction: A systemic review and meta-analysis.

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Prepectoral versus subpectoral implant-based breast reconstruction: A systemic review and meta-analysis. Edvin Ostapenko, MD^{1,2}, Larissa Nixdorf, MD¹, Yelena Devyatko, MD¹, Ruth Exner, MD¹, Kerstin Wimmer, MD¹, Florian Fitzal, MD¹ ¹Department of General Surgery and Breast Health Center, Medical University of Vienna, Vienna, Austria. ²Faculty of Medicine, Vilnius University, Vilnius, Lithuania

Abstract Background Implant-based breast reconstruction (IBBR) is still standard and most popular option for women undergoing breast reconstruction after mastectomy worldwide. Recently, prepectoral IBBR has resurged in popularity, despite limited data comparing prepectoral with subpectoral IBBR. **Methods** A systematic search of PubMed and Cochrane Library from January 1, 2011, to December 31, 2021, was performed following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) reporting guideline, data were extracted by independent reviewers. Random and fixed-effect models were applied to obtain pooled proportions and 95% CIs. The Risk of Bias in Nonrandomized Studies- of Interventions (ROBINS-I) tool was used for critical appraisal of cohorts and funnels plots, and the Egger bias test were used for evaluating the publication bias. Studies that compared prepectoral IBBR with subpectoral IBBR for breast cancer were included. **Results** Overall, 15 studies with 3101 patients were included in this meta-analysis. Our results showed that patients receiving prepectoral IBBR experienced fewer capsular contracture (odds ratio [OR], 0.54; 95% CI, 0.32-0.92; P=.02), animation deformity (OR, 0.02; 95% CI, 0.00-0.25; P=.002), and prosthesis failure (OR, 0.58; 95% CI, 0.42-0.80; P=.001). There was no significant difference between prepectoral and subpectoral IBBR in overall complications (OR, 0.83; 95% CI, 0.64-1.09; P=.19), seroma (OR, 1.21; 95% CI, 0.59-2.51; P=.60), hematoma (OR, 0.76 95% CI, 0.49-1.18; P=.22), infection (OR, 0.87; 95% CI, 0.63-1.20; P=.39), skin flap necrosis (OR, 0.70 95% CI, 0.45-1.08; P=.11), and recurrence (OR, 1.31; 95% CI, 0.52-3.39; P=.55). Similarly, no significant difference was found in Breast-Q scores between prepectoral and subpectoral IBBR groups. **Conclusion** The results of our

systematic review and meta-analysis demonstrated that prepectoral implant-based breast reconstruction is a safe modality and have similar outcomes with significantly lower rates of capsular contracture, prosthesis failure and animation deformity compared to subpectoral implant-based breast reconstruction. Future research should include randomized clinical trials or well-designed prospective matched studies with adequate follow-up to assess long-term as well as oncologic outcomes between comparative groups. Key Words: immediate implant-based breast reconstruction, breast cancer, outcomes, prepectoral, subpectoral;

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Edvin Ostapenko, MD: No financial relationships to disclose

Larissa Nixdorf, MD: No financial relationships to disclose

Yelena Devyatko, MD: No financial relationships to disclose

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P2-15-06

Light-based bioprinting of vascularized fatty tissue for the development of biological breast implants

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Although multi-modal and ablative treatment strategies for breast cancer are becoming more popular, partial or full mastectomy is still a most common intervention. While proving to be effective in curing the cancer, it leaves the patient disfigured, which can pose a considerable psychological burden. Hence, reconstructive breast surgery is continuing to increase in importance as it offers the possibility to at least partially restore the original look of the breast. Autologous adipose tissue transfer techniques, amongst them the surgical gold standard flap surgery and liposuction-based fat grafting, present natural solutions with the patient's own tissue, but either produce a considerable secondary wound or are insufficient to address larger defects. Synthetic solutions like silicone implants on the other hand can also be used to fill large defects and only require minimal surgical intervention, but suffer from foreign body-associated complications like fibrosis. Tissue engineering biological breast implants of arbitrary size with no or minor insult to the patient's body and excellent biocompatibility, exclusively using biomaterials and patient-specific adipose cells, could open a new chapter for breast reconstruction. Such an approach has become an intriguing possibility through the rise of powerful biofabrication technologies in the last two decades, namely three-dimensional bioprinting. Bioprinting marries additive manufacturing with biomaterials and living cells with the aim to create life-mimicking tissues and organs, and while it is mainly focused on research today, current endeavors push for application in regenerative medicine. In our work we sought to fabricate adipose tissue constructs using light-based bioprinting to investigate the potential application of such technology for future reconstructive breast surgery. The engineered tissue blocks were designed to mimic native human adipose tissue by comprising fat, connective tissue and endothelial cells. Being specifically placed by the bioprinter within extracellular matrix-like hydrogels, the cells were cultured in vitro and differentiated within the cultivation time

of up to 4 weeks to form an adipose-like tissue. Live imaging showed high viability of bioprinted tissue blocks over the whole cultivation period and pronounced cellular reorganization. Confocal and histological analyses revealed a dynamic tissue maturation process with increasing proportions of differentiated adipocytes, ECM remodeling and formation of microvascular structures. In conclusion, the obtained results gave proof to the concept of engineering adipose tissue through bioprinting and could lay the groundwork for the development of all-natural biological breast implants.

Disclosure(s):

Nina Hedemann, n/a: No financial relationships to disclose

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Marion van Mackelenbergh, MD: Amgen: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); GenomicHealth: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); GSK: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Molecular Health: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Mylan: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pierre Fabre: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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P2-15-07

Current status of latissimus dorsi flaps with or without implants for breast reconstruction in patients with breast tumor: A single-center retrospective study

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Background: Asian women have relatively small breast sizes compared to European American women, so the latissimus dorsi flap (LDF) is the most commonly used autologous flap for breast reconstruction in Chinese patients with breast tumor. To explore the current status of LDF with or without implants (IMP) breast reconstruction in China, we conducted this study. Methods: This study was a single-center retrospective study that included breast tumor patients who underwent LDF breast reconstruction in Fudan University Shanghai Cancer Center (FUSCC) from 2000 to 2019. The basic clinicopathological information, the timing and type of reconstruction, postoperative hospitalization time and serious complications requiring surgical intervention were analyzed. Continuous variables were expressed as mean values or median values, while categorical variables were expressed as frequencies. Data were analyzed by using Chi-square and Kruskal-Wallis tests. All P values reported were two-sided and were calculated at a significance level of 0.05. Results: A total of 2868 patients who underwent breast reconstruction for breast tumor were analyzed in this study, 785 (27.4%) patients used LDF for breast reconstruction, and 397 (13.8%) patients underwent autologous breast

reconstruction utilizing abdominal flap. The number of breast reconstruction patients and the diversity of reconstruction procedures were increasing year by year. Breast reconstructions utilizing LDF have decreased as a percentage of breast reconstructions, but have increased in number in the past few years. Among patients with LDF breast reconstruction, the majority (97.3%) underwent immediate reconstruction, 11 patients underwent delay reconstruction, and 10 patients underwent immediate-delay reconstruction. 448 patients underwent expanded LDF breast reconstruction, and 337 (42.9%) patients underwent LDF combined with IMP breast reconstruction. 13 patients underwent restoration of reconstructed breast with LDF, 12 of which were changed to LDF±IMP reconstruction due to unsatisfactory outcome of expander reconstruction or failed implant reconstruction, and one patient was changed to LDF reconstruction from failed abdominal flap reconstruction. In terms of pathological type, 629 (80.1%) patients had invasive carcinoma, 129 (16.4%) had carcinoma in situ, 18 (2.3%) patients had phyllodes tumor and 9 (1.1%) patients had other malignancies. The median reconstruction age of the patients was 37 years old, the mean BMI was 21.76kg/cm², and the mean postoperative length of stay was 11.13 days. There were no significant differences in postoperative hospitalization time, reconstruction age, BMI, pT, ER, PR, HER2, Ki67, and radiotherapy between patients with expanded LDF and LDF combined with IMP breast reconstruction. Patients with neoadjuvant therapy (P=0.045), phyllodes tumors or other malignant tumors (P=0.023), and those with more metastatic lymph nodes (P=0.031) were tent to expanded latissimus dorsi flap reconstruction. Serious complications requiring surgical intervention occurred in 13 patients (1.65%), including 7 patients who underwent surgical debridement or scar repair due to wound infection and poor healing, and 3 patients who removed the implant due to implant infection. The reconstructed latissimus dorsi flaps necrosis occurred in 3 patients, and the reconstructed breasts were removed in these patients. There was no significant difference in the incidence of serious complications requiring surgical intervention between patients with expanded LDF and those with LDF combined with implant reconstruction, P=0.79. Conclusions: LDF±IMP breast reconstruction is a mature breast reconstruction procedure in our center with high safety. Whether combined with implant reconstruction did not affect the postoperative hospitalization time and the incidence of serious complications.

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P2-15-08

Aesthetic Incisions and Early Complications for Nipple-sparing Mastectomy followed by Immediate Breast Reconstruction

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Introduction: Nipple-sparing mastectomy (NSM) is a surgical alternative for patients who are not candidates for breast-conserving therapy in early breast cancer or even for women who are candidates for risk-reducing mastectomies, facilitating immediate breast reconstruction. Aesthetic incisions such as through the inframammary fold (IMF) or periareolar (PA) are viable options for radial scars, with better cosmetic results and less visibility. Little is known about early surgical complications between these two techniques. Objectives and methods The aim of this study was to evaluate early complications (NAC necrosis [mild, partial or total], infection, seroma, hematoma, dehiscence and reconstruction failure) in patients undergoing NSM via esthetic incisions (IMF or PA) and immediate breast reconstruction in a unique Brazilian institution. A retrospective analysis was performed at Hospital Geral de Fortaleza (HGF) between 2015 and 2022, including patients with a minimum follow-up of 3 months and complete data in the medical records. The following demographic parameters were evaluated: age, body mass index, co-morbidities, use of direct implant or tissue expander, breast weight and pre-pectoral or submuscular reconstruction. Pearsons chi squared tests and t-test were performed and a p value of < 0.05 was considered statistically significant. Results A total of 180 NSM through IMF (n=106) or PA (n=74) incisions were included and 43 cases (23.9%) of complications were observed: 27 in the PA group (62.8%) and 16 in the IMF (37.2%), with this difference being significant (p=0.0002). Regarding NAC necrosis, 65.4% were observed in the PA incision (n=17; 22.4%), compared to 34.6% in the IMF (n=9; 8.7%) (p=0.0023). There was no significant difference in relation to other complications (n=7 [IMF] vs n=10 [PA]), just as there was no difference in relation to the demographic parameters evaluated, except for the pre-pectoral and direct-to-implant reconstruction, which were more frequently performed in the IMF group: 19 (18.3%) vs 3 (4%) and 52 (50%) vs 24 (31.6%) cases respectively. Only 2 patients had breast reconstruction failure, both in the PA cohort. Conclusions Both incisions are viable

options for accessing the NSM, with an acceptable rate of complications. The PA incision is related to a higher complication rate compared to IMF, based mainly on the NAC necrosis rate. More studies are needed for a better understanding of this scenario.

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P2-15-09

Impact of neoadjuvant chemotherapy on the short- and long-term outcomes in patients who underwent immediate breast reconstruction after mastectomy

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Background and Purpose In breast cancer patients receiving neoadjuvant chemotherapy (NAC), the use of immediate breast reconstruction (IBR) as a breast cancer treatment option remains controversial. The Japanese breast cancer society conducted retrospective multicenter

cohort study in the era of IBR, and we assessed the impact of NAC on surgical and oncological outcomes in patients underwent IBR. Methods Between January 2008 and December 2016, 473 (10.0%) breast cancer cases received NAC of 4726 cases underwent IBR after mastectomy. The clinicopathological and survival data of patients who received NAC (the NAC group) and those who did not receive NAC (the control group) were compared in terms of postoperative complications (infection, hemorrhage, seroma, dehiscence, tissue expander or implant loss, flap or skin necrosis) and oncologic safety. Results Eight-hundred forty cases had minor or major complications. NAC did not increase the risk of complications after IBR (OR 1.20; 95%CI 0.95 - 1.53; p = 0.13). Smoking (OR 1.35; 95%CI 1.14 - 1.62; p = 0.001), overweight (BMI \geq 25) (OR 1.94; 95%CI 1.61 - 2.35; p < 0.001), PMRT (OR 1.54; 95%CI 1.20 - 1.99; p = 0.01) increased risk of complications. At the median follow-up time of 76.5 months, 36 patient (7.6%) in the NAC group and 147 patients (3.5%) in the control group had local recurrence. 35 patient (7.4%) in the NAC group and 147 patients (2.0%) in the control group had regional recurrence. Conclusion Immediate breast reconstruction after NAC is a safe procedure with post-operative complication profile. It can be performed safely and therefore should be considered as a strategy preferred for patients with local advanced breast cancer.

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P2-15-10

Impact of the withdrawal of textured breast implants from the market on breast reconstruction practices

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Background: In November 2018, the SOFCPRE (Société Française de chirurgie plastique, reconstructrice et esthétique) recommended that textured Biocell© implants should no longer be used because of a potential risk of anaplastic large cell lymphoma (ALCL). This decision was confirmed in April 2019 by the French Medicines Agency (ANSM, Agence nationale de sécurité du médicament), and the French Medical Regulatory Authority. In the Georges-François Leclerc Cancer Center (Dijon, France), we suspended the use of textured Biocell© implants from November 2018 onwards, in favour of smooth surface, round implants.

Objective: To assess the impact of textured implant withdrawal on surgical practices in breast reconstruction (BR) in a single French cancer center.

Methods: This is a retrospective, single-centre study in the Georges-François Leclerc Cancer Center (Dijon, France). Surgical practices of BR and complications were compared between 2 periods : before the withdrawal of textured implants from the market (Period 1 : September 2017-November 2017) and after (Period 2 : December 2018-March 2020). Patients were included if they were operated on for the first time for immediate or secondary BR in either period. Univariate analysis was performed to compare before vs after groups, and to analyse surgical practices (rates of autologous techniques and breast implant) of BR and complications ((defined as any complication grade IIIB or higher according to the Clavien Dindo classification) between the 2 periods.

Results: Data from 168 and 159 BR were collected from Periods 1 and 2 respectively. Characteristics were comparable between groups. The rate of BR with implants was significantly lower in period 2 compared with period 1 (23.9% vs 53.6% ; $p < 0.001$). Similarly, autologous BR increased significantly in period 2 for muscle sparing latissimus dorsi (2.4% vs 12.6% ; $p < 0.001$) and exclusive fat grafting (9.5% vs 21.5% ; $p < 0.01$). Others autologous techniques was comparable between the two periods (DIEP and latissimus dorsi). The number of complications decreased in period 2 (10% vs 18.4% in period 1, $p = 0.04$).

Conclusion : After the withdrawal of textured implants, we observed a significant change in surgical practices for BR in our center. The rate of reconstruction with implants decreased in favour of autologous techniques. This change in practice was accompanied by a decrease in

complications.

Surgical techniques for breast reconstruction between the two periods

	Period 1 (n=167)	Period 2 (n=159)	p
Breast reconstruction with implant	90 (53.9%)	38 (23.9%)	<0.001
Autologous reconstruction	77 (46.1%)	121 (76.1%)	<0.01
DIEP	27 (16.2%)	33 (20.8%)	0.36
Latissimus dorsi flap	30 (18%)	34 (21.4%)	0.52
Muscle sparing latissimus dorsi flap	4 (2.4%)	20 (12.6%)	<0.001
Exclusive lipofilling	16 (9.6%)	34 (21.4%)	<0.01
Timing of breast reconstruction			0.08
Immediate	81 (48.5%)	61 (38.4%)	
Secondary	86 (51.5%)	98 (61.6%)	
Contralateral symmetrization			
Mastopexy	56 (33.5%)	50 (31.4%)	0.52
Breast augmentation with implant	11 (6.6%)	2 (1.3%)	0.04
Average number of operations (mean ± SD)	2.74 ±1.60	2.59 ±1.42	0.36
≤ 3 operations	123 (73.7%)	119 (74.8%)	0.91
> 3 operation	44 (26.3%)	40 (25.2%)	0.91

Period 1 : September 2017-November 2017;Period 2 : December 2018-March 2020. DIEP, Deep Inferior Epigastric Perforator; SD, Standard deviation

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

P2-16-01

The Kinesin-like protein Kif11 is essential for the Survival of TP53-mutant Triple Negative Breast Cancer Cells

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Background: Breast cancer is the most commonly diagnosed non-cutaneous malignancy in American women and one of the leading causes of cancer deaths. Breast cancer can be divided into several subtypes, the most aggressive of which is Triple-Negative Breast Cancer (TNBC), a disease with few targeted therapies. TP53 mutations are found in 80% or more of TNBCs. However, direct targeting of mutant TP53 has been difficult. To identify drugs that can specifically induce the death of TP53-mutant breast cancers, we conducted a drug screen in TP53-mutant and TP53-wild type breast cancer cells. Through this combined in silico and in vitro drug screen, we discovered that TP53 mutant TNBC cells have an increased sensitivity to KIF11 inhibition as compared to TP53 wild-type cells. Hypothesis: We hypothesize that TP53 mutational status confers sensitivity of triple-negative breast cancer cells to KIF11 inhibition. Methods: We obtained data on TP53 mutational status, KIF11 mRNA expression levels, and clinical characteristics from publicly-available TCGA, METABRIC, and CCLE datasets. To demonstrate the effect of KIF11 inhibition on cell growth, we treated TP53 mutant and wild-type breast cancer cell lines with the small molecule KIF11 inhibitor SB-743921 and KIF11 siRNAs. Cell counts were obtained through staining with DAPI or Hoechst nuclear stains and imaging on the MetaXpress PICO instrument. To determine protein expression of p53 and Kif11 across various cell lines, western blotting was performed. We then investigated the biological mechanisms of growth inhibition by DRAQ7 staining and flow cytometry analysis following Annexin V-PI staining. Results: Using cell growth assays we demonstrated that TP53 mutant cells are more sensitive to KIF11 inhibition. We next utilized cell lines in which TP53 mutations had been introduced into TP53 wild-type cells to show that overexpression of a TP53 mutant gene can sensitize cells to KIF11 inhibition. Using assays of proliferation and apoptosis, we showed that TP53 mutant breast cancer cells treated with a KIF11 inhibitor undergo cell death. Using publicly-available datasets of breast cancers, we showed that KIF11 is upregulated in TNBCs and TP53 mutant cancers, and that high expression of KIF11 in breast cancer is correlated with poorer clinical prognosis. Conclusions: Our results show that the Kif11 protein is essential for the survival of TP53 mutant TNBC cells. Inhibitors of Kif11 induce death of TP53 mutant TNBCs and thus, this kinesin-like protein involved in cell spindle mechanics is a potential target for the treatment of these aggressive cancers. Research reported in this publication was supported by the National Center for Advancing Translational Sciences of the

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P2-16-02

TXNIP-dependent tumor suppressive pathways in breast cancer growth and progression

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Thioredoxin-interacting protein (TXNIP) plays a critical role in glucose metabolism and redox signaling through negatively regulating thioredoxin activity. Over the past decade, TXNIP has emerged as a novel tumor suppressor in various cancer models. In search of the molecular targets mediating the anticancer effect of an epigenetic drug UNC0642, we found TXNIP to be consistently upregulated by UNC0642, which was coupled with significant suppression of MDA-MB-231 breast cancer cell proliferation in vitro and tumor growth in vivo. TXNIP knockdown increased MDA-MB-231 cell proliferation and in vivo tumor growth and metastasis. In contrast, TXNIP-reconstitution in TXNIP-deficient HCC1954 breast cancer cells suppressed cell proliferation and migration that is coupled with increases in reactive oxygen species, strongly supporting TXNIP's potent antitumor function. TXNIP-reconstitution also decreased mitochondrial respiration and glycolysis in HCC-1954 cells as determined by using the Agilent Seahorse XF Cell Energy assays. To understand the molecular targets through which TXNIP exerted its antitumor activity, we performed co-immunoprecipitation studies and proteomic analyses to identify TXNIP-interacting proteins in UNC0642-treated MDA-MB-231 cells. Besides thioredoxin, we identified peroxiredoxin-6 (PRDX6), another modulator of cellular redox signaling, as a major TXNIP-interacting protein. While Prdx6-knockout mice develop normally, PRDX6 is frequently upregulated in breast cancer patients that is significantly associated with aggressive tumor subtypes and poor overall survival. The mechanism underlying the role of PRDX6 in breast oncogenesis remains elusive. Our findings suggest that TXNIP might exert its antitumor activity through binding and inhibiting PRDX6 activity in breast cancer cells to alter ROS signaling, thus providing novel therapeutic targets and potential prognostic biomarkers for breast cancer patients.

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Jasvinder Singh, n/a: No financial relationships to disclose

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P2-16-03

The Speckle-type POZ protein (SPOP) inhibits breast cancer malignancy by destabilizing oncogene TWIST1

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Epithelial-mesenchymal transition (EMT) inducing transcription factor TWIST1 plays a vital role in cancer metastasis. How the tumor-suppressive E3 ligase, Speckle-type POZ protein (SPOP), regulates TWIST1 in breast cancer remains unknown. In this study, we report that SPOP physically interacts with, ubiquitinates, and destabilizes TWIST1. SPOP promotes K63- and K48-linked ubiquitination of TWIST1, predominantly at K73, thereby suppressing cancer cell migration and invasion. Silencing SPOP significantly enhances EMT, which accelerates breast cancer cell migration and invasiveness in vitro and lung metastasis in vivo. Clinically, SPOP is negatively correlated with the levels of TWIST1 in highly invasive breast carcinomas. Reduced SPOP expression, along with elevated TWIST1 levels, is associated with poor prognosis in advanced breast cancer patients, particularly those with metastatic triple-negative breast cancer (TNBC). Taken together, we have disclosed a new mechanism linking SPOP to TWIST1 degradation. Thus SPOP may serve as a prognostic marker and a potential therapeutic target for advanced TNBC patients.

Disclosure(s):

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MNX1 promotes tumor sensitivity to HER2-targeted therapy in HER2-positive breast cancer

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Background: Female breast cancer has been the world's leading cancer incidence among women. HER2-positive breast cancer accounts for about 15%~20% of all breast cancer, with a high degree of malignancy and easy metastasis and recurrence. With the development of medical technology and the continuous innovation of HER2 targeting drugs, patients with HER2-positive breast cancer have more treatment options and their prognosis had been greatly improved. However, there is still a lack of biomarkers for HER2-positive early breast cancer in clinical practice. Methods: This study prospectively collected single-center (Fudan University Shanghai Cancer Center, FUSCC) preoperative core needle biopsy samples of breast cancer patients from July 2017 to July 2018 who received neoadjuvant paclitaxel, carboplatin plus with trastuzumab (PCH). The patients were divided into pCR and non-pCR groups, and 81 patients were enrolled. The differential expression of genes was screened and validated by RNA-seq. The gene expression data for GSE181574 (this database has a total of 105 cases of breast cancer tissue samples were collected by core needle biopsy before neoadjuvant treatment. 52 cases underwent Ado-trastuzumab emtansine plus pertuzumab, 9 cases of paclitaxel plus trastuzumab, and 44 cases of paclitaxel plus trastuzumab and pertuzumab), GSE52707 (SK-BR-3 Lapatinib resistance cell group vs control group), and GSE15043 (BT474 Herceptin-resistant cell group vs control group), were downloaded from the Gene Expression Omnibus (GEO) database. Cell cloning formation, proliferation assay, and drug sensitivity experiments were conducted in MNX1 ectopic and knockdown cell lines. Co-IP assay, RNA-Seq, and ChIP-Seq analysis were used to explore the downstream pathways that MNX1 might be involved. Results: High-throughput sequencing results of core needle biopsy samples from 81 HER2-positive breast cancer patients were divided into pCR and non-pCR groups. Using DEseq2 packet analysis to screen differentially expressed genes, P-value < 0.05, | log2FoldChange | > 1 as the filter, there were 620 up-regulated genes and 715 down-regulated genes in the pCR group. The same method was used for the analysis of the GSE181574 data set. Combined the two datasets used P values and log2FoldChange (P-value < 0.05, | log2FoldChange | > 1.2) as selection criteria, we found the MNX1 and PNMT expressions were significantly higher in the pCR group. Subsequently, differential analysis of GSE52707 and GSE15043 datasets showed that MNX1 and PNMT expression levels were reduced in drug-resistant cell lines. Considering the P-value and | log2FoldChange |, we ultimately selected motor neuron and pancreatic homeobox 1(MNX1) gene as the target factors for follow-up studies. In the cloning formation and proliferation assay, overexpression of MNX1 inhibits proliferation and clonal formation of HER2-positive breast cancer cells. In the drug sensitivity experiments overexpression of MNX1 enhances the sensitivity of HER2-positive breast cancer cells to tyrosine kinase inhibitors (TKI)

such as lapatinib and pyrotinib. MNX1 knockdown reduces the sensitivity of HER2-positive breast cancer cells to TKI. Through RNA-seq and ChIP-seq, we found that CD-M6PR might be a downstream target gene regulated by MNX1. Verification by Dual-Luciferase Reporter Assay MNX1 was found to positively regulate CD-M6PR transcription. By Co-IP assay, it was found that MNX1 interacted with EEF1D, and EEF1D stabilized MNX1. MNX1 and CD-M6PR affect the proliferation and drug sensitivity of breast cancer cells by down-regulating the PI3K-AKT-mTOR pathway. Conclusion: Overexpression of MNX1 increases the sensitivity of HER-2 positive cells to TKI. MNX1 binds to EEF1D and is stabilized by EEF1D. MNX1 positively regulates M6PR and affects the proliferation of breast cancer cells and the sensitivity of breast cancer cells to TKI through the PI3K-AKT-mTOR pathway.

Disclosure(s):

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P2-16-05

Targeting EZH2 to overcome chemoresistance in Triple Negative Breast Cancers Employing Combinatorial Approach.

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Objective: Triple Negative Breast Cancers (TNBC) are highly invasive and 46% of patients develop distant metastases, leading to higher mortality. Chemotherapy remains the most efficacious option, however, there is still a largely unmet need to identify novel therapeutic targets in TNBC to increase treatment options and improve patient outcomes, survival. Enhancer of zeste homologue 2 (EZH2), a member of the catalytic subunit of the polycomb repressive complex 2, is a histone methyltransferase and its canonical function is to methylate lysine 27 of histone 3. EZH2 is a potential driver of TNBC metastasis, and its high expression strongly associates with the TNBC phenotype as compared with other molecular subtypes of breast cancer. Despite the advancement in the discovery of inhibitors for EZH2 that attenuate its catalytic activity. Currently, several EZH2 inhibitors are under development and undergoing clinical trials and these compounds have been proved to be effective in the treatment of hematological malignancies, sarcomas and malignant rhabdoid tumors. However these inhibitors do not affect the intrinsic protein stability of EZH2, but typically competes with the cofactor S-adenosylmethionine (SAM) and binds to the SET domain of EZH2. Hence, the EZH2 inhibitors are only effective for some malignant blood tumors, and have poor efficacy for solid tumors, such as TNBC. Several studies have shown the involvement of neurotransmitter dopamine in proliferation, apoptosis, tumor angiogenesis, and drug resistance among different cancers, including the breast¹. Dopamine D1 receptor activation in TNBC cell line induces apoptosis, autophagy and phosphorylation of eukaryotic translation initiation factor 2-alpha (eIF2a)². Also, D1R agonists inhibits the invasion of breast cancer cell lines MDA-MB-231 and BT-20 and regress mammary tumors³. The oncogenic nature of EZH2 in driving aggressiveness in TNBC cells led us to simultaneously target dopamine D1 receptor and EZH2 to completely ablate tumor growth and metastasis. Methods: Schrodinger protein modeling software was employed for docking studies. TNBC cells MDA-MB-231 cells were treated with the EZH2 inhibitor GSK126 and/or D1R agonists A77636 and SKF38393 for assessing cell viability, migration. Immuno precipitation to investigate if the combination could disrupt the PRC2 complex in TNBC cells. To model tumor burden and the effects of combination therapy on tumor growth in vitro, we tested the combinatory effect of GSK126 and D1R agonists in a 3D culture system of MDA-MB-231 cells encapsulated in calcium-alginate microgels seeded from a microfluidic droplet generator. Cell death was determined by Yo-pro-Propidium Iodide staining. Result: In silico analysis confirmed that D1R agonists exhibited strong stabilization of protein structures upon binding to the EZH2 catalytic active site, albeit with slightly weaker affinity than GSK126. Combination treatment with GSK126 and dopamine agonists A77636 or SKF 38393 led to significant and synergistic inhibition of cell viability ($p < 0.01$), migration, invasion, and EZH2 activity ($p < 0.01$) in TNBC cells. In addition, MDA-MB-231 cells formed tumor spheroids that were subjected to the EZH2 inhibitor alongside dopamine agonists, indicating tumor reduction relative to single agent treatment in 3D culture ($p < 0.0001$). The combination also led to increased necrotic cell death ($p < 0.05$). Immunoprecipitation of EZH2 in the presence of GSK126 and SKF38393 and A77636 dissociated the physical interaction between EZH2, EED, and SUZ12 in MDA-MB-231 cells. Conclusion: Our data suggest that the combination of GSK126 and Dopamine D1 agonists synergistically inhibits TNBC proliferation by disrupting EZH2 functions leading to necrotic cell death. (This work is supported by DOD: W81XWH2010065, for Eswar Shankar). 1) PMID: 21531818 2) PMID: 29773888 3) PMID: 26477316

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P2-16-06

Protein expression and subcellular localization of a clathrin adaptor AP-1 associate with tumor growth activity in breast cancer

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[Introduction] Breast cancer is the fifth leading cause of cancer-related death among women, and its prevalence is the highest in all cancers of Japanese women. To improve the prognosis of breast cancer patients, new diagnostic and therapeutic tools need to be developed. Adaptor protein complex-1 (AP-1) is one of the clathrin adaptor molecules regulating intracellular transport of specific cargos between the trans-Golgi network (TGN) and endosomes. Although the detailed mechanisms have been poorly elucidated, previous reports suggest that AP-1 expression is related with cell proliferation and cancer metastasis. The purpose of this study is to investigate the association between AP-1 expression in tumor tissue measured with immunohistological analyses and surrogate markers of cancer aggressiveness, such as Ki-67 labeling index and/or breast cancer subtypes. [Materials and methods] The records of 207 primary breast cancer patients surgically treated at Fukushima Medical University Hospital from 2011 to 2014 were reviewed. Paraffin embedded sections of these patients were processed for immunohistochemistry examination using antibody against γ -adaptin, a subunit of AP-1, and then its immunoreactivity was quantified. The staining patterns were also graded into 4 grade: Negative (Neg) = 1, Perinuclear (PN) = 2, Scattered (Sc) = 3, and Diffuse (Dif) = 4. The association of the stain characteristics, such as intensity and patterns, and clinicopathological factors, including Ki-67 labelling index and tumor subtypes, were assessed. In addition, the detailed intracellular localization of AP-1 was examined with double immunofluorescence microscopy using markers for the TGN and endosome. [Results] AP-1 intensity was associated with Ki-67 index ($p < 0.005$) and subtypes ($p < 0.0001$). Patients with high Ki-67 index showed significantly higher AP-1 intensity than those with low Ki-67 index ($p < 0.05$). Regarding the tumor subtypes, HER2 type ($p < 0.001$) and TNBC ($p < 0.05$) showed significantly higher AP-1 intensity than Luminal A. HER2 type also showed significantly higher AP-1 intensity than Luminal B ($p < 0.01$). In terms of the staining pattern, AP-1 distribution was also significantly associated with Ki-67 index ($p < 0.0001$) and subtype ($p < 0.0001$). The staining pattern grade of high Ki-67 index patients was significantly higher ($p < 0.0001$) than that of low Ki-67 index patients. Regarding the association with subtypes, the grades in Luminal B ($p < 0.0001$), HER2 type ($p < 0.0001$), and TNBC ($p < 0.005$) were significantly higher than that of Luminal A, and HER2 type also showed higher score than Luminal B ($p < 0.01$). In tumor cells with Sc pattern, AP-1 was mainly localized in EEA1-positive endosomes, but the localization in TGN was not apparent. [Conclusion] Although further confirmative studies are needed, these results suggest that the protein expression and the endosomal localization of AP-1 are likely related to the cellular proliferation activity in breast cancer tissues. Aberrant AP-1 distribution could be a predictive marker of the tumor growth potential.

Disclosure(s):

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P2-16-07

Overexpression of the alpha subunit of the epithelial sodium channel in MDAMB231 breast cancer cells reduces cell migration and proliferation

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Breast cancer is the most common cancer diagnosed in women worldwide and leads to 600,000+ deaths annually. The vast majority of breast cancer-related deaths are attributed to metastasis from the primary site in the breast to visceral organs or the brain. Therefore, understanding how these cells achieve metastasis is vital. Ion channels, such as the epithelial sodium channel (ENaC), are emerging as new targets for cancer research due to their role in regulating cell functions such as the process that allows cancer cells to undergo phenotypic changes necessary for metastasis. Ion channel dysregulation may be crucial in cancer development due to the ion channels' potential role in controlling cancer cell characteristics such as migration and proliferation. There is limited research investigating the role ENaC may have in breast cancer. We have shown that more migratory, mesenchymal breast cancer cell lines have reduced mRNA and protein expression of ENaC compared to more epithelial breast cancer cell lines. Importantly, higher expression levels of the pore-forming alpha-ENaC subunit is correlated with an increased breast cancer survival in patients (n=1705) included in the SCAN-B data set. Bioinformatic analysis, using the SCAN-B data set, showed an increase in the expression of alpha-ENaC mRNA correlated with lower expression levels of migration and proliferation markers, suggesting ENaC has a role in breast cancer cell proliferation and migration. Therefore, this research examines the influence of stably overexpressing the pore-forming subunit of ENaC, alpha-ENaC, in breast cancer cells on their cell migration and proliferation ability. We hypothesised that increasing the expression of ENaC will restore the cells to a more epithelial state, thus reducing cell migration and proliferation. MDAMB231 breast cancer cells were engineered via a stable transfection to overexpress alpha-ENaC or to express an empty vector control. Several clones were isolated and expanded and using RTqPCR, alpha-ENaC mRNA overexpression was confirmed to consistently have 200-fold

increased mRNA expression compared to control cells (n=9, p=0.0006). An increase in alpha-ENaC protein expression was also confirmed via western blotting. Using an EdU assay the alpha-ENaC overexpressing cells were shown to have a significant reduction in proliferation compared to the control cell line (n=3, p=0.0048). The alpha-ENaC overexpressing cells showed reduced migratory ability when examined in two established migration assays. In scratch wound assays, the alpha-ENaC overexpressing cells had a significant reduction in cell migration at 24 hours post scratch (n=4, p=0.0001). In Boyden chamber assays, the number of alpha-ENaC-overexpressing cells that migrated through the membrane was significantly reduced compared to the control cell line (n=4, p=0.02). Our results suggest that increased sodium entry into the cell through ENaC has a role in preventing the development of metastatic breast cancer cells, and highlights ENaC as a potential target for future breast cancer therapies.

Disclosure(s):

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7:00 AM - 8:15 AM

P2-16-09

Dual Specific Phosphatase-7 (DUSP7/PYST2) and its role in regulating vascular endothelial functions

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Dual Specific Phosphatase-7 (DUSP7/PYST2) and its role in regulating vascular endothelial functions Wenxiao Ji, Wen G. Jiang, Lin Ye, Tracey A. Martin CCMRC, Cardiff University School of Medicine, Cardiff, Wales, UK Introduction. Dual specific phosphatases (DUSPs) are a large family of enzyme able to trigger tyrosine phosphorylation, and phosphorylation of serine and/or threonine. This feature of a dual phosphorylation pattern by DUSPs, renders them with diverse roles in cells, from cytoskeletal regulation of cell migration, regulation of multiple kinases in cell signalling, to regulation of proteins such as microtubules and cell growth. We have investigated DUSP family members, in particular DUSP-7 (otherwise known as PYST2), identified from our studies as being one of prominent DUSPs found to be highly aberrant in certain cancer types including gastric cancer and pancreatic cancer. In breast cancer cells, DUSP7 has been reported as a potential factor linked to drug sensitivity. The role played by DUSP7 in vascular endothelial cells has been poorly studied. Here, we present our findings on the role of DUSP-7 in the regulation of biological functions of vascular endothelial cells.

Methods. Human vascular endothelial cells were used in the present study. Cell sub-models were created by knock down of DUSP7. The cells were evaluated for their biological response to loss of DUSP7, including proliferation, migration, matrix adhesion and response to downstream signalling. DUSP7 responses to various exogenous factors were also evaluated by a protein kinase platform. Results. Knock down of DUSP7 in human endothelial cells rendered them manifesting significantly reduced matrix adhesiveness ($p < 0.05$) and most strikingly, reduced cellular migration ($P < 0.0001$, control versus DUSP7 knock down). Interestingly, there was little change with the rate of cell growth. When cells were tested by inhibiting a tight junctional molecule, HAVcr1, the endothelial cells responded with markedly reduced DUSP7 (reduction of 46%). Likewise, the cells were also exhibited reduced levels of DUSP7 after being challenged by exogenous metastasis related Kisspeptin, indicating that DUSP7 may participated the wide network of signalling and functional regulations shared with the tight junction regulator HAVcr1 and possibly utilising Mitogen-activated protein kinase 3 (MAPK3 or Extracellular signal regulated kinase-1). Conclusion. Dual specific phosphatase-7 has an

important role to play in vascular endothelial cells, primarily on cell matrix adhesion and cellular migration. A possible route of regulation is by targeting the extracellular signalling network.

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Targeted CRISPR screen to identify synthetic lethal combinations between APOBEC3B and DNA repair

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APOBEC-catalyzed deamination of cytosine bases is the largest enzymatic and second largest overall source of mutation in cancer. One member from the APOBEC family of enzymes, APOBEC3B (A3B) is overexpressed and dysregulated in many different cancer types. In addition to hallmark C-to-T transitions and C-to-G transversions, APOBEC-catalyzed uracil lesions can be processed into single- and double-strand DNA breaks. Therefore, A3B-positive tumors are under continual stress to repair DNA breaks and may be vulnerable to DNA repair inhibition. Previous results from the Harris lab have identified UNG2, DNA uracil glycosylase 2 (UNG2), initiator of the base excision repair pathway, as synthetic lethal pair with A3B. The genetic disruption of UNG2 combined with high expression of A3B, causes cell death. This provides the rationale to hypothesize that also other DNA repair proteins could be putative synthetic lethal pairs with A3B, when its expression and activity are high. To test this hypothesis, CRISPR guide RNA library targeting 237 DNA damage repair and response genes was used in doxycycline-inducible TREX-293-A3Bi-eGFP cell line. Cells expressing or not A3B were harvested for DNA extraction and sequencing at different time points. Comparison of guide RNA abundance between doxycycline and H₂O treated cells revealed the dropout guides that disrupt genes and create putative synthetic lethal combinations with A3B. The screen design and overall results will be presented

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P2-17-02

SMC6 down-regulation: marker of genetic instability and poor outcome in breast cancer

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Genetic instability commonly found in tumors may be a consequence of imbalance in homologous recombination (HR), a mechanism of DNA double-strand break (DSB) repair dependent on the formation and resolution of Holliday junctions' structures for genomic stability maintenance. The SMC6 is involved in DSB repair. The SMC6 gene is structurally located very close to the GEN1 gene in a head-to-head organization sharing a bi-directional promoter, and the encoded protein is also involved in HR. Herein, we explored the association between SMC6 expression, genomic instability, and prognosis of breast cancer (BC). SMC6 and GEN1 expression and Copy Number Variation (CNV) data measured by qRT-PCR and CGH array, respectively, were assessed in 33 BC of women non-carrier BRCA1/BRCA2-mutations. The SMC6 protein expression was evaluated on a Tissue Microarray containing 74 BC samples classified as low (negative/weak) or high (moderate/strong) according to SMC6 nuclear staining. SMC6 and GEN1 expressions were directly correlated ($p=0.821$). Moreover, SMC6-low tumors tend to show higher CNV. Yet, the SMC6-low group presented poorer disease-free survival (DFS) than the SMC6 high group ($\log\text{-rank}=0.008$). Further, SMC6 expression broke the DFS ER+ cohort in groups of distinct prognoses ($\log\text{-rank}=0.029$). By in silico data analysis,

SMC6 downregulation was also associated with worse prognosis in some BC subtypes. Our findings point to a possible association between SMC6 down-regulation and BC poor outcomes, suggesting that SMC6 may serve as an indicator of tumor genetic instability for BC patients. Supported by Fapesp and CNPq.

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P2-17-03

Preclinical study of trastuzumab deruxtecan (T-Dxd; DS-8201a) in combination with DNA damage response pathway inhibitors in HER2-low/Hormone receptor negative breast cancer patient-derived xenograft models

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Background: Triple negative breast cancer (TNBC), defined by negative hormone receptor (HR) status and the lack of HER2 gene amplification, is a significant clinical challenge because of its aggressive clinical course and association with a poor prognosis. Recent studies demonstrated that approximately a third of TNBC has low expression of HER2, so called HER2-low TNBC, which could be targeted by the new generation HER2-directed antibody-drug conjugate (ADC). Trastuzumab deruxtecan (also known as T-Dxd, DS-8201a) is a novel HER2-directed ADC with a topoisomerase 1 inhibitor payload and a tetrapeptide-based cleavable linker, which has been FDA approved for patients with metastatic HER2-positive, or amplified breast cancer. T-Dxd has also shown to improve survival outcomes when compared to physicians' choice chemotherapy in patients with metastatic HR-negative/HER2-low breast cancer in the Phase 3 DESTINY-Breast04 trial. However, resistance is invariable. We hypothesize that small molecule inhibitors against DNA damage response (DDR) pathways could potentiate the DNA damaging effect of T-Dxd and improve its anti-tumor activity in HER2-low TNBC. Method: We conducted preclinical experiments to assess the anti-tumor activity of T-Dxd and each of the DDR pathway inhibitors, including the ATR inhibitor AZD6738, the ATM inhibitor AZD1390, and the PARP inhibitor olaparib, as well as the Wee 1 inhibitor AZD1775, either alone or in combination,

compared to the vehicle treatment, in a panel of HER2-low TNBC PDX models in vivo, as well as mechanistic studies using HER2-low TNBC cell lines in vitro. HER2-low was defined as 1+ or 2+ on HER2 immunohistochemistry. Results: Four HER2-low TNBC PDX models, including WHIM2 (TP53 mutated, basal-like), WHIM6 (TP53 WT, basal-like), WHIM12 (TP53, PIK3CA, and PTEN mutated, claudin-low), and WHIM30 (BRCA1 and TP53 mutated, basal-like), as well as a panel of 4 TNBC cell lines with variable HER2 expression were included in the study. We demonstrated that the addition of DDR pathway inhibitors to T-Dxd led to further tumor shrinkage and delayed tumor progression in HER2-low TNBC PDX models in vivo and induced synergistic anti-tumor effects in vitro. Enhanced DNA damaging effect and apoptosis induction were observed with combination therapies in vitro. Biomarker analysis on xenograft tumors harvested 3 days following treatment with either Vehicle, T-Dxd, olaparib, or T-Dxd plus olaparib in WHIM6, was also performed, which demonstrated that the addition of olaparib enhanced DNA damage (increased pH2AX), and promoted apoptosis (increased cleaved PARP). Further mechanistic studies in HER2-low TNBC cell lines demonstrated the formation of DNA topoisomerase 1 covalent complexes (Topolcc) following treatment with T-Dxd. Interestingly, while the formation of Topolcc was reduced with the addition of either ATR or ATM inhibitor, no reduction was observed with the addition of olaparib. Additionally, we observed that combination therapies reduced cell migration in vitro. The combination of olaparib with T-Dxd, in particular, reduced mammosphere formation and Epithelial Mesenchymal Transition (EMT) modulation markers, including SNAIL, SLUG and/or TWIST. Conclusion: Our study demonstrated that the combination of T-Dxd and DDR pathway inhibitors induced additive or synergistic anti-tumor effect in HER2-low TNBC. Our data from the studies of cell lines and PDX models provided preclinical rationale for the combination of T-Dxd and DDR pathway inhibitors in patients with HER2-low TNBC. The olaparib combination showed unique mechanistic characteristics compared with other DDR inhibitors, which are being further examined in additional HER2-low TNBC models.

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P2-17-04

Pharmacological inhibition of LY6K induced cell cycle arrest and DNA damage by disrupting the LY6K-Histone-Aurora B signaling axis

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Pharmacological inhibition of LY6K induced cell cycle arrest and DNA damage by disrupting the LY6K-Histone-Aurora B signaling axis Benson C. Selvanesan^{1,2}, Sheelu Varghese^{1,2}, Justyna Andrys⁵, Ricardo H. Arriaza⁶, Rahul Prakash⁶, Purushottam B Tiwari⁷, Cara Olsen⁸, Daniel Hupalo^{2,4}, Yuriy Gusev⁵, Megha N. Patel⁶, Sara Contente¹, Miloslav Sanda⁹, Aykut Uren⁷, Matthew D. Wilkerson^{3,4}, Clifton L. Dalgard^{3,4}, Linda S. Shimizu⁶, Maksymilian Chruszcz⁶, Tomasz Borowski⁵, Geeta Upadhyay^{1,3,7}. Affiliations 1 Department of Pathology, 2 Henry M. Jackson Foundation, 3 Murtha Cancer Center, 4 Department of Anatomy, Physiology, and Genetics 8 Department of Preventive Medicine and Biostatistics Uniformed Services University of the Health Sciences, Bethesda, MD, USA. 5 Jerzy Haber Institute of Catalysis and Surface Chemistry Polish Academy of Sciences, Cracow, Poland. 6 Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC, USA. 7 Department of Oncology, Georgetown University Medical Center, Washington, DC, USA. 9 Max Planck Institute for Heart and Lung Research, Ludwigstrasse, 43, 61231 Bad Nauheim, Germany. Correspond
Disclaimer The opinions expressed herein are those of the authors and are not necessarily representative of the official policies of the Uniformed Services University of the Health Sciences (USUHS), the Department of Defense (DOD), the United States Army/Navy/Air Force, the U.S. Government, or any other funding agencies Conflict of Interest None
Acknowledgments NIH, NCI, R01 CA227694. NIH, NCI, R21CA256424. DOD, USUHS, VPR-NFP-74-9824. Biomedical Instrumentation Center, USUHS. The American Genome Center, USUHS. Antibody Characterization Program, Clinical Proteomics Tumor Analysis Consortium (CPTAC), National Cancer Institute, National Institute of Health. The Polish Grid Infrastructure, Cracow, Poland. NIH P30CA51008 and 1S10OD019982-01 to Biacore Molecular Interaction Shared Resource (BMISR), Georgetown University. ABSTRACT Increased expression of LY6K is significantly associated with poor survival outcomes in many solid cancers, including triple-negative and estrogen receptor-positive breast, ovarian, gastric, head and neck, neuroblastoma, bladder, and lung cancers. Inhibition of LY6K signaling is an ideal therapeutic approach for cancer, since the LY6K protein is not involved in vital organ function. Previously, we identified the small molecule NSC243928 as a binder of LY6K using surface plasmon resonance screening and showed that its activity was dependent on LY6K expression in triple-negative breast cancer cells. Here, we demonstrate the structural basis of the molecular interaction of NSC243928 with LY6K protein and the subsequent inhibition of LY6K function in mitosis and cell division via Aurora B-histone pathway. We observed that LY6K interacts with phosphorylated histones and Aurora B kinases during mitosis and that this interaction was disrupted in the presence of NSC243928. Disruption of LY6K function in mitosis/cytokinesis leads to DNA damage, senescence, and apoptosis of cancer cells. We observed that NSC243928 led to increased binding of LY6K to phosphorylated gammaH2X at S139, which was dependent on NSC243928 interaction with LY6K on phenylalanine 79. Furthermore, we observed increased levels of phosphorylated gammaH2X at S139 and increased caspase-3 activation in the tumor isografts of 4T1 and E0771 mammary tumors treated with NSC243928.

These data reveal that LY6K is a novel cell cycle target for therapeutic development in triple-negative breast cancer and other solid cancers with high expression of LY6K, such as bladder cancer, head and neck, and lung cancer.

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**Matched Single-Cell RNA-seq and Single-Cell ATAC-seq of Male Breast Cancers
Nominate Salient Cancer-Specific Enhancers**

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Although male breast cancer accounts for less than 1% of all breast cancer cases, overall survival is worse for men compared to women. This is due, in part, to the older age of patients at the time of diagnosis and the increased presence of comorbidities in the male population. While male breast cancer presents with similarities to certain female breast cancers, the paucity of data available on male breast cancer makes it difficult to establish targeted therapies, and to date, most male breast cancers are treated according to the standards in place for female breast cancer. Thus, investigating the transcriptional and epigenetic landscape of male breast cancer with improved resolution is crucial for understanding the tumor heterogeneity of this rare cancer type and can lead to the discovery of new therapeutic targets. In this study, we present matched transcriptional (scRNA-seq) and epigenetic (scATAC-seq) profiles of two male breast cancer tumors at single-cell resolution. Using scRNA-seq, we determine differentially expressed genes between male and female breast cancer tumors, specifically in the malignant cell populations, and highlight several genes that may have therapeutic implications within male breast cancer. We then leverage the scATAC-seq data to link variation in chromatin accessibility to changes in gene expression and show that certain highly expressed genes in the tumor-epithelial cells of male breast tumors are linked to highly active enhancer elements that drive their expression. Finally, we examine transcription factor motifs in the tumor-epithelial regulatory regions of male breast cancer tumors to further investigate the regulatory logic of these cell types. Overall, this dataset exposes clinically relevant regulatory networks in male breast tumors, providing a useful resource to the field of breast oncology that expands on the current knowledge of male breast cancer genetics.

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Promoter hypomethylation associated upregulation of MEN1 mRNA expression and its correlation with pathological parameters in Indian breast cancer patients

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Background: Breast cancer in the recent years has accounted to be most frequently reported cancer across the globe. Nearly 11.7% of total cancer cases were of breast cancer and 6,84,996 deaths were reported in the year 2020. Multiple endocrine neoplasia type 1 gene that encodes for menin protein is known to be involved in numerous signaling pathways and is also reported to show its interactions with histone modifiers. MEN1 is frequently reported to be dysregulated in the cancer including neuroendocrine tumors, lung cancer and melanoma. However, the role of MEN1 in case of Breast cancer has not been well understood. Lifestyle, environmental conditions and ethnicity play crucial role in epigenetic modulation of gene expression. In the current scenario with high increase in number of cancer cases, there is need to develop more personalized course of treatment rather than generalized approach. Thus, discovery of new biomarkers will aid in designing better diagnostic and therapeutic strategy to treat cancer. Aims and Objective: In this study we aim to find MEN1 mRNA expression and its connection with the MEN1 promoter methylation in case of Indian breast cancer patients and to correlate our findings with the pathological parameters of the patients to understand the role of MEN1 gene in breast cancer progression. Material and methods: The ethical approval for the study was procured from Institutional ethical committee of AIIMS, New Delhi and Jamia Millia Islamia, New Delhi. The study comprises of 44 pair of Breast tissue samples including cancer

and adjacent normal tissue collected at department of surgical oncology AIIMS, New Delhi and were stored in RNA later and PBS at -80°C for RNA and DNA extraction respectively. DNA was extracted through PCI (Phenol-Chloroform-Isoamyl alcohol) method and was further confirmed by Agarose gel electrophoresis. TRIZOL method was used to extract RNA from tissue samples and was quantified using nanodrop. Moreover, cDNA synthesis was carried out using Verso cDNA synthesis kit. To investigate the MEN1 mRNA expression, RT-PCR was carried out with LightCycler96 SYBR Green I Master (Roche) using specific primers. To analyze the promoter methylation status of MEN1 promoter region, CT-conversion was done and MS-PCR was performed using Methylation and Unmethylation specific primers. Statistical analysis was done using Graph Pad and SPSS to correlate our findings with clinical parameters. Results: In our study we found 27 out of 44 patients to exhibit up-regulation of MEN1 mRNA in the breast cancer tissue as compared with the normal tissue. MEN1 promoter unmethylation was detected in 25 out of 44 cases, which revealed its significant correlation with the upregulated MEN1 gene. Further on correlation of our data with the clinical parameters, we found its significant association with the estrogen receptor status and age of menopause of the patients. Conclusion: Our results of the MEN1 mRNA expression study and its association with MEN1 promoter methylation in case of breast cancer suggests the tumorigenic role of MEN1 in breast cancer. Our findings thereby indicate the possible role of MEN1 gene in progression of the disease. Further study on large sample size will aid in better understanding the role of MEN1 gene in Breast carcinoma.

Disclosure(s):

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Characterization of fully human internalizing anti-HER2 monoclonal antibodies that compete with Trastuzumab for binding to HER2

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The human epidermal growth factor receptor (HER) family of receptors plays a significant role in the pathogenesis of several human cancers. Among them, HER2 is overexpressed in several cancers. In particular, overexpression with or without gene amplification occurs in 15-30% of breast cancers and this has both prognostic and predictive implications. HER2 overexpression and amplification is associated with shorter disease-free and overall survivals and with resistance to certain hormonal agents as well as increased risk of metastasis to the brain. Two types of treatment targeting HER2 biological activity have been developed: anti-Her2 monoclonal antibodies and small molecule tyrosine kinase inhibitors such as lapatinib and neratinib targeting HER2 and EGFR and Afatinib targeting all HER family members. Trastuzumab is a humanized anti-HER2 monoclonal antibody that binds to domain IV of HER2 extracellular segment and blocks its signaling. It is the first therapeutic antibody targeting Her2 overexpression approved by the FDA. It is administered in combination with standard of care chemotherapy. More recently, since it was shown that Trastuzumab was an internalizing antibody, two antibody drug conjugates using trastuzumab have been approved and used in the standard of care: Ado-Trastuzumab-Emtansine (Kadcyla) consisting of trastuzumab conjugated to the drug mertansine DM1 and fam-trastuzumab-deruxtecan-nhki (Enhertu). Enhertu is

another antibody drug conjugate using Trastuzumab to deliver a topoisomerase inhibitor deruxtecan. Our laboratory has been focused in developing fully human internalizing anti-Her2 antibodies that compete or not with trastuzumab for binding to Her2. These antibodies have been developed by immunizing fully human mice with recombinant Her2 protein. Human Ab producing Tc mice (TC-mAb mice) stably maintain a mouse-derived engineered chromosome containing the entire human Ig heavy and kappa chain loci in a mouse Ig knockout background. After production of hybridoma secreting fully human immunoglobulins, the screening process included inhibition of binding of trastuzumab to Her2 by enzyme linked immunoassay and by Octet epitope binning as well as internalization assay. Several internalizing antibodies with Kd ranging from 10⁻⁹ M to 10⁻¹² M were selected. They were stratified by their ability to compete or not with trastuzumab. They were further characterized for their ability to deliver a cytotoxic payload in Her2 overexpressing cells as well as for their efficacy to inhibit proliferation, signaling and migration of Her2 overexpressing breast cancer cells. Data related to these antibodies will be presented here. In conclusion, the use of fully human TC mice in our laboratory represents an attractive approach to develop fully human monoclonal antibodies to high value cancer targets that can by-pass the need for humanization and affinity maturation of antibodies.

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Androgen mediated signaling induces epithelial to mesenchymal transition phenotype in MDA-MB-453 breast cancer cells and human breast tumors

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Background: Epithelial-mesenchymal transition (EMT) phenotype is a complex process and plays a central role in tumor progression, aggression, invasion, metastasis, and resistance to therapy. Role of androgen receptor (AR) and androgens in inducing EMT has been well established in experimental systems of prostate cancer. AR is widely expressed in all subtypes of breast cancer (BC) and is considered to have context dependent role based on the steroid hormone microenvironment. Previous studies have shown AR as the only sex steroid receptor detectable in BC metastases and in metastatic lesion. We investigated the role of androgens in driving the EMT phenotype and association of AR induced genes with EMT in BC tumors using public dataset. Methods: We treated AR positive breast cancer cell line MDA-MB-453 with the androgen, dihydrotestosterone (DHT) followed by AR antagonist bicalutamide (Bic) and examined the expression levels of AR induced genes by quantitative real time PCR (qPCR) and AR induced protein GCDFP-15 by western blot. AR driven genes (SEC14L2, C1orf116, FKBP5, UGT2B11, UGT2B28, KCNMA1, PIP and ABCC11) were identified by bioinformatic pipeline using a systematic bioinformatic approach from public microarray data sets derived from AR positive breast cancer cell lines (S Rajarajan et al, SABCs 2021). Mesenchymal phenotype of the cell lines under DHT/ Bic was evaluated morphologically and expression levels of EMT markers (ZEB1, Slug, Vimentin) and E-cadherin was estimated by qPCR, western blot and

immunofluorescence. Migratory potential of the cell line under treatment was evaluated by wound healing assay and proliferation was examined by the MTT assay. Association of AR induced genes and levels of enzymes involved in intracrinial testosterone metabolism (SRD5A1 & SRD5A3) with EMT in breast tumors was evaluated using transcript data from METABRIC database. EMT scores were derived from previous publications (Byers et al, 2013, Mak et al, 2016) and correlation was tested with AR induced genes. Results: The MDAMB-453 cell line was treated with 10nM DHT for 72hrs and this increased the expression of AR downstream protein GCDP-15 by 31.47% ($p=0.022$) when compared to the control. Further, a significant increase in the expression levels of AR driven genes with a fold change >2 was observed in the DHT treated cells ($p < 0.05$). The expression of GCDP15 protein ($p=0.028$) and the AR downstream genes ($p < 0.05$) were significantly repressed upon treatment with bicalutamide. DHT treatment also showed a significant higher expression of EMT master regulator, SLUG (fold change >3 , $p=0.045$) and a wound healing assay showed a 22% increase in migration ($p=0.027$). The expression of SLUG was significantly repressed ($p=0.003$) and the migratory ability of the DHT treated cells reduced upon treatment with bicalutamide ($p=0.145$). We also observed a significant loss of E-cadherin protein (by 23.65%; $p=0.024$) with DHT treatment and this was completely reversed upon treatment with bicalutamide ($p=0.047$). No significant change in proliferation was observed among the different treatment conditions. A significant positive correlation was observed between AR induced genes and the EMT scores ($p < 0.05$). Expression level of SRD5A3 was also positively correlated with EMT score ($p=0.043$) and AR induced genes ($p < 0.05$), except SEC14L2. Conclusion: Androgen receptor plays an important role in the biology of breast cancer and is considered a useful marker for prognosis. However, antiandrogen therapies haven't seen the expected success in clinical trial settings. Our results support the controversial role played by AR in higher androgenic environment within breast cancer and warrant the consideration of the intratumoral levels of sex steroid hormones.

Disclosure(s):

Savitha Rajarajan, Ph.D scholar: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-20-01

Patient-derived triple-negative breast cancer organoids as a platform for glucocorticoid receptor-mediated mechanisms of immunotherapy response and resistance

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Background: In early-stage triple-negative breast cancer (TNBC), high glucocorticoid receptor (GR) expression correlates with worse relapse-free survival across TNBC subtypes, induces oncogenic gene expression and tumor cell survival, and potentiates anti-inflammatory or an anti-immunogenic phenotype. Immune checkpoint therapy has increased pathologic complete response rates in the neoadjuvant setting, however response to immunotherapy remains modest overall and the explanatory mechanisms for this phenomenon are incompletely understood. We sought a three-dimensional model of the TNBC immune microenvironment using patient-derived organoids (PDOs) that capture tumor heterogeneity, partially recapitulates tumor microenvironment, and can be established for longer-term in vitro/in-vivo translational study after exposure to immunotherapy. We hypothesize that during chemoimmunotherapy treatment of early-stage triple-negative breast cancer, high glucocorticoid receptor activity mediates an immunosuppressive phenotype and glucocorticoid receptor modulation can restore anti-tumor immunity. Methods and Results: We are successfully growing 5 PDOs out of 8 surgically resected samples tumors from patients with early-stage triple-negative breast cancer treated with chemotherapy vs. chemoimmunotherapy as per KEYNOTE-522.

Interrogation of complementary TNBC cell line data revealed that GR activation downregulates the expression of immune checkpoint genes (PD-L1, B7-H3, B7-H4), while GR knockdown or treatment with a selective GR modulator restores expression of these immune checkpoint genes. TNBC-intrinsic GR activation increases the proportion of regulatory T cells vs. CD8+ T cells. In a coculture system of TNBC spheroids and T cells, GR activation in TNBC results in decreased activated CD8+ CD137+ T cells and use of the selective GR modulator increases the proportion of activated CD8+ CD137+ T cells. Conclusions and Future Directions: In early-stage triple-negative breast cancer, GR activation downregulates expression of immune checkpoint genes and reduction of GR activity restores expression. In a coculture system that recapitulates T cell repertoire found in triple-negative breast cancer, tumor-intrinsic GR activation results in increased regulatory T cell population and reduction of GR activity increases activated CD8+ CD137+ T cells. Ongoing analyses of TNBC organoid-immune coculture systems modeling high GR states will be used to (i) define cooperativity amongst immune checkpoint proteins in costimulation vs. coinhibition of anti-tumor responses and (ii) define novel pairs of receptor-ligands amongst TNBC:CD8+ vs. TNBC:Treg vs. CD8+:Treg as discovery of potential new therapeutic targets.

Disclosure(s):

Christine Shiang, MD, PhD: No financial relationships to disclose

Candace Frerich, Ph.D.: No financial relationships to disclose

Ishrat Durdana, Masters of Science in Biomedical Engineering: No financial relationships to disclose

Cheryl Lewis, Ph.D.: No financial relationships to disclose

Lynda B. Bennett, Ph.D.: No financial relationships to disclose

Carlos Arteaga, MD: Arvinas: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Research Funding (Ongoing); MERCK: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); OrigiMed: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Research Funding (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing); TAIHO Oncology: Consulting Fees (e.g., advisory boards) (Ongoing); Takeda: Research Funding (Ongoing)

Suzanne D. Conzen, MD: BostonGene Corporation: Consulting Fees (e.g., advisory boards) (Ongoing); Corcept Therapeutics: Receipt of Intellectual Property Rights / Patent Holder (Ongoing)

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7:00 AM - 8:15 AM

P2-20-02

Enrichment of atypical memory double negative (CD27— IgD—) tumour infiltrating B cells following neoadjuvant chemotherapy for early-stage breast cancer

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Background: Humoral immune responses have previously been associated with improved outcomes, with B cell infiltrates able to independently predict pathologic complete response to neoadjuvant chemotherapy (NACT). B cells represent a diverse population of cells and the complex interplay between specific B cell subsets in the context of chemotherapy treated breast cancers remains unclear. Here, we investigate the dynamic changes in the B cell immune landscape before and after NACT treatment across different breast cancer subtypes. Methods: Treatment naïve, mid-treatment and post-NACT breast tumour tissue samples were dissociated into single cells, stained with two panels of B cell-specific antibodies recognising a total of 24 target proteins, and analysed by flow cytometry. In addition, PMBC before and after NACT were also profiled. B cell subsets were classified as either naïve (CD27—IgD+), class-switched memory (CD27+IgD—), unswitched memory (CD27+IgD+) or double negative (DN)(CD27—IgD—). DN B cells were further characterised into DN1 (CXCR5+CD21+) and DN2 (CXCR5—CD21—) subsets. In vitro co-cultures of breast cancer cell line spheroid and PBMC were carried out. Results: In both treatment naïve and chemotherapy treated samples, we observed a significant expansion in the DN B cell population within the TME compared to the periphery. DN B cells represented on average 40.96% of B cells in treatment naïve tumours vs 9.48% in PBMCs ($p < 0.0001$), and 71.80% vs 6.34% of B cells in post-NACT tumour vs PBMC samples respectively ($p < 0.05$). Interestingly, in treatment naïve PBMC and tumour tissue samples, the largest proportion of the DN subset consisted of DN1 cells, 69.35% and 64.11% respectively. In contrast, following NACT, DN2 cells constituted the majority of the DN population both within the TME (86.30%) and in the periphery (50.44%). Although the specific functions of these B cell subsets remain unclassified, deeper phenotyping suggests DN1 cells more closely resemble the phenotype of class-switched memory cells, whilst DN2 cells are thought to have antibody-secreting properties and more closely resemble the plasmablast phenotype. scRNA sequencing

of B cells pre- and post NACT is currently underway. Conclusion: To our knowledge, this work is the first to identify an expanded population of DN B cells in breast tumour tissue and highlights the requirement for further investigation into these cells to decipher their role in the context of chemotherapy treatment and resistance in breast cancer.

Disclosure(s):

Esme Carpenter, MRes: No financial relationships to disclose

Thanussuyah Alaguthurai, MSc: No financial relationships to disclose

Farhana Hossain, BSc: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-20-03

Combination Therapy with an Anti-GD2 Antibody, Transforming Growth Factor Beta Imprinted Natural Killer Cells and Gemcitabine Improve Tumor Control and Survival in a Triple Negative Breast Cancer Model

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Background: Intrinsic resistance to immunotherapy observed in breast cancer is attributed to low neoantigen levels, defective antigen presentation, low mutational burden, reduced programmed death ligand (PD-L1) expression and the presence of immunosuppressive signals like transforming growth factor-beta (TGF β) in the tumor microenvironment (TME). These collectively attenuate the effector functions of T cells and natural killer cells (NK cells). NK cells are an important component of innate immunity. While generally TGF β dampens the NK cell response in the breast cancer TME, chronic stimulation in vivo with TGF β during the expansion process of donor NK cells produces TGF β imprinted NK cells which exhibit high cytotoxicity and resistance to suppression by TGF β due to down regulation of SMAD3 and hypersecretion of interferon gamma and tumor necrosis factor alpha. NK cell activation also promotes antibody dependent cellular cytotoxicity (ADCC) and augments monoclonal antibody directed killing. GD2 is a disialoganglioside and a tumor-associated antigen with limited expression in healthy tissues and overexpression in a variety of cancers, including breast cancer. Up to 60% of high grade breast cancers have GD2 expression with higher expression linked to worse overall survival. Given GD2 expression in aggressive BC subtypes and the role of NK cells in ADCC and antigen presentation, there is a strong rationale for evaluating an anti-GD2 antibody along with NK cells in the immunosuppressive breast TME. Based upon established preclinical data, we hypothesized that combining (1) an IgG1 anti-GD2 monoclonal antibody (anti-GD2), (2) TGF β imprinted, IL-21 expanded allogenic universal donor NK cells (TGF β iNK) and (3) the

standard chemotherapy agent gemcitabine (gem) which has immunomodulatory effects including improved NK cell function, will improve tumor control and survival in a TNBC mouse model. Methods: First, we evaluated if anti-GD2 treatment would increase ADCC against MD-MBA-231 tumor cells. To do this, tumor cells with or without anti-GD2 were cocultured with TGFβiNK + anti-GD2 and evaluated by real time cell analysis (RTCA). Next we evaluated the effect of gem on both tumor and immune cells. Finally to evaluate the effect of our novel combination therapy, female NSG mice were injected with 1x10e6 MDA-MB-231 cells into the mammary fat on day 0 and tumor burden was followed for 83 days. On day 21, mice were divided into 4 groups: control, gem only (standard of care), TGFβiNK+anti-GD2 (NK-GD2), and gem+TGFβiNK+anti-GD2 (G-NK-GD2) and tumor growth was measured weekly. Mice were observed for toxicity and bioluminescence evaluation for NK cells were performed prior to each cycle. Results: RTCA data confirmed anti-GD2 treatment increased ADCC mediated cell lysis by TGFβiNK. Furthermore, at clinically relevant doses, gem did not alter GD2 expression by flow cytometry on MDA-MB-231 tumor cells but induced MICA expression which suggests potential improved NK cell activity. In the mouse model, monitoring of mouse weights showed greater weight stability in the G-NK-GD2 group, suggesting a tolerable regimen. Serial measurement of tumors showed a significant reduction in tumor growth in NK-GD2 and G-NK-GD2 arms when compared to Gem or control. Additionally, mice who received G-NK-GD2 or NK-GD2 had significantly improved survival. Histological evaluation and immune assessment of the mice are ongoing. Conclusion: Our data showed no significant toxicities in the murine model and improved efficacy of G-NK-GD2 over the standard of care gemcitabine. Our preclinical data supports moving forward with a phase 1b/2 Bench-To-Bedside clinical trial, that will evaluate this combination in patients with aggressive subtypes of metastatic breast cancer where there is a great clinical need for effective treatments.

Disclosure(s):

Marcelo Pereira, PhD: Kiadis Pharma: Royalty (Ongoing); Merck, Fate Therapeutics, Sorrento Therapeutics, Moderna: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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12/7/2022

7:00 AM - 8:15 AM

P2-20-04

Vaccination against HIF1 α /c-MET peptides overcome lapatinib resistance and inhibits tumor growth by immunomodulating in HER2 positive breast cancer.

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Human Epidermal growth factor Receptor 2 (HER2) is overexpressed in 20% to 30% of breast cancers and is associated with poor prognosis. Patients with advanced HER2-type breast cancer are treated with HER2-directed tyrosine kinase inhibitors as well as antibodies, but many patients finally acquire therapeutic resistance. Therefore, it is important to develop new treatment strategies that circumvent HER2 positive resistant breast cancer. Among the suggested mechanisms of resistance to HER2-targeted therapeutics, tumor hypoxia and relevant biological factors are known as important players. In this study, we aimed to explore the role of tumor hypoxia in the development of resistance to HER2-targeted therapeutics, and whether the role of an immunological therapy targeting this could contribute to overcoming resistance. To this end, we established lapatinib-resistant HER2 positive breast cancer cells in vitro (SKBR3, BT-474 for human and MMC for murine cells). First, we examined if lapatinib-sensitivity is different according to oxygen concentration using lapatinib-resistant cell lines (LR-SKBT3, LR-BT-474, LR-MMC) compared with parent cell lines. Resistant cells were resistant both in normoxic and hypoxic conditions, but parent cells were highly sensitive in both of the oxygen concentration. In the Western blot analysis, HIF1 α and c-MET were overexpressed in the resistant cells compared with parent cell lines in both normoxic and hypoxic condition. Interestingly, treatment with lapatinib had reduced HIF1 α and c-MET expression at normoxia in parent cell lines but not in resistant cell lines. Under the hypoxic conditions, the difference in expression of HIF1 α and c-MET was more pronounced between parent cell lines and resistant cell lines treated with lapatinib. These results indicate that the expression of HIF1 α and c-MET was involved in lapatinib-resistant. In a previous study, we have identified epitopes from HIF1 α /c-MET and demonstrated effect of delayed bone metastasis in triple negative breast cancer model when used as peptide vaccine. Herein, we evaluated whether the immunization using HIF1 α /c-MET peptide vaccine is effective in inhibition of lapatinib-resistant HER2 positive breast cancer growth in vivo. MMTVneu-transgenic mouse model was used and 6- 8 weeks old mice were injected with LR-MMC subcutaneously. Immunization using the HIF1 α /c-MET

peptide vaccine significantly inhibited growth of LR-MMC cells in MMTVneu-transgenic mice compared with controls. HIF1 α /c-MET specific IFN- γ -secreting T cell responses in the splenocytes were significantly higher in the immunized group than controls. Immunohistochemical staining of T cells revealed that expression of tumor HIF1 α and c-MET was significantly decreased, while the number of CD8+ T cell was increased in the tumors from immunized animals compared with control tumors. In conclusion, our study demonstrated that the vaccine targeting HIF1 α /c-MET might be a promising cancer immunotherapy in lapatinib-resistant HER2 positive breast cancer. In vivo study to evaluate efficacy of combination therapy (lapatinib and HIF1 α /c-MET vaccine) is ongoing.

Disclosure(s):

Ji Min Lee, n/a: No financial relationships to disclose

Jin Hwa Hong, n/a: No financial relationships to disclose

Soon Young Lim, n/a: No financial relationships to disclose

Ju Won Kim, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-20-05

Personalized tumor vaccine can suppress tumor growth and metastasis in the syngeneic mouse breast cancer model

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Objective Immunotherapy using the tumor-specific antigens (TSAs) is a promising strategy in breast cancer. Studies have suggested that the in vivo exposures to certain tumors can induce adaptive anti-tumor immunity in syngeneic tumor models. In this study, we show the efficacy of the tumor lysate vaccine and peptide-based vaccine against tumor neoantigen in suppressing tumor growth and metastasis in 4T1 syngeneic tumor models. Method We used BALB/c mice and its syngeneic tumor cell lines to evaluate the anti-tumor effect induced by the transient exposure to the tumor cells. For tumor vaccines, we synthesized the tumor lysate vaccine by the freeze-thaw method or synthetic peptide against the selected tumor neoantigens identified by exome sequencing. We systemic and local immune remodeling was investigated by using immunohistochemistry, flow cytometry, and single cell RNA sequencing. Results We observed a significant reduction of tumor growth and metastasis in 4T1 syngeneic tumors when the mice were previously exposed to the same cells (pre-exposure group). This anti-tumor effect induced by the exposures to the tumor was cell line-specific. The 4T1 tumor lysate vaccines administered prior to the tumor cell injection also showed significant inhibitory effect on tumor

growth and metastasis. T lymphocytes, isolated from the tumor tissues of the 4T1 pre-exposure mice and lysate vaccine-treated mice, showed higher levels of TNF- α and IFN- γ when compared to the control those from the control tumors. The lysate vaccine treatment resulted in a substantial remodeling of tumor microenvironment including reduction of myeloid-derived suppressor cells and M2 tumor-associated macrophages. On the other hand, the numbers of M1 tumor-associated macrophages and effector memory CD8+ T cells were increased by the lysate vaccine. While the peptide vaccine showed no inhibitory effect on the primary tumor growth, it also suppressed spontaneous lung metastasis. Finally, we administered lysate tumor vaccine after the tumor establishment to determine the therapeutic effect. The lysate vaccine significantly suppressed the tumor growth and lung metastasis of the syngeneic 4T1 tumors. Conclusion Tumor lysate vaccine can suppress the tumor growth and metastasis in the 4T1 syngeneic mouse models by inducing substantial remodeling of tumor immune microenvironment. Additionally, tumor lysate vaccine can elicit similar anti-tumor immune response when administered after the establishment of the primary tumor suggesting a potential therapeutic value.

Disclosure(s):

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7:00 AM - 8:15 AM

P2-20-06

Anti-B7-H3 Antibody (T-1A5) Blocks Immunomodulatory Function of B7-H3 and Enhances NK and T Cell–Mediated Cytotoxicity against Breast Cancer Cells

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One of the main factors contributing to breast cancer (BC) initiation and metastasis is immune suppression by tumor cells. Immune checkpoint blockade has recently been shown to overcome tumor-induced immune suppression, but a significant proportion of patients do not respond, implying that more effective cancer immunotherapies are required. B7-H3 belongs to B7 family of immune checkpoint proteins that is overexpressed in various human malignancies. Here, we hypothesize that blocking B7-H3 using monoclonal antibodies (mAbs) enhances immune cell proliferation and function. To test our hypothesis, B7-H3 expression was determined using RNA-seq data from primary and metastatic breast tumors, and adjacent normal tissues, from the TCGA and METABRIC databases. To assess B7-H3 protein expression in BC, we performed immunohistochemistry (IHC) on frozen primary tumor tissues (n=50) and adjacent normal tissues (n=23) from TNBC patients. In addition, to investigate the immunomodulatory effect of B7-H3 in BC, we performed IHC for T-cell markers in subsets of patient tissues with high and low levels of B7-H3 expression. Next, we assessed B7-H3 expression in over 13 BC cell lines, including TNBC and ER+, PR+, and HER2+ cell lines, as well as TNBC PDX-derived cells. Moreover, to determine the effect of B7-H3 knockdown on NK- and T-cell activity, we co-cultured control and B7H3-KD BC cells in the presence and absence of NK and T cells and measured the induction of apoptosis in BC cells through IncuCyte live-cell imaging system. The effect of a novel B7H3-blocking mAb (clone T-1A5, isotype IgG1) on NK-cell and T-cell-mediated cytotoxicity in BC cell lines was examined using live-cell imaging. In the TCGA and METABRIC databases, B7-H3 was found to be significantly overexpressed ($P < 0.0001$) in tumor tissues than in adjacent normal tissues of BC patients. A survival analysis by the log-rank test indicated that patients with B7-H3^{high} tumors had significantly lower progression-free ($P=0.01$) and relapse-free ($P=0.0026$) survival than patients with B7-H3^{low} tumors. Moreover, B7-H3 is significantly upregulated in all the BC subtypes including basal, luminal A, luminal B and Her2-enriched with highest expression in basal type BC. Relative mRNA quantification and flow cytometry analysis demonstrated strong B7-H3 expression in most of the BC cell lines including TNBC and ER+, PR+, and HER2+ cell lines, as well as TNBC PDX-derived cells. Furthermore, IHC analysis revealed that compared to the matched normal tissue, B7-H3 expression was substantially higher in tumor tissue ($N=16$, $P < 0.001$). Also, patients with high B7-H3 expression had significantly lower numbers of CD3+, CD4+, and CD8+ T-cell, compared to patients with low B7-H3 expression ($P < 0.001$), indicating immunosuppressive role of B7-H3. Furthermore, NK cell and T cell mediated killing was significantly higher in B7H3-KD BC cell lines compared to control cells. We observed a significant increase in the killing of BC cells by NK cells and T cells in the presence of anti-

B7H3 mAb T-1A5 in a concentration dependent manner ($P < 0.001$), suggesting that anti-B7H3 antibodies suppress the immunomodulatory function of B7-H3 and enhance NK and T cell-mediated ADCC in BC. To determine the antibody-dependent cell-mediated cytotoxicity, we developed a human-mouse chimera of T-1A5 (chT-1A5) and tested in combination with NK cells. Interestingly, we found a concentration and time dependent increase in ADCC in BC cells in the presence of chT-1A5 antibody. Our data suggests that B7-H3 is overexpressed in primary BC and inhibits immune-cell infiltration. Moreover, blocking the immunomodulatory functions of B7-H3 using anti-B7H3 antibody T-1A5 enhances NK and T cell-mediated killing of BC cells.

Disclosure(s):

Vivek Anand, PhD: No financial relationships to disclose

Anudishi Tyagi, PhD: No financial relationships to disclose

Venkata Lokesh Battula, PhD: Daiichi Sankyo: Contracted Research (Ongoing); Nektar Therapeutics: Contracted Research (Terminated, April 15, 2022); Y-mAbs Therapeutics: Contracted Research (Ongoing)

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7:00 AM - 8:15 AM

P2-20-07

Immunotherapy becomes a treatment option in cryoablated Luminal A breast cancers

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Background: Most breast cancers are not inherently immunogenic, and as a result are difficult to treat with immunotherapy. However, recent research has shown that triple-negative breast cancer (TNBC) and HER-2 positive (HER2) breast cancers can stimulate some level of an immune response. In contrast, the most common form of breast cancer, the luminal A (hormone receptor-positive (HR+)/HER-2 negative), has shown low involvement of tumor-infiltrating lymphocytes (TILs) and low expression of immune checkpoint inhibitors specifically programmed death-ligand-1 (PD-L1). Cryoablation, the destruction of cells using ultra-low temperatures, has been used as a primary treatment method for benign breast tumors and is in clinical trials to evaluate its use for invasive breast cancer. A secondary effect of cryoablation is the release of cellular proteins that can function as neoantigens and are in their native folded state. We hypothesize that release of these native neoantigens might trigger an immune response capable of preventing/reducing metastasis and local relapse. In this pilot study, we evaluated biopsy material, cryoablated specimens and sentinel lymph nodes (SLN) from patients enrolled in the ACOSOG Z1072 trial at Lankenau Medical Center (LMC) [N=18] with cancers < 2 cm. Responses were compared to patients treated with surgical resection. Methods: After obtaining IRB approval for retrospective analyses of specimens from the ACOSOG Z1072 trial, these samples were evaluated with immunohistochemistry (IHC) using commercially available antibodies and standard techniques to determine changes in CD4, CD8, CD20, CD21, CD1c levels, as well as the immune checkpoint regulators PD-1, PD-L1 and CTLA-4, and the immune modulator IDO1. Patient samples included biopsy, surgical material,

and SLN collected from the patients and were compared with patients of similar age, tumor characteristics and time to surgery. Per the ACOSOG trial protocol, tumors had to be surgically removed within 28 days of cryoablation, but the exact time was left to the surgeon's discretion. Participating surgeons at LMC preferred to remove tumors on average 24.7 days after ablation resulting in an average time from diagnosis to surgical removal of 43.3 days. Results: Cryoablation of the tumors resulted in coagulative necrosis presenting as a gelatinous mass surrounded by a fibrous capsule. The ACOSOG trial demonstrated effective cryoablation-induced destruction of ER+ invasive ductal carcinoma lesions in 92% of patients (N=86). On IHC staining of the cryoablated samples, more CD8+ lymphocytes were identified compared to CD4+, which was consistent with pattern among non-cryoablated tumors, albeit to a lesser degree. Though no difference in percentage of PD-1 positive cells were observed between treatment modalities, positive cells in cryoablated tumors had mostly moderate-to-strong staining. We observed a 20% increase in cells positive for PD-L1 after cryoablation with predominantly strong staining. Though IDO1 had fewer positive cells in the tumor mass, the expression in SLN was higher with nearly all cells exhibiting strong staining. Compared to the patients who were treated with surgery alone, the SLNs of cryo patients had higher levels of CD20+ B cells as well as CD21+ follicular dendritic cells. CTLA-4 was seen sporadically, but with a slight preference for the surgery patients. Conclusion: We show that cryoablation of breast cancer lesions in vivo can induce an immune response in HR+ tumors, turning an immunogenically cold tumor into an immunogenically hot, tumor potentially responsive to check-point inhibitors and immune modulators. Possibly providing less toxic treatment options for elderly patients and/or patients with comorbidities All local cryo patients in the clinical trial are currently disease-free (F/U 5 - 13years), while 1 surgical patient is alive with late recurrence (11 years post-surgery).

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P2-20-08

Expression of ACVRL1 in a subset of recruited tumor-associated macrophages drives resistance to PD-1 therapy in human breast cancer.

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The activin-like kinase receptor 1 (ALK1, encoded by ACVRL1) is a member of the transforming growth factor β (TGF- β) superfamily. Expression of ALK1 has been historically associated with endothelial cells, thus serving as a potential target for antiangiogenic therapy in cancer. Despite promising preclinical results with a ligand trap (RAP-041/dalantercept), clinical trials did not show additional benefit of dalantercept when combined or contrasted with the standard of care.

This outcome raises the question about patient selection and optimal combination partner in the clinical setting. Moreover, from the biological perspective, how ALK1 signaling shapes the features of a tumor is still largely uncharted. Based on our previous observations, we confirmed that the genetic network correlated with ACVRL1 expression is associated with immune processes in human breast cancer. Next, we validated that inhibition of ALK1 altered the immune landscape in experimental primary breast cancer (MMTV-PyMT model), providing a rationale for a combined regimen with immunotherapy. After developing and validating a murine model of adjuvant therapy with RAP-041 (syngeneic E0771 and 4T1 cell lines), we discovered that ALK1 blockade potentiated immune checkpoint inhibitors. Based on bulk RNA-sequencing and a multicolor FACS approach, addition of RAP-041 to immunotherapy significantly reduced the number of intratumoral macrophages compared with either treatment alone. Notably, these changes were coupled with systemic alterations in peripheral blood cell composition, with the combined administration suppressing circulating monocytes. Interestingly, ALK1 signaling appears to be a pivotal contributor to this phenotype, as fewer circulating monocytes were also detected in the RAP-041 cohort. Based on our in vitro characterization, we revealed that ALK1 expression is not limited to endothelial cells, as different myeloid populations readily expressed *Acvrl1*, suggesting a direct functional role of ALK1. Stimulation of ALK1 did not alter macrophage polarization, even though different levels of mediators downstream of ALK1 characterized the M1/M2 states. Furthermore, apoptosis and necrosis did not seem to be affected upon activation of ALK1, while the effect on the cell cycle awaits confirmation. In vitro genetic modulation of ALK1 activity is ongoing, with co-culture systems, transendothelial adhesion and migration being currently assessed. Inspection of several human sc-RNA-sequencing datasets confirmed the existence of ACVRL1-positive monocytes in human PBMCs from healthy individuals as well as in human solid cancers, including breast cancer. Focusing on the immune compartment, ACVRL1 expression characterized recruited tumor-associated macrophages (TAMs) and their cycling counterpart. In light of this feature, longitudinal follow-up of patients exposed to chemotherapy and/or anti-PD-1/PD-L1 revealed that expression of ACVRL1 decreased following exposure to chemotherapy. Notably, high ACVRL1 expression and an increased proportion of ACVRL1-positive TAMs were found at progression with anti-PD-1 treatment. In agreement with our preclinical data, ACVRL1-positive cells were depleted from circulation upon recurrence, indicating a migration from blood to tumors. Finally, survival analysis determined that ACVRL1^{hi} signature in macrophages correlated with a significantly lower survival in a 5-year follow-up in breast cancer. In conclusion, our work sheds light on the value of ALK1 as a promising dual antiangiogenic and immunomodulatory target for precision medicine in cancer.

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12/7/2022

7:00 AM - 8:15 AM

P2-20-09

Enhancement of anti-tumor immunity in ER+ breast cancer through dual inhibition of MCL1 and caspases.

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Breast cancer is one of the most commonly diagnosed cancer types and a leading cause of cancer death in women in the United States. However, it is difficult to treat with immunotherapy because of its immunological “cold” status. This underscores the importance of a novel clinical approach to increase efficacy of immunotherapy including acute upregulation of Type I Interferon (IFN) response. One strategy to enhance Type I IFN response is by release of damage-associated molecular patterns (DAMPs) from mitochondria, including mitochondrial DNA, RNA and oxidized proteins that are recognized by pattern recognition receptors (PRRs) in cytoplasm and activate downstream IFN signaling. Because many cancers including breast cancer experience increased and dysregulated mitochondrial biogenesis at baseline, they contain significantly higher levels of DAMPs compared to normal cells, but these substrates are sequestered in mitochondria and not accessible to PRRs. We set out to develop a strategy to exploit increased levels of DAMPs in cancer cell mitochondria to enhance Type I IFN response. While DAMPs are released from mitochondria upon apoptosis caused by mitochondrial outer membrane permeabilization (MOMP), Type I IFN response is still silenced due to cleavage of PRRs by activated caspases. One way to induce MOMP is by inhibition of Myeloid Cell Leukemia-1 (Mcl-1), an anti-apoptotic family protein that is frequently upregulated in breast cancer. Interestingly, breast cancer cell lines showed the highest dependency on Mcl-1 among solid cancers and inhibitors of Mcl-1 have shown efficacy in breast cancer early clinical trials. Based on our preliminary observations showing that Mcl-1 inhibition activates a robust Type I IFN response in MCF7 breast cancer cells deficient for caspase 3, we hypothesized that combining Mcl-1 inhibitors with caspase inhibitors would greatly enhance Type I IFN response in a robust and specific manner by facilitating release of DAMPs into the cytoplasm while preventing inactivation of PRRs. Strikingly, in contrast with Mcl-1 inhibitor treatment alone, combination treatment led to dramatic increase in expression levels of IFN- β and interferon-stimulated genes (ISGs) in MCF7 and ZR-75-1 ER+ breast cancer cell lines with minimal effects on cytotoxicity. In addition, T47d, a breast cancer line highly resistant to Mcl-1 inhibition due to compensation by other Bcl-2 family proteins, showed greatly enhanced Type I IFN response upon combined Mcl-1, Bcl-2 and caspase inhibition. Because reduced expression of MHC class I molecules on cell surface is one of the most important immune escape mechanisms in tumors including breast cancer, we examined whether the proposed combinatorial treatment would overcome this by enhancing expression of MHC class I. Immunofluorescence (IF) staining confirmed that the combination treatment dramatically increased total HLA-ABC protein expression on plasma membrane of ZR-75-1. Furthermore, combinatorial treatment upregulated transcription of most genes responsible for antigen presentation, a multistep process consisting of antigen peptide generation and loading of MHC class I molecules. Lastly, we sought to examine how elevated chemokine expression may impact patients with breast cancer. We examined association of cytokines highly upregulated by the combination treatment with immune cell infiltration using a TCGA dataset that included

over a thousand breast cancer samples. This analysis was performed by xCell algorithm and demonstrated strong association of that cytokine expression with CD8+ T, B and DC infiltrate. Our results demonstrate that the combination of Mcl-1 and caspase inhibitors greatly enhances Type I IFN response and may improve anti-tumor immunity. We plan to further test this drug combination in immunocompetent mouse models, laying the foundation for a clinical trial assessing the combination treatment in patients with metastatic ER+ breast cancer.

Disclosure(s):

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P2-20-10

Prognostic impact of lymphocyte-Activation Gene-3 (LAG-3) expression in triple negative breast cancer

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Introduction Recent advances in breast cancer treatment strategies have improved survival outcomes in metastatic breast cancer (mBC). Targeting immune checkpoint, especially programmed death 1 (PD-1)/programmed death ligand 1 (PD-L1), has made a breakthrough in treating advanced malignancies including breast cancer. Immune checkpoint inhibitors (ICIs), such as pembrolizumab and atezolizumab, in combination with chemotherapy have prolonged survival outcomes in mBC with triple negative subtype. However, the low response rate and resistance of ICIs with anti-PD 1/PDL-1 antibodies is a major limitation and a challenge. Lymphocyte Activation Gene-3 (LAG3; CD223) is a potential cancer immunotherapeutic target due to its negative regulatory role on T cells and cytokines, thereby ensuring immune homeostasis. Several studies suggested that combination immunotherapy of anti-LAG-3 and anti-PD-1 has shown promising efficacy in fighting PD-1 resistance. Therefore, we evaluated the prognostic role of LAG3 in metastatic TNBC (mTNBC) treated with ICIs to figure out resistance mechanism of ICIs. **Methods** mTNBC patients with available archival tumor tissues, who has received ICIs in Samsung Medical Center, were enrolled in this study. For the evaluation of LAG3 expression in tumor microenvironment, Vectra Polaris Multispectral Imaging and Whole Slide Scanning technique (PerkinElmer, Inc. Hopkinton, MA) was used. **Results** In total, 64 mTNBC patients were treated with ICI's with or without cytotoxic chemotherapy between 2019.02- 2021.11. Of 70 mTNBC patients, 41 patients had archival tissues and finally 40 patients were included in this study. Median age was 43.0 years of age (range: 24.5 ~ 64.5). Recurrent mTNBC was 92.5% and only 7.5% was de novo mTNBC. Geremline BRCA1 pathogenic variants were detected in 4 (10.0%) patients. Among 37 recurrent mTNBC patients, 72.5% were treated with neoadjuvant chemotherapy with anthracycline (97.3%) and taxane(97.3%). Among ICI's, 52.5% were treated with pembrolizumab and 47.5% of

atezolizumab. LAG3 expression varies among mTNBC tissues (median cell density: 366, range: 48, 2861 cells/mm²). Among cells expressing LAG3, LAG3 was expressed more in CK+ cells compared with CK- cells (median:150 (20, 2503) cells/mm² in CK+ cells, median: 88 (2, 806) cells/mm² in CK- cells, p=0.005). Patients with high LAG3 expression in CK+ cells showed short progression free survival(PFS) compared to those with low LAG3 expression in CK+ cells (median PFS of high vs. low LAG3 expression [months]:1.9 vs. 4.2, p=0.01). On the contrary, patients with high LAG3 expression in CK- cells had 9.1 months of PFS compared to 3.1 months of PFS in patients with low LAG3 expression in CK- cells (p=0.10). In addition, patients with high LAG3 in CK- cells had longer overall survival(OS) compared to those with low LAG3 expression in CK- cells (median OS of high vs. low LAG3 expression [months]: not reached, 15.7, p=0.05). Conclusion LAG3 expression was associated with PFS in patients with mTNBC treated with ICI's independent of PDL-1 expression. And the prognostic significance of LAG3 expression was different between CK+ cells and CK- cells. These findings need to be proved in large scale clinical trials.

Disclosure(s):

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Jeehyun Kim, n/a: No financial relationships to disclose

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Yeon Hee Park, MD, PhD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Invited speaker (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Dong-A ST: Contracted Research (Ongoing); Everest Medicine: Principal Investigator (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Menarini: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Invited speaker (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Invited speaker (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Invited speaker (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Invited speaker (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing)

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7:00 AM - 8:15 AM

P2-20-11

Progesterone impacts the growth and immune cell infiltration of murine mammary gland tumors

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Clinical studies have linked usage of progestins (synthetic progesterone) to breast cancer risk. However, little is understood regarding the role of native progesterone (P4), signaling through the progesterone receptor (PR), in breast tumor formation. Recently, we demonstrated that P4 treatment or PR overexpression can drive changes in immune cell populations in the murine mammary gland and that PR overexpression leads to increased development of mammary gland tumors in mice. Given these findings, we sought to investigate whether P4 impacts tumor growth and immune cell infiltration of mammary gland tumors. We utilized syngeneic mammary gland tumor models to evaluate the effect of P4 on PR+ mammary gland tumor growth, which

revealed that P4 promoted tumor growth and impacted immune cell infiltration of PR+ mammary gland tumors. Of note, numbers of tumor-infiltrating dendritic cells were decreased and exhausted T cells and regulatory T cells were increased with P4 treatment in PR+ tumors. To determine if anti-progestin therapies could reverse the growth-promoting effect of P4 on mammary gland tumors, mice bearing PR+ mammary gland tumors were treated with the anti-progestin onapristone. Onapristone treatment led to significantly decreased tumor volumes in two syngeneic mammary gland tumor models and reversed the effect that P4 had on tumor-infiltrating regulatory T cells. To determine if inhibition of tumor growth by onapristone was immunologically mediated, SCID mice bearing PR+ mammary gland tumors were treated with onapristone. Results revealed a decreased ability of onapristone to inhibit tumor growth in SCID mice compared to immunocompetent mice, suggesting that inhibition of tumor growth is, in part, immunologically mediated. These findings offer a novel mechanism of P4-driven mammary gland tumor development and provide rationale in investigating the usage of anti-progestin therapies to promote immune-mediated elimination of mammary gland tumors.

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P2-20-12

Abundance of tumor-infiltrating lymphocytes is associated with pathologic complete response to neoadjuvant chemotherapy but not with survival in ER-positive/HER2-negative breast cancer

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INTRODUCTION: Abundance of tumor infiltrating lymphocytes (TILs) is well known to be associated with achievement of pathologic complete response (pCR) after neoadjuvant chemotherapy and is a surrogate of better survival in triple negative breast cancer (TNBC). However, the association remains unclear in ER-positive/HER2-negative, which is the most common subtype in breast cancer. Further, pathological quantification of TILs is known for its ambiguity. We hypothesized that abundance of TILs, quantified by transcriptomic signatures, in ER-positive/HER2-negative is associated with different biology and is not a surrogate of survival unlike in TNBC. **METHODS:** A total of 6035 primary breast cancer patients from three cohorts (TCGA, METABRIC, and SCAN-B) with full transcriptome and clinical data were analyzed. Lymphocyte fractionation in the tumor microenvironment of a bulk tumor was estimated from the transcriptome using two different deconvolution tools, CIBERSORTx and xCell. **RESULTS:** First, the correlation between TIL score measured histologically on TCGA patients and gene expression of CD3D, CD3E, CD3G, CD8A, CD4, and total lymphocytes, and total T-cells measured by xCell or CIBERSORTx were analyzed. Total sum of lymphocytes by xCell correlated the strongest, thus it was adopted as the TIL score. The TIL score strongly correlated with CD3G, CD3E, CD3D, CD8A, and CD4 gene expressions in both TCGA and GSE96058 cohorts (all $r > 0.48$). Among the infiltrated cells; M1 and M2 macrophages, dendritic cells, mast cells and monocytes were all higher, and microvascular endothelial cells and pericytes were lower in TIL score high tumors in ER-positive/HER2-negative (all $p < 0.01$) where M2 and mast cells were not in HER2+ and TNBC in both 2 cohorts. Enrichment of immune related gene sets IL2/Stat5 signaling, IL6/Jak/Stat3 signaling, inflammatory response, and Complement were less in high TIL group of ER-positive/HER2-negative than HER2 and TNBC. In agreement, cytolytic activity was lower in TIL high of ER-positive/HER2-negative

compared from TNBC. On the other hand, high TIL group in ER-positive/HER2-negative had significantly higher intratumor heterogeneity, homologous recombination deficiency, mutation burden, and neoantigens, which were not the case in the other subtypes. In agreement, all the cell proliferation-related gene sets; E2F targets, G2M checkpoint, mitotic spindle, Myc targets v1 and v2, were more strongly enriched in high TIL group of ER-positive/HER2-negative compared from HER2+ and TNBC. MKI67 gene expression and Nottingham histological Grade were uniformly elevated with high TIL regardless of subtypes. In three independent neoadjuvant cohorts, we found that pathologic complete response rates of high TIL group. On the other hand, high TIL group did not show any survival benefit compared with low TIL group in ER-positive/HER2-negative, unlike in HER2+ or TNBC. CONCLUSION: High tumor-infiltrating lymphocytes in ER-positive/HER2-negative breast cancer was associated with less immune response and higher genetic alteration and cell proliferation compared to the other subtypes, leading to better response of neoadjuvant chemotherapy, but no benefit in survival outcome.

Disclosure(s):

Rongrong Wu, n/a: No financial relationships to disclose

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12/7/2022

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P2-20-14

Relationship of HIF-1 α and tumor infiltrating lymphocytes in patients with HER2-negative early-stage breast cancer treated with neoadjuvant chemotherapy

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Title: Relationship of HIF-1 α and tumor infiltrating lymphocytes in patients with HER2-negative early-stage breast cancer treated with neoadjuvant chemotherapy Authors: Grabinski VF, Oza HH, Gilkes DM, Shah MY, Cimino-Mathews A, Gabrielson E, Zhi I, Pipa Z, Lehman J, Ibanez HE, Ke S, Tsai HL, Stearns V, Santa-Maria CA Introduction: Hypoxia inducible factor 1 α (HIF-1 α) is an oxygen-dependent transcription factor expressed in areas of hypoxia associated with

regulation of immune escape mechanisms, metabolism (CAIX), and results in cancer treatment resistance. High stromal tumor infiltrating lymphocytes (sTILs) are associated with pathologic complete response (pCR) to neoadjuvant chemotherapy (NACT) in breast cancer. We investigated associations between HIF-1 α , sTILs and their relationship with pCR after NACT in patients with HER2-negative early-stage breast cancer. Methods: We identified patients with early-stage HER2-negative breast cancer at the Johns Hopkins Sidney Kimmel Comprehensive Cancer Center from 2000-2009 who received NACT, and had accessible breast tissue from biopsy and/or surgery. A pathologist scored nuclear HIF-1 α (0, 1, 2, or 3), membranous CAIX (0, 1, 2, or 3), sTILs (0-100) from baseline (ie pre-NACT) and surgical tissue (if non-pCR). Statistical analysis considered the following variables: age, histology, race, menopausal status, tumor size, and node status. Chemotherapy regimens were divided into either anthracycline AND taxane versus anthracycline OR taxane. Wilcoxon rank-sum, Fisher exact, and Jonckheere trends tests were utilized to assess differences between groups. Results: 43 patients met the predefined criteria and were included in the analysis, 16% (n=7) obtained a pCR. Patient race, ethnicity, clinical tumor size, histology, clinical subtype (estrogen receptor positive (ER+) vs. triple negative (TN)), and NACT regimen were not associated with pCR. Older age (p=0.019), postmenopausal status (p=0.009), smaller surgical tumor size (p < 0.001), and surgical node-negative status (p < 0.001) were associated with pCR. Mean TILs score was 32.5% in patients achieving pCR versus 20% in those with non-pCR (p=0.46); mean HIF-1 α was 2.42 in pCR group versus 2.57 in non-pCR (p=0.84). There was a trend of lower baseline sTILs with increasing nuclear HIF-1 α score (p=0.085). Membranous CAIX was not associated with nuclear HIF-1 α or baseline TILs, however, in the small proportion of patients (n=11) with CAIX scoring, higher membranous CAIX score at baseline (1 vs. 0) was associated with pCR (p=0.024). Conclusions: We observed that patients with pCR had a numerically higher sTILs level at baseline consistent with other studies, but did not find a correlation of HIF-1 α and pCR. Patients with higher HIF-1 α scores tended to have lower sTILs, suggesting that hypoxia may be leading to an immunosuppressive tumor microenvironment. Further characterizing the HIF-1 α pathway and its effects on the immune microenvironment may help identify resistance mechanisms to chemotherapy and immunotherapy.

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Victoria Grabinski, BA: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-20-15

Proteolytic regulation of CD73 by TRIM2 orchestrates tumor immunogenicity

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Proteolytic regulation of CD73 by TRIM2 orchestrates tumor immunogenicity Ziyi Fu^{1,2}, Siqi Chen³, Yueming Zhu⁴, Donghong Zhang⁴, Ping Xie³, Qiao Jiao⁴, Shipeng Xu¹, Yifan Xue⁶, Xinhua Lu⁶, Xinxin Song⁷, Massimo Cristofanilli⁸, William J Gradishar³, Kevin Kalinsky⁵, Yongmei Yin², Bin Zhang³ and Yong Wan^{4,5*} ¹Department of Obstetrics and Gynecology, Department of Pharmacology, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, USA. ²Department of Oncology, The First Affiliated Hospital of Nanjing Medical University, China ³Department of Medicine, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, USA. ⁴Department of Pharmacology and Chemical Biology, Winship Cancer Institute, Emory University School of Medicine, USA. ⁵Department of Hematology and Medical Oncology, Winship Cancer Institute, Emory University School of Medicine, USA. ⁶Department of Biomedical Informatics, University of Pittsburgh School of Medicine, USA. ⁷Department of Surgery, UT Southwestern Medical Center, Dallas, TX, USA. ⁸Department of Medicine, Weill Cornell Medicine, USA. **ABSTRACT** Despite the rapid utilization of immunotherapy, emerging challenges to the current immune checkpoint blockade need to be resolved. Here, we report that uncontrolled elevation of CD73 levels due to its aberrant turnover is tightly correlated with poor prognosis in immune-cold triple negative breast cancers (TNBCs), which impedes the efficacy for chemotherapy and immunotherapy. We have identified TRIM21 as a E3 ligase that governs CD73 destruction. Disruption of TRIM21 stabilizes CD73 that in turn enhances CD73-catalyzed production of adenosine, resulting in the suppression of CD8+ T cell function. The immunostaining demonstrated the cytosolic colocalization between TRIM21 and CD73. Molecular mapping further identified the amino acid stretches from 340-476 on TRIM21 and residues from 176-224 on CD73 mediated the interaction between TRIM21 and CD73. Replacement of lysine 133, 208, 262 and 321 by arginine on CD73 attenuated CD73 ubiquitylation and degradation. Moreover, TRIM21 is upregulated but CD73 is downregulated in response to IFN- γ secreted from activated CD8+ T cells in a feedback manner. Importantly, in preclinical animal models, diminishing of CD73 ubiquitylation remarkably promotes tumor growth and impedes antitumor immunity. In addition, a TRIM21^{high}/CD73^{low} signature in a subgroup of human breast malignancies was associated with a favorable immune profile. Collectively, our findings uncover a novel mechanism that governs CD73 proteolysis and point to a new therapeutic strategy by modulating CD73 ubiquitylation.

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7:00 AM - 8:15 AM

P2-20-16

Hormone receptor expression is associated with specific immunological profiles in the breast cancer microenvironment

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Purpose: Elucidating the unique immunomodulatory mechanisms in breast cancer microenvironment should provide useful insights to aid the development of new therapeutic strategies for this disease. Some studies suggested the immune regulatory function of hormone

receptor such as estrogen receptor- α (ER) and androgen receptor (AR), but their mechanism has not been fully understood because of the complexity of immune milieu in breast cancer microenvironment. In this study, we systematically analyzed the relationships between ER, progesterone receptor (PgR), and AR expression and the immunological profile in breast cancer tissue. Methods: Gene set enrichment analysis (GSEA) was used to screen the biological processes associated with the expression of human sex hormone receptor genes (ESR1, PGR, and AR), using a gene expression profile dataset of the Molecular Taxonomy of Breast Cancer International Consortium (METABRIC). Then, using METABRIC and a gene expression profile dataset of The Sweden Cancerome Analysis Network - Breast (SCAN-B), the correlation between the immune cell composition in breast cancer tissue (estimated with the CIBERSORTx) and hormone receptor expression was analyzed. In our previous study of 45 breast cancer tissues, we evaluated the level of human tumor infiltrating lymphocytes (hTILs), expression of human programmed death-ligand 1 (hPD-L1), and infiltration of 11 types of immune cells, using hematoxylin–eosin staining, immunohistochemistry (IHC), and multicolor flow cytometry, respectively. In this study, the levels of ER, PgR, and AR expression were further evaluated using IHC, and their relationship with the immunological profile of breast cancer tissues was analyzed. Results: GSEA showed that the expression levels of the ESR1, PGR, and AR genes were negatively correlated with multiple immunological processes, including “INFLAMMATORY RESPONSE.” Analysis of the correlations between the immune cell composition and hormone receptor gene expression showed that ESR1 expression was inversely correlated with Macrophage M1, CD4 memory activated T cells, Macrophage M0, CD8 T cells, and CD4 memory resting T cells; PGR expression was inversely correlated with Macrophage M1, CD4 memory activated T cells, and Macrophage M0; and AR expression was inversely correlated with Macrophage M0 and Macrophage M1. Immunohistochemical evaluation of ER and AR expression revealed both receptors to be inversely associated with hTIL, hPD-L1 expression, and leukocyte infiltration in breast cancer tissue. Analysis of the immune cell composition in these tissues revealed that ER expression was associated with the decreased infiltration of total T cells, CD4+ T cells, monocytes/macrophages, myeloid-derived suppressor cells, dendritic cells, and myeloid dendritic cells; PgR expression was associated with the decreased infiltration of dendritic cells; and AR expression was associated with the decreased infiltration of CD4+ T cells, monocytes/macrophages, nonclassical monocytes, myeloid-derived suppressor cells, dendritic cells, myeloid dendritic cells, and minor natural killer cells. Conclusion: The correlation of hormone receptor expression with specific immunological profiles in the breast cancer microenvironment both at the genetic and protein levels strongly suggests that hormonal signals may preferentially affect certain subsets of immune cells.

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12/7/2022

7:00 AM - 8:15 AM

P2-20-17

Eribulin is an immune potentiator in breast cancer by up-regulation of human leukocyte antigen class I

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Background: Eribulin, an anticancer drug that increases the overall survival (OS) of patients with metastatic recurrent breast cancer, inhibits microtubule polymerization, although the mechanism is different from that of other microtubule inhibitors (taxanes). A subgroup analysis revealed a low neutrophil-to-lymphocyte ratio (NLR) (< 3) to be a prognostic factor of eribulin treatment. NLR has also been reported to be a predictive marker for cancer immunotherapy. Checkpoint inhibitor-based cancer immunotherapy is currently available for breast cancer. We hypothesized that eribulin improves breast cancer cell immune response. Immunological effector cytotoxic T lymphocytes (CTLs) recognize antigenic peptides presented by human leukocyte antigen (HLA) class I; HLA class I downregulation is frequently observed in breast cancer. Here, we evaluated the CTL response in eribulin-treated breast cancer cells. Materials and Methods: HLA class I expression before and after eribulin treatment was evaluated using immunohistochemistry in tumors from patients, and by immunofluorescence, flow cytometry, western blotting, and quantitative RT-PCR (qRT-PCR) in breast cancer cells (MDA-MB231 and MCF7). Factors that upregulate HLA class I were screened using RNA-seq. To evaluate T cell recognition, we generated cancer testis antigen (NY-ESO-1)-specific T cell receptor transduced-T cells (TCR-T cells). NY-ESO-1 cDNA was stably transduced into MCF7 and

MDA-MB-231 cells. TCR-T cell reactivity with MCF7/NY-ESO-1 cells was analyzed using an ELISPOT assay. A combinatorial therapy model was established using eribulin and TCR-T. Results: HLA class I was upregulated after eribulin treatment in clinical samples. To confirm this, we treated breast cancer cells with eribulin and evaluated HLA class I expression. Eribulin increased HLA class I expression, as evidenced by immunofluorescence, flow cytometry, western blotting, and qRT-PCR. RNA-seq results on eribulin-treated cells showed that eribulin upregulated NLRC5, a master regulator of HLA class I. IFN γ ELISPOT assay revealed that eribulin increased IFN γ secretion by TCR-T cells ($p < 0.01$), indicating that eribulin enhanced the immune response. These results suggest that eribulin and immunotherapy had a synergistic effect. Therefore, we established an eribulin and NY-ESO-1 combinatorial therapy model and showed that the combination group had a significantly lower number of viable cancer cells than the eribulin- and TCR-T-only groups ($p < 0.01$). Conclusions: Eribulin increased the expression of HLA class I, probably by upregulating NLRC5 in breast cancer cells. It also enhanced TCR-T recognition in breast cancer cells. The combinatorial therapy model revealed the synergistic effect of eribulin and TCR-T. These results indicate that eribulin might be an immune potentiator and that combination therapy with immunotherapy can be effective for the treatment of breast cancer.

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7:00 AM - 8:15 AM

P2-21-01

Decoding Inter- and Intra-Tumor Heterogeneity in Lobular Breast Cancer Using Spatial Transcriptomics and Clustering Analysis

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Background: Invasive lobular breast carcinoma (ILC) represents 5 to 15% of all invasive breast cancers. Recent studies showed the importance of tumor microenvironment (TME) heterogeneity on patient outcome. Here, we aim to characterize TME spatial heterogeneity by performing clustering analysis on spatial transcriptomics (ST) data. Methods: Frozen tumor samples from 43 primary estrogen receptor positive, HER2-negative ILCs were characterized using ST (Visium, 10x Genomics), each ST slide containing 4992 spots. Hematoxylin/eosin (H&E) stained ST slides were annotated (QuPath software) reaching single cell resolution. After performing normalization, hierarchical clustering (STUtility R package) across all samples was carried out on principal components computed using highly variable genes. Clusters were characterized using morphological annotation and gene set enrichment analysis for hallmark gene sets from MSigDB (FGSEA R package). A cluster of spots was defined as tumoral or stromal if the average proportion of pixels annotated as tumor or stroma across its constitutive spots was higher than the average proportion of tumor or stroma pixels across all spots of our cohort. Spatial heterogeneity was assessed by comparing the number of contacts between spots belonging to the same cluster (homo-contacts) and the number of contacts between spots belonging to different clusters (hetero-contacts). Comparisons between groups were assessed using Wilcoxon test. Results: Out of the 43 ILC samples, 19 were T2 or T3, 13 were node-positive and 34 were grade 2. Of note, 9 patients experienced disease relapse. Morphological annotation revealed that an average of 20.4%, 61.12%, 11.5%, 0.45%, 3% of the tissues in our dataset corresponded to tumor, stroma, adipose tissue, immune infiltrate and normal structures (vessels, normal breast), respectively. Bioinformatics analysis revealed 7 tumor, 11 stroma, and 6 normal structures clusters, as well as 8 mixed clusters with no predominant morphological structure, with a median of 22 clusters per sample. Tumor and stroma clusters were either shared across all samples or present only in specific samples. Overall, tumor clusters were characterized by an enrichment in estrogen and androgen response related pathways. Moreover, tumor clusters enriched in oxidative phosphorylation, G2M checkpoint and MYC targets were more present in samples with higher histopathological grade ($p=0.016$), whereas tumor clusters enriched in interferon alpha/gamma response related pathway were associated with a higher tumor stage ($p=0.007$). A higher number of hetero-contacts among tumor spots were associated with disease relapse ($p=0.02$). Similarly, a higher number of hetero-contacts among stroma spots including immune and adipose related clusters was also found in samples from patients who experienced disease relapse ($p=0.01$). Overall, these findings suggest a role of both tumor and stroma spatial disorganization and heterogeneity in tumor progression. Furthermore, clusters capturing the presence of normal breast and in situ carcinoma were enriched in samples from patients who did not relapse ($p<0.001$). Conclusion: Our results revealed the substantial inter- and intra-patient heterogeneity of ILC both at the tumor and microenvironment levels. Different tumor and stroma clusters characterized by specific hallmarks were associated to specific clinical features and disease outcome, unraveling potential new targets for optimizing ILC care. Further validation is needed.

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7:00 AM - 8:15 AM

P2-21-02

Longitudinal tumor-immune microenvironment changes in patients with clinical luminal A early breast cancer treated with neoadjuvant palbociclib and endocrine therapy: results from the Swedish randomized PREDIX Luminal A trial

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Introduction: The use of preoperative CDK4/6 inhibitors combined with endocrine treatment remains investigational in breast cancer (BC), while their effect on tumor-immune microenvironment (TIME) in luminal BC is the subject of few published studies. The aim of this study was to characterize the treatment-induced changes of TIME at a spatial proteomic and bulk tumor transcriptomic level in clinical luminal A BC patients treated with neoadjuvant palbociclib and endocrine treatment. **Methods:** The PREDIX Luminal A phase II randomized clinical trial (NCT02592083) included patients with stage 2-3 BC and IHC-defined luminal A biology (ER+ and PR+, HER2-, low proliferation) treated with preoperative ET (tamoxifen or aromatase inhibitor) with or without the addition of CDK4/6i palbociclib, based on the early change of Ki67 levels. A core biopsy was obtained at baseline, after 10 weeks of treatment (on-treatment) and at surgery. The study was closed after the inclusion of 10 patients due to slow accrual. By using formalin-fixed paraffin-embedded tissue from all timepoints, we performed the GeoMx® Digital Spatial Profiling (DSP, NanoString, Seattle, WA, USA) for the spatial profiling of 27 immune cell and tumor markers (immune cell profiling core and pan-tumor panels) both at intra-epithelial and stromal tissue segments. Upon data normalization, a linear mixed model was adopted for differential marker expression assessment between the different timepoints and treatment arms, using the DSP Suite® software. RNA was also extracted from fresh-frozen biopsies and the nCounter® Breast Cancer 360™ panel (NanoString) was used for gene expression profiling of 776 targets and data analysis was performed using the nSolver® software. **Results:** A total of 7 patients received palbociclib + ET and 3 were treated with ET only. All patients experienced an on-treatment radiological partial response while no patient achieved pathological complete response. While ET suppressed the ER axis in both palbociclib-treated and untreated patients, treatment with palbociclib additionally led to cell-cycle arrest as evidenced by a decrease in proliferation and downregulation of cell-cycle gene pathways. Immune-related protein markers were enriched in the stroma segments and pan-tumor markers were enriched in the intra-epithelial segments at all timepoints. In palbociclib-treated patients, immune cell markers (e.g. CD45, CD68, CD20, CD4, HLA-DR) were significantly enriched in on-treatment samples (n=3) both in tumor and stromal segments, while these expression changes were reversed between on-treatment and surgery. In the ET-treated patients immune markers reflecting e.g. T-, B- and/or antigen-presenting-cells were significantly enriched at the operation samples (n=2), in the intra-epithelial but not in the stromal areas. This finding was confirmed also at the gene level, where immune-related pathways (e.g. chemokine and cytokine activity and receptor binding) were upregulated in the palbociclib-treated patients on-treatment but they were partially abrogated at surgery. The ET-only treated patients presented with enhanced immune activation gene sets at both on- and post-treatment timepoints **Conclusion:** The findings of this small hypothesis-generating study indicate an upregulation of immune function during treatment with palbociclib and ET and an altered tumor microenvironment. The prognostic and potential therapeutic implications of sensitizing tumors to subsequent chemotherapy and immunotherapy need to be further investigated in larger studies.

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P2-21-03

Unique Collagen Peptide Signatures between Ductal Carcinoma in Situ and Invasive Breast Cancer by Mass Spectrometry Tissue Imaging

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Ductal carcinoma in situ (DCIS) is characterized by inter-tumor heterogeneity that poses a therapeutic challenge due to its unpredictable recurrence and progression to invasive breast cancer (IBC). Recent publications have implicated the crucial role of the tumor microenvironment particularly stromal differences between DCIS patients who progress to IBC (progressors) and those that do not (non-progressors). However, spatial regulation of the collagen proteome has yet to be investigated in the context of disease progression in DCIS. In this study, we hypothesized that the collagen proteome was significantly altered between DCIS

and IBC and that differentiating collagen peptide signatures could be related to clinical outcomes. Our initial studies investigated collagen peptide signatures in lumpectomies (n=13) annotated as DCIS, DCIS and invasive ductal carcinoma (IDC), or IDC only. We leveraged our previously published method for spatial imaging of collagen proteomics on tissue to report collagen types and collagen post-translational modifications including 40 other extracellular matrix (ECM) proteins involved in the regulation of collagen fibers. Over 1000 peaks were found to be linked to annotated pathologies or adjacent regions. Initial comparison of DCIS to IDC lesions demonstrated 63 differentially expressed peaks between these regions by unpaired, two-tailed t-test ($p < 0.001$). Image segmentation of the 315,541 pixels demonstrated 16 high-level hierarchical groups designating unique spatially localized ECM proteomic groups. Notably, these groups overlaid with histopathological features and pathological annotations. Next, we investigated collagen peptide signatures in a subset of DCIS samples from the Resource of Archival Breast Tissue (RAHBT) (n=37). Samples were histologically diverse within the tissue microarrays, with cribriform, micropapillary, papillary, solid, and comedo necrosis architectural patterns. In our preliminary analysis, we found two peptide peaks that could distinguish the solid subtype (n=22) from comedo necrosis (n=4) and one peak that could discriminate between the cribriform (n=8) and solid subtype (n=22) by area under the receiver operating curve (AUROC) ≥ 0.75 and Wilson/Brown t-test ($p < 0.05$). Evaluated per clinical outcome, four ECM peptides showed significantly different peak intensities in progressors with IBC recurrence (n=7) compared to non-progressors (n=26) (AUROC ≥ 0.75 ; Wilson/Brown t-test $p < 0.05$). One peptide had significantly different peak intensities between progressors with contralateral IBC recurrence and DCIS recurrence (n=5) and non-progressors (n=26) (AUROC ≥ 0.75 ; Wilson/Brown t-test $p < 0.05$). Overall, the data suggest that unique collagen signatures in DCIS could be useful for understanding recurrence and progression to IBC. Further investigation of the spatial distribution of the collagen proteome within DCIS pathologies and relative to clinical outcome is warranted.

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The tumor immune microenvironment composition and prognostic value in breast cancer during pregnancy is dynamic during the gestation period

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Introduction: Breast cancer (BC) during pregnancy (PrBC) is an uncommon malignancy characterized by a more aggressive clinical course compared to pregnancy-unrelated BC. Specific patterns of tumor-infiltrating lymphocytes (TILs) subpopulations have been observed in these patients, with significant prognostic roles. Previous studies demonstrated the varying histopathologic and prognostic profiles of PrBC by gestational age. However, the underlying immune landscape dynamics has never been investigated. Here, we sought to provide comprehensive insights into the association between gestational age at breast cancer diagnosis and tumor immune microenvironment (TIME) composition. **Materials and Methods:** A total of 110 PrBC were selected from our Institutional registry and categorized based on the trimester in which they were diagnosed. All cases were subjected to TILs profiling according to the International TILs Working Group recommendations. Immunohistochemistry for CD4, CD8, forkhead box P3 (FOXP3), and PD-L1 (clone 22C3) on a Dako Omnis platform was performed. Fisher's and Chi-squared tests, multinomial logistic regression models, ROC curve, and survival analyses were performed. **Results:** The proportion of patients with high histologic grades incremented with the increase in gestational age (1st, n=24, 53%; 2nd, n=27, 69.2%; 3rd trimester, n=20, 87.0%; p=0.02). Neither breast cancer subtypes nor the hormone receptor (HR) and HER2 status changed significantly according to the pregnancy trimester. In HR+/HER2- subtype, the proportion of TILs+ tumors were higher in the early phases of pregnancy (1st, n=29, 100%; 2nd, n=17, 89.5%; 3rd trimester, n=9, 81.8%; p=0.04) imprinted by FOXP3 positivity where more FOXP3+ TILs were seen in the first months and decreased progressively (1st, n=10, 55.6%; 2nd, n=2, 11.8%; 3rd trimester, n=0, 0%; p< 0.01). While in the triple negative breast cancer (TNBC) population, the proportion of PD-L1+ tumors (i.e. CPS>1) was significantly higher in the later stages of pregnancy (1st, n=2, 16.7%; 2nd, n=2, 18.2%; 3rd trimester, n=5, 71.4%; p=0.03). Patients who relapsed after a BC diagnosis during the 1st and 2nd trimesters lacked more frequently FOXP3+ and CD8+ cells, unlike those with no disease recurrence (n=21, 77.8% vs. n=17, 48.6%; p=0.02 and n=18, 66.7% vs. n=10, 28.6%; p< 0.01, respectively). **Conclusions:** TIME dynamics of PrBC are different according to the gestational age in both HR+ and TNBC PrBC. Our results suggest that immune tolerance events are likely to involve PrBC at later gestational age. Specific escape mechanisms (i.e., TILs and FOXP3 decrease in HR+ and PD-L1 expression in TNBC) might explain the aggressiveness of PrBC diagnosed during the later gestational age.

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7:00 AM - 8:15 AM

P2-21-05

Vascular effects of Platelet-derived growth factor-B (PDGFB) in breast cancer metastasis to the brain

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Brain metastases are associated with shortened survival and poorer quality of life in breast cancer patients. Recently, the importance of platelet-derived growth factor-B (PDGFB) and its stromally localized cognate receptor, platelet-derived growth factor receptor-beta (PDGFR β) in promoting breast cancer metastasis to the brain was identified by our group. Historically, PDGFB-to-PDGFR β signaling is known to promote angiogenesis and vessel maturation both in normal physiology and in cancer, but the mechanism(s) behind this tumor stromal interplay in brain metastasis is poorly understood. Based on our previous work and the work of others, we hypothesized that breast tumor-derived PDGFB directly modulates both brain endothelial and blood brain barrier (BBB) function by altering angiogenesis and endothelial permeability. To test this directly, we over-expressed PDGFB ligand in MDA-MB-231 and HCC1187 triple negative

breast cancer cell lines and compared the angiogenic potential of the conditioned medium (CM) from these cells. We utilized both a 3D in vitro (human brain microvascular endothelial cell, HBMEC) spheroid angiogenesis model and a tri-culture BBB system (HBMECs in direct interaction with human astrocytes and human pericytes) to test the BBB vasculature. CM harvested from PDGFB overexpressing cells significantly increased the sprouting angiogenesis potential of 3D HBMECs and the migration of 3D tri-culture BBB spheroids compared to CM obtained from parental cells. In addition, CM from PDGFB overexpressing cells caused the surface of BBB spheroids to exhibit significantly increased permeability to high molecular weight dextran compared to CM from parental cells. In agreement with these findings, the tight junction protein ZO1 was diminished. Importantly, in vivo BBB permeability was also tested upon intracardiac injection of MDA-MB-231 cells with and without PDGFB overexpression. These studies revealed that Evans blue dye fluorescence intensity was significantly higher in the brains of mice injected with PDGFB overexpressing cells compared to parental cells. Overall, these studies reveal a previously unrecognized role for PDGFB-to-PDGFR β signaling in brain vascular remodeling and BBB permeability, which has clinical implications for women with PDGFB-positive breast cancer.

Disclosure(s):

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7:00 AM - 8:15 AM

P2-21-06

The relationship between the gene expression difference of fibroblasts in the tumor microenvironment and metastasis of triple-negative breast cancer

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Background Triple negative breast cancer (TNBC) is a breast cancer subtype with increased risk of distant metastasis, especially to lung and liver. In addition to the intrinsic characteristics of tumor cells, the molecular features of the tumor microenvironment cells can also regulate the metastasis process of TNBC. In this study, we tried to characterize the transcriptomic features of microenvironment fibroblasts associated with the distant metastasis of TNBC. Method We established PDX models by obtaining tumor tissues from 26 triple-negative breast cancer patients and transplanting them into the mammary fat pads of immunodeficient mice. When the PDX tumors grew sufficiently in the fat pads, we excised them and saved the mice to assess whether each PDX tumor was capable of developing spontaneous distant metastasis. We used bulk RNA sequencing and single cell RNA sequencing to determine the transcriptomic features associated with the distant metastasis. Results We classified the 26 TNBC PDX models based on their in vivo metastasis capacity and the clinical outcomes of the corresponding patients. Non-metastatic PDX models were defined as the lack of developing distant metastasis in either mouse experiment or clinical follow-up data (n=5). PDX models were defined as metastatic models when they developed distant metastasis in both mouse and human (n=4). We performed single cell RNA sequencing using the nine PDX tumors and observed a substantial gene expression differences of fibroblasts in the tumor microenvironment between the metastatic and non-metastatic PDX models. The fibroblasts of the metastatic PDX models showed up-regulation of genes involved in the response to hypoxia, inflammatory response, neutrophil chemotaxis, cellular response to IL-1, positive regulation of cell proliferation, and negative regulation of apoptotic process. Moreover, this difference of gene expression between metastatic and non-metastatic TNBC PDX models were not identified by the bulk RNA sequencing data. Conclusion By using the single cell RNA sequencing using the TNBC PDX models, we identified key features of fibroblasts in the tumor microenvironment that contributes to the metastasis capacity of TNBC. Further studies are on-going to elucidate the underlying mechanisms.

Disclosure(s):

Woo Hang Heo, n/a: No financial relationships to disclose

Woochan Lee, n/a: No financial relationships to disclose

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P2-21-07

Exploring spatial correlations in Breast invasive Lobular Carcinoma subtypes using a novel CAF multiplex immunofluorescence panel

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Background:

Recent advances in immunotherapy led to development of new technologies to identify topographical distributions and correlations in the tumor microenvironment, enabling a better understanding of the tumor immune landscape.

Based on the 2019 WHO classification Invasive lobular carcinoma (ILC) has various histological presentations. The pleomorphic variant has been reported to be biologically different to the classical counterpart.

Cancer associated fibroblasts (CAFs) secrete cytokines and growth factors aiding in tumor growth. CAFs have been shown to express alpha-smooth muscle actin (α -SMA), Thy1, fibroblast activation protein (FAP), S-100. IHC based studies have shown differences in CAFs subpopulation between ILC and IDC. Here, we explored different CAFs subpopulations between Pleomorphic and Classical ILC using multiplex immunofluorescence (mIF).

Study design:

Multiplex immunofluorescence (mIF) was performed on formalin-fixed paraffin-embedded (FFPE) tissue sections [(n=6, classic ILC; n=6 pleomorphic ILC)] stained with Opal 7-color Kit using an automated system. Sections were stained consecutively with Pancytokeratin, CD45, A-SMA, FAP, S100, Thy-1. Slides were scanned using the Vectra 3.0 spectral imaging system (PerkinElmer). Five tumor ROIs were examined with Phenochart (Akoya/PerkinElmer) viewer and subsequent images were analyzed to explore spatial distances of CK+ cells to the CAFs. Data was generated using InForm and Phenoptr softwares (Akoya Labs) as a median value. Statistical analysis data correlation was performed using SPSS version 24.0 (IBM Corp)

Results:

Twelve invasive lobular carcinomas cases were evaluated. All cases with classical features were nuclear grade 2 and all pleomorphic cases (n=6) were nuclear grade 3. Six were Luminal B, five were Luminal A and one case was triple negative invasive lobular carcinoma. We studied nineteen different phenotypes of CAFs in the tumor, stroma, and overall tissue compartments. We found statistically significant differences (p -value < 0.05) between the distances of CAFs from the tumor cells in classic and pleomorphic ILC in three phenotypes. The A-SMA+, A-SMA+/S100+ phenotypes were closer to the tumor cells in classic subtype and the S100 only phenotype was closer to the tumor cells in pleomorphic carcinomas. In addition, there were two other phenotypes namely A-SMA+/Thy-1+(closer to tumor cells in classic ILC) and FAP+/S-100+ (closer to tumor cells in pleomorphic ILC), which showed a trend of significance (Table 1)

Discussion:

TME studies in invasive breast lobular carcinoma have been primarily based on chromogenic IHC. Multiplex immunofluorescence quantifies cell phenotype's densities and positions in different tissue compartments (tumor vs stroma vs total tissue). Knowing the proximity of an individual TME cells to the tumor cells, aids in pinpointing possible therapeutic targets. Fibroblast dysregulation in cancers, enhances their pro-tumorigenic and anti-tumorigenic potential. Due to their heterogeneity, they can express a wide array of markers. Identifying the full possibility of CAF subsets is one of the keys to discovering actionable targets. Our results showed Alpha- SMA positive, Alpha-SMA/S-100 positive, Alpha SMA/ Thy-1 positive CAFs in closer proximity to the classic ILC tumor cells as compared to pleomorphic ILC. Additionally, S-100 positive and FAP/S-100 positive CAFs showed a closer proximity to tumor cells in the pleomorphic subtype. Based on these results we hypothesize that pleomorphic ILCs are closely associated with pro-tumorigenic CAFs as compared to classic ILCs. Larger datasets are needed to confirm this.

In conclusion we utilized an objective approach to quantify, phenotype and spatially correlate each cell in the tumor microenvironment. This has helped identifying CAFs subsets that differs in the spatial correlation to tumor cells in ILC subtypes, which can be potential actionable targets.

Table 1

Distance of CK+ cells from CAF subtype	p-value
Total FAP	0.093
Total Alpha-SMA	0.026
Total Thy1	0.132
Total S100	0.310
Alpha-SMA/FAP	0.132
Alpha-SMA/FAP/Thy1	0.400
Alpha-SMA/FAP/S100	0.093
Alpha-SMA/FAP/S100/Thy1	1.000
Alpha SMA only	0.699
Alpha-SMA/Thy1	0.067
Alpha-SMA/S100	0.02
Alpha-SMA/S100/Thy1	1.000
FAP only	0.310
FAP/S100	0.065
FAP/S100/Thy1	0.229
FAP/Thy1	0.485
S100 only	0.009
S100/Thy1	0.792
Thy1 only	0.394

Phenotypes of Cancer associated fibroblasts and their statistical correlation between classic vs pleomorphic invasive Lobular carcinomas.

Disclosure(s):

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P2-21-08

Digital spatial profiling of RNA and protein in the invasive lobular breast cancer microenvironment

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Invasive lobular breast cancer (ILC) is an understudied subtype of breast cancer with late recurrence, metastasis to serosal surfaces, such as the peritoneum, and dismal long-term outcome. We previously reported better patient outcome in ER+ breast cancers with high glucocorticoid receptor (GR) expression (Pan et al 2011). Preliminary data suggests more favorable patient outlook in the ILC subtype when tumors express higher levels of GR. The dynamic interaction between a tumor and its microenvironment leads to phenotypic changes in stromal cells and the extracellular matrix to promote growth or invasion of malignant cells. ILC is histologically distinct from invasive ductal carcinoma and is characterized by discohesive tumor cells that grow as "Indian files" due to lack of the cell adhesion molecule E-cadherin. Because of these differences we expect the tumor microenvironment (TME) to be quite unique in ILC compared to other breast cancer subtypes. We hypothesized that differing levels of expression of nuclear receptors by tumor cells would impact cells residing within the stroma, presumably through paracrine signaling. Immunohistochemistry for 25 ILC biopsies revealed a wide variation in GR expression, ranging from completely negative to strongly positive. Our goal was to gain insight into how GR presence or absence in ILC cells might impact gene and

protein expression in malignant cells and their TME. We were inspired to examine how crosstalk between the GR-positive or GR-negative cancer cells and their respective tumor microenvironment (TME) differentially impact stromal cell gene expression as well as the immune cell milieu. Bulk expression profiling is inadequate to examine molecular profiles of the tumor and stroma separately. Therefore, we used nanoString GeoMx® high-plex digital spatial profiling of RNA and protein expression in GR-positive and GR-negative primary ILC. We first performed spatial gene expression using the Whole Transcriptome Atlas (WTA) for six primary ILC, two of which were strongly positive for GR, two GR-negative and 2 tumors harboring both GR-positive and GR-negative regions. To examine the tumor cells and the stroma independently we segmented regions into panCK-positive and panCK-negative segments and analyzed those separately. Intriguing differences were observed between GR-positive and negative ILC, for the tumor cells as well as for the TME. Implementation of the Spatial Deconvolution script embedded within the GeoMx® software revealed striking differences in the abundance of immune cells, endothelial cells and fibroblasts in the stroma of GR-positive vs GR-negative ILC. Macrophages and other myeloid subsets were present in significantly higher numbers in the TME of GR-positive compared to GR-negative ILC. The contribution of B- and T-cell subsets as well as endothelial cells and fibroblasts were also notably different. To more precisely define the spatial distribution and abundance of various cell subtypes and their association with tumor cells, we are including protein DSP as an added layer to complement the WTA. We are also performing RNA and protein DSP for an additional ten GR-positive and ten GR-negative ILC. Thus, we will test our initial observations and expand our investigation to generate comprehensive molecular profiles of ILC tumors and stromal cells and acquire a deeper understanding of how GR expression/activation influences the crosstalk between ILC cells and their TME. We anticipate that differences in gene and protein expression will provide clues as to how GR activation affects proliferative and adhesive properties of ILC through modification of the TME.

Disclosure(s):

Lynda B. Bennett, Ph.D.: No financial relationships to disclose

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Suzanne D. Conzen, MD: BostonGene Corporation: Consulting Fees (e.g., advisory boards) (Ongoing); Corcept Therapeutics: Receipt of Intellectual Property Rights / Patent Holder (Ongoing)

12/7/2022

7:00 AM - 8:15 AM

P2-21-09

Detailed analyses of pro-metastatic and anti-metastatic microenvironments of murine breast tumors in syngeneic mice

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Despite the advances in early diagnostics and therapeutics, women with metastatic breast cancer have limited treatment options. Women with TNBC, who constitute 15-20% of breast cancer patients, are often diagnosed with aggressive/metastatic disease. Advanced studies implicated immunosuppressive tumor microenvironment (TME) in aggressive/metastatic properties of TNBC subtype. Alternatively activated immature myeloid cells including tumor-associated macrophages (TAM), tumor-associated neutrophils (TAN), tumor-associated dendritic cells (TADC) and myeloid derived suppressor cells (MDSC) constitute a major component of TME. However, anti-tumorigenic microenvironment is also reported and that may have clinical relevance in early TNBC patients. Therefore, our hypothesis is that myeloid cells polarize to become immunosuppressive and infiltrate tumors and pre-metastatic niches in patients with advanced disease, while patients with early TNBCs may elicit anti-tumor immune response eliminating disseminated tumor cells (DTC). The utilization of syngeneic immunocompetent mouse models has contributed to our current understanding of immunosuppressive or immunomodulatory TME. Using these models, we have demonstrated that tumor dissemination and growth at metastatic sites is facilitated by MDSC's. Emerging technologies; single cell RNA sequencing (scRNA-Seq), mass cytometry (CyTOF) or cellular

indexing of transcriptomes and epitopes sequencing (CITE-Seq) has been powerful platforms for detailed characterization of tumors and TME compartments. We performed scRNA-Seq and CyTOF analyses of the myeloid cell populations of tumors and spleens from metastatic 4T1 and non-invasive EMT6 tumor-bearing mice. Tumors and spleens from 4T1 tumor-bearing mice exhibited a marked expansion of myeloid cell subsets that are characterized by the expression of immunosuppressive as well as progenitor markers. On the contrary, indicated tissues from EMT6 mice were enriched in NK cells, T and B lymphocytes and they were lacking immunosuppressive myeloid cell subsets. Furthermore, we identified a distinct differentiation pattern of immature myeloid cell subsets from neutrophil progenitors (NP) in 4T1 tumor-bearing mice. Using the murine TNBC models in syngeneic mice, we provide evidence that early TNBC tumors may elicit anti-tumor immune responses and thus the survival outcome in those patients is substantially increased after complete surgical resection of the primary tumors. Whereas immunosuppressive tumor microenvironment contributes to the poor overall survival in patients with advanced TNBCs. Therefore, identifying an anti-tumor immune signature in early TNBC patients may be utilized as a clinical biomarker before surgical intervention as well as improve the survival outcome.

Disclosure(s):

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7:00 AM - 8:15 AM

P2-21-10

Tumour associated macrophages in Breast Cancer - Are they critical players in response to Neo Adjuvant Chemotherapy?

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Background Breast Cancer (BC) patients who do not obtain pathologic complete response (pCR) after neoadjuvant chemotherapy (NACT) present higher rate of relapse and worse overall survival. Recent evidence suggests that chemotherapy (CT) efficacy relies on the capacity of chemotherapeutic agents to interact with the immune system. BC features a unique tumor microenvironment (TME) comprising of multiple immune cell types including Macrophages that share a double-edged relationship with cancer as they get polarised from M1 (anti-tumour) to M2 (Pro-tumour). Pro-tumour M2 macrophages are referred to as tumor-associated macrophages (TAMs) and are implicated extensively in angiogenesis, metastasis and therapy resistance. Establishing role of TAMs, facilitates the emergence of novel strategies that exploit them as theranostic targets/tools of interest for treating cancer. Utility of using Drugs like Zoledronic Acid, Trabectedin, Rebastinib in combination with 5-fu have shown promising anti-TAM activity and improved response to CT in clinical trials. In this study, we have characterized presence of M2-TAM and its correlation to NACT response in matched primary

and residual tumours by examining expression of several biomarkers . Methods Treatment naïve primary and their matched residual tumour specimens from 45 women treated at a single center were accessed through IERB approved protocols. The study included locally advanced HR+HER2-ve and TNBC tumours treated with standard NACT regimes between 2018 to 2020. To determine the association of TAM population with response to NACT, expression levels of CD68 (pan macrophage marker) & CD163 (marker of M2 macrophages), were detected by immunohistochemistry (IHC) and represented as combined H score. We also performed gene expression of chemokines, inflammatory cytokines and interleukins involved in M1-M2 polarization by q-RT-PCR. Residual Cancer Burden Scoring was used to assess response and patients were divided into three groups (complete responders, partial responders and non-responders). Univariate and multi variate analysis were performed between gene expression groups and IHC groups with clinicopathological parameters. Findings from this study was validated on public data bases like TCGA, METABRIC and GEO. Results: 20% of all patients included in the study were complete responders. We arrived at a Macrophage Polarisation Score (MPS) by Gene expression and also a combined H score by IHC. MPS and H-score had a positive correlation ($p=0.083$) overall. Interestingly, Combined analysis of H-Score and MPS with response to treatment showed a greater and statistically significant correlation with residual tumours as compared to treatment naïve tumours ($p=0.009$). We also observed that high MPS and high combined H score in residual tumours were associated with increased tumour size and LVI ($p=0.055$ and $p=0.03$). Other clinicopathological parameters like receptor status, grade and stage at diagnosis were not significantly associated with H score or MPS. Taken together we found that 11% of patients who exhibited high TAM score by both H sascore and MPS fell into the non-responders category. We therefore report TAMs in residual tumours being more indicative for response to therapy compared to primary tumours. Conclusion Although primary tumours are useful for building predictive models to therapy response, we have demonstrated that there is utility in examining residual tumours as well for choice to adjuvant chemotherapy, since the tumour is constantly evolving through the NACT period. More work to arrive at a “TAM score” that could aid in choice of additional adjuvant treatment strategies is underway. We believe our work is helping us to move one step closer to Precision Medicine in a low and middle income country like India that has a higher burden of locally advanced disease. Our analysis also lends itself to becoming a clinical test since it is performed on an FFPE specimen

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

P2-21-11

A high content imaging and analysis approach to screen compounds for novel drug targets in 3D breast cancer co-culture model

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The desired effect of cancer therapeutics can only be conceived when applied to complex multicellular structures with different cell types and extracellular matrix (ECM) in three-dimensional (3D) space. Therefore, 3D cell culture systems have become very popular in drug screening and discovery. There is an immense demand for highly efficient and easy methods to produce 3D spheroids in any cell format. However, heterogeneity in size, extended cultivation times, and reproducibility for high throughput assays are limiting factors in the generation of spheroids. Recently we have established a naturally transformed breast cancer cell line, KAIMRC1 (1), from ductal breast carcinoma. We have developed a novel and easy method to produce spheroids (2) from KAIMRC1 cells in vitro, which can be used as a 3D model to study proliferation, differentiation, metabolism, cell death, and drug response of cells in the tumor microenvironment. We developed an in-vitro high content imaging (HCI) based cellular assay using commercially available compound panels to perform initial drug screening in the KAIMRC1 spheroids model. Our approach allows rapid screening of a panel of drugs to assess inhibitory effects on the growth of tumor cells in 3D cultures. To mimic the actual in-vivo tumor microenvironment, we are now developing an HCI-based assay utilizing 3D KAIMRC1 spheroids co-cultured with patient-derived fibroblast cells. 1. Ali, Rizwan, et al. "Isolation and Characterization of a New Naturally Immortalized Human Breast Carcinoma Cell Line, KAIMRC1." *BMC Cancer* 17 (2017) 2. Rizwan Ali et al., (2021) New Born Calf Serum (NBCS) can induce spheroid formation in breast cancer KAIMRC1 cell line. *Front. Mol. Biosci.* DOI: 10.3389/fmolb.2021.769030

Disclosure(s):

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7:00 AM - 8:15 AM

P2-21-12

Targeting ADAM8 dependent maintenance of the myCAF phenotype in the breast cancer tumor microenvironment

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Background: Cancer associated fibroblasts (CAFs) regulate breast cancer growth, differentiation and metastasis. Targeting the signaling pathways between myofibroblast CAFs (myCAF) and cancer cells required for myCAF maintenance provides a mechanism to reverse engineer the tumor microenvironment to inhibit cancer growth and metastasis.

Methods and Results: We co-cultured human triple negative breast cancer (MDA-MB-231) with human mesenchymal stem cells (MSC). After 72h, MSC mRNA expression of the myCAF markers, alpha-smooth muscle actin (α -SMA) / vimentin (Vim) / tenascin C (Ten-C) are all significantly increased. In parallel, MB-231 mRNA expression of stemness markers, SRY-Box Transcription factor 2 (Sox2) / Octamer-binding transcription factor 4 (Oct4) / Nanog, are also significantly increased. Migration assay and morphology imaging confirm the induction of the myCAF phenotype to promote MB-231 cancer stemness. shRNA lentivirus was used to knock down Sox2 gene expression in MB-231. We performed RNA-seq in MB-231 first comparing MB-231 vs. MB-231+MSC and then MB-231(-/-sox2)+MSC vs. MB-231+MSC. There are 104 overlapping genes in MB-231+MSC from the two analyses indicating upregulation with myCAF differentiation and cancer stemness. Using the Human Cancer Secretome Database, 9 genes are either membrane or secreted proteins. Using antibody blockade in co-culture, antibody depleted co-culture medium, and adding activated proteins to culture, A Disintegrin And Metalloprotease 8 (Adam8) gene was found to be required for myCAF maintenance. Using SELEX, we isolated 5 RNA aptamers targeting the human Adam8 soluble MP domain. Using in vitro quantification of Adam8 MP activity with human Adam8 fluorogenic peptide substrate and recombinant human Adam8 protein, Adam8 Apt-1 with IC₅₀=33nM and K_d=29nM was selected. APt-1 does not inhibit human Adam 10 or 17 MP activity and remains extracellular. The core inhibitory domain of Apt-1 aptamer contains 23nt. Following induction of the myCAF phenotype and cancer stemness in MB-231+MSC coculture, addition of Apt-1 significantly decreased myCAF and cancer stemness markers. In murine NOD/scid xenograft model, 10⁶ luciferase-MB-231 and 10⁶ MSC were implanted in the R3 position at week 0. Apt1 was administered (10mg/kg via tail vein every 2 days) from week 3 to week 6. MB-231 volume (bioluminescence) was significantly decreased following Apt1. (Table)

Conclusion: Adam8 is expressed in MB-231 breast cancer cells in the context of MSC/myCAF coculture and MB231 stemness and is required for MB-231 cancer growth. Aptamer ablation of Adam8 extracellular activity reverses MB-231 growth.

MB-231 and MSC Murine Xenograft Model

	MB-231 and MSC Xenograft Model					
	MB-231 Bioluminescence Photo Flux (p/s)					
	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
Saline Control (n=3)	35492 ±165	63729 ±130	91648 ±123	117481 ±1397	126042 ±1923	151524 ±600
Apt1 (n=3)	35551 ±133	63694 ±159	52678 ±184 *p<0.01 vs Control	20027 ±4270 *p<0.01 vs Control	14659 ±3748 *p<0.01 vs Control	9507 ±1041 *p<0.01 vs Control

In murine NOD/scid xenograft model, 10^6 luciferase-MB-231 and 10^6 MSC were implanted in the R3 position at week 0. Apt1 was administered (10mg/kg via tail vein every 2 days) from week 3 to week 6.

Disclosure(s):

Zhiyong Mi, PhD: No financial relationships to disclose

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P2-22-01

Nuclear long non-coding RNA LINC00355 expression and treatment using antisense oligonucleotides in Estrogen Receptor positive late-stage relapse breast cancer

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Late-stage relapse also known as late recurrence breast cancer is a metastatic disease that occurs more than five years after initial adjuvant endocrine therapy treatment. The 5-year relative survival rate is less than 30% and there are limited treatment options for patients with late-stage relapse because of poor performance status. We hypothesize that long non-coding RNA (lncRNA) protein interactions regulate genes to promote late-stage relapse and these interactions can be targeted using RNA therapeutics. To address this, we used RNA-sequencing to identify LINC00355 to be up-regulated in 24 late-stage relapse samples compared to a unique cohort of 72 primary breast cancer samples. Analysis of 480 primary breast cancer samples from The Cancer Genome Atlas (TCGA) also shows decrease expression of LINC00355 compared to late-stage relapse. To better assess LINC00355 cell type expression, we analyzed 26 publicly available primary breast cancer single cell sequencing data samples and detected 0.90% or less of cells expressing LINC00355, which was restricted to cancer epithelial cells. Due to cellular localization playing an important role in lncRNA function, we isolated nuclear and cytoplasmic lysates and orthogonally validated with RNAscope in situ hybridization (RNA-ISH) to show that LINC00355 is located in the nucleus of MCF7 long-term estrogen deprived (MCF7 LTED) cells. LTED cells are deprived of estrogen for longer than three years meant to recapitulate the acquired resistance to aromatase inhibitors.

Next, we determined that LINC00355 binds to MENIN protein to regulate p27KIP expression to promote proliferation with UV crosslinking immunoprecipitation and chromatin immunoprecipitation qPCR of LINC00355 overexpression and mutant constructs. Furthermore, RNA-ISH assays validated high nuclear expression of LINC00355 and RNA-ISH protein co-detection assays showed co-localization of LINC00355-MENIN interaction in a panel of late-stage relapse breast cancer patient tissues compared to primary tissues. Lastly to determine clinical significance, we treated MCF7 LTED cells with two locked nucleic acid antisense oligos (ASOs) targeting LINC00355 to observe a significant decrease in proliferation, cell viability, and invasion. Overall, this is the first study to show the importance of lncRNA-protein interactions and therapeutically target lncRNAs with ASOs in late-stage relapse breast cancer. Moving forward, we intend to further understand how LINC00355 contributes to the progression of late-stage relapse with the intent of creating novel cancer diagnostics and therapies.

Disclosure(s):

DeAnna Wells, n/a: No financial relationships to disclose

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The role of circular RNAs in triple-negative breast cancer and chemotherapy resistance

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Background: Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer-related death among women worldwide. Triple-negative breast cancer (TNBC) is an aggressive subtype representing 15-20% of all breast cancers. TNBC often ends with a poor clinical outcome due to high histological grade and recurrence rates with few treatment options. Chemotherapy remains the standard of care for TNBC treatment, but unfortunately, patients frequently develop resistance, and alternative treatment strategies for the chemoresistant disease remain a major unmet need. circRNAs are newly identified non-coding RNA molecules with covalently closed circular structures. Recently, an increasing number of studies have indicated that circRNAs play crucial roles in regulating tumor development and chemoresistance. However, the role of circRNAs in the process of TNBC chemotherapy resistance is not yet fully clear. Materials and methods: To study the molecular functions of circRNAs in TNBC chemoresistance, identify alternative biomarkers for chemotherapy-resistant disease, and elucidate novel therapeutic targets, doxorubicin-resistant (Doxo-R) and paclitaxel-resistant (Taxol-R) cell lines were generated using TNBC models. Results: Doxo-R and Taxol-R cells exhibited a 3- and 12-fold decrease in sensitivity to their respective chemotherapeutic agents. We identified a large spectrum of gene expression changes that were acquired in Doxo-R and Taxol-R cells. The expression of circRNAs was profiled using circRNA microarrays, and top hits were validated using RT-PCR. We identified 429 and 310 circRNAs that were differentially expressed in Doxo-R and Taxol-R resistant cells respectively compared to the parental chemosensitive cell line ($|FC| \geq 1.5$; p value < 0.05). Of these, 66 were commonly differentially expressed between the two chemotherapy resistant models. Conclusions: These results revealed that Doxo-R and Taxol-R TNBC cell lines were successfully established and serve as good models for studying the mechanisms of chemotherapy resistance and the regulatory roles of circRNAs in the development of chemoresistance in TNBC. Increasing knowledge of the important functions of circRNAs underlying drug resistance will provide new opportunities for developing efficacious therapeutic strategies and prognostic/predictive biomarkers for TNBC.

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Effect of miR-660-5p in breast cancer progression

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Background: Breast cancer (BC) is the most diagnosed cancer in women worldwide. MicroRNAs (miRNAs) are involved in different processes of BC and their deregulation can cause them to act as oncogenes or tumor suppressors, participating in cancer progression or also as therapeutic target. Using The Cancer Genome Atlas (TCGA) database, we found that miR-660-5p is significantly overexpressed and associated with poor survival in patients with this pathology. Moreover, it is reported that miR-660-5p can induce BC progression through transcription factor CP2 (TFCP2) and the down regulation of tet-eleven translocation 2 (TET2). In this project, we propose to identify the role of miR-660-5p in proliferation, migration, invasion, angiogenesis, and possible targets involved in these processes in BC cell lines. Methods: Basal levels of miR-660-5p were determined in BC cells MDA-MB-231 and MCF-7, and in human epithelial breast cells MCF-10A by RT-qPCR. The effect of miR-660-5p was evaluated on proliferation, migration, and invasion processes using MDA-MB-231 and MCF-7 cells. HUVEC cells were used to assess angiogenesis. All cell lines were transfected with miR-660-5p inhibitor. Analysis of nine miRNA-target prediction databases was made to identify targets of

miR-660-5p. We selected the target genes predicted by at least three of these programs, and their expression was evaluated by RT-qPCR in a customized 384-well plate. Results: We found that miR-660-5p is significantly upregulated in MDA-MB-231 and MCF-7, compared to MCF-10A cells. In addition, we observed a significant decrease in proliferation, migration, and invasion of BC cells transfected with miR-660-5p inhibitor, compared to non-treated cells and miRNA inhibitor negative control treated cells. Similarly, we observed a significant decrease in angiogenesis of HUVEC cells transfected with miR-660-5p inhibitor. Furthermore, of all the miR-660-5p targets identified by prediction databases 21 were selected, and of these, 7 were observed upregulated and 1 downregulated. Conclusions: The results show that miR-660-5p is upregulated and involved in proliferation, migration, invasion, and angiogenesis of BC, which may lead us to suggest that this miRNA act as an onco-miRNA. In addition, seven potential miR-660-5p target genes were identified, but further validation assays are needed to clarify their implication in this disease.

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Functional effect of miR-1307-3p on breast cancer progression

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Background: MiRNAs are non-coding RNA molecules and its function is the regulation of gene expression. In cancer, the deregulation of miRNAs allows them to act as oncogenes or tumor suppressors. From an analysis of the expression of miRNAs in breast cancer (BC) in The Cancer Genome Atlas (TCGA), it was identified that miR-1307-3p is significantly overexpressed in the tumor tissue compared to healthy tissue from patients. So far, in BC, it has only been reported that this miRNA inhibits SMYD4 and that it is involved in resistance to cisplatin through its effect on Mdm4. In this project we propose to identify the role of miR-1307-3p in proliferation, migration, invasion, angiogenesis, and possible targets involved in these processes in BC cells. Methods: RT-qPCR was used to evaluate basal levels of miR-1307-3p in the BC cell lines MDA-MB-231 and MCF-7, and the human epithelial breast MCF-10A cells. Later, we determined the effect of miR-1307-3p on proliferation, migration, and invasion in MDA-MB-231

and MCF-7, and angiogenesis in the HUVEC endothelial cells. All assays were carried out using the miR-1307-3p inhibitor. Finally, nine miRNA-target prediction databases were analyzed to identify potential miR-1307-3p target genes, and their expression was analyzed by RT-qPCR in a designed 384-well plate. Results: We found that miR-1307-3p is overexpressed in MDA-MB-231 and MCF-7, compared to MCF-10A cells. We also identified that transfection with the miR-1307-3p inhibitor causes a significant decrease in the processes of proliferation, migration, invasion, and angiogenesis, when compared with untreated or negative control transfected cells. For its part, prediction databases analysis allowed us to identify 19 potential targets of miR-1307-3p. Finally, by RT-qPCR, the overexpression of 3 and the downregulation of 2 genes were confirmed. Conclusions: MiR-1307-3p is overexpressed in BC cells. Furthermore, miR-1307-3p induces the processes of proliferation, migration and invasion in BC cells, and angiogenesis in HUVEC cells. These observations suggest that miR-1307-3p can acts as an onco-miRNA. In addition, the expression of 5 of the predicted target genes were altered by miR-1307-3p inhibitor. Further analysis to validate the implication of this miR-1307-3p targets are needed to understand its importance in BC.

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Patient-derived xenografts allow deconvolution of single agent and combination chemotherapy responses in triple-negative breast cancer

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Background: Triple-negative breast cancer (TNBC) patients frequently receive combination chemotherapy treatment, but a direct comparison of response to carboplatin, docetaxel, and their combination in 50 TNBC patient-derived xenografts (PDXs) showed that combination treatment was largely ineffective at generating enhanced responses over the best single agent. This suggests de-escalation of chemotherapy may be possible if molecular mechanisms and biomarkers underlying response to individual treatments can be identified. To this end, we performed multi-omics profiling for the 50 TNBC PDXs. Methods: Orthotopic TNBC PDXs were treated with four weekly cycles of docetaxel, carboplatin, or the combination. Changes in tumor volume after 4 weeks of treatment were assessed quantitatively and by modified RECIST criteria. Genomic, transcriptomic, and mass-spectrometry-based proteomic profiling were performed on baseline tumors prior to treatments to identify associations with chemotherapy response at the gene and pathway level. ProMS was used to integrate both RNA and protein data to select a 5 RNA feature combination for optimized prediction of carboplatin response in a logistic regression model. Publicly available neoadjuvant chemotherapy clinical datasets with transcriptomic data and response information used for validation/testing included TNBC samples from: GSE18864, I-SPY2 (GSE194040), and BrighTNess (GSE164458). Results: Proteogenomic profiles revealed distinct genes associated with response to each agent and their combination, respectively, suggesting distinct molecular mechanisms underlying response to each treatment. A substantial number of genes associated with single agent and combination treatment were validated in multiple independent patient cohorts receiving platinum and taxane containing neoadjuvant therapy, confirming clinical relevance of our PDX panel. For the same treatment, different types of molecular data identified distinct sets of associated genes,

providing highly complementary information. At the pathway level, RNA and protein data converged to metabolic and E2F/G2M related pathways which were upregulated in PDXs resistant or responsive to all treatment types, respectively, while variable levels of MYC-related proliferation pathways were observed across all treatments suggesting pathways that are common across and unique to different treatments. Several individual genes found to be higher in PDXs with better response to either single-agent had discriminatory power in external clinical TNBC datasets treated with similar neoadjuvant chemotherapy regimens. In addition, a logistic regression-based carboplatin response prediction model trained to select a group of 5 RNA markers (TKT, MAGI2, ATF6B, MCM7, LRP6) using both RNA and protein data performed the best in predicting response to cisplatin in a clinical TNBC dataset vs predicting response to other datasets with taxane and platinum + taxane combination containing chemotherapy regimens, demonstrating specificity of the prediction model. These results suggest potential individual biomarkers or biomarker combinations to select TNBC tumors that may respond to either single agent carboplatin, docetaxel, or their combination. PDXs refractory to all treatment arms had higher levels of proteostasis-related pathways including proteasome degradation and the unfolded protein response (UPR) related to endoplasmic reticulum stress and altered levels of chromatin regulation. Subsequent pharmacological targeting of the UPR pathway and targeting HDACs enhanced chemotherapy response. Conclusion: Proteogenomic characterization identifies molecular mechanisms and putative biomarkers for stratifying TNBC tumors for single or combination chemotherapy treatments, suggests targeted therapies to augment chemotherapy response, and provides a valuable resource for researchers and clinicians.

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Genomic Evaluation of Malignant Phyllodes Tumors Reveals Multiple Targetable Opportunities

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Background: Malignant phyllodes tumors (MPT) are rare fibroepithelial breast tumors that disproportionately affect young women. Despite high local and distant recurrence rates, treatment is almost exclusively surgical. With no known effective chemotherapy or targeted systemic therapy options, metastatic progression portends dismal prognosis. Current national guidelines do not recommend biomarker testing in the non-metastatic setting. Management of metastatic disease follows principles of soft tissue sarcoma recommending Next-Generation Sequencing on an individual basis for patients who may qualify for clinical trials or are refractory to standard therapies. In the largest genomic profiling effort of MPT to date, we sought to describe the genomic landscape of MPTs through comprehensive genomic profiling (CGP) and immunotherapeutic biomarker analysis.

Methods: Cases of sequenced MPT were identified from a CLIA-certified, CAP-accredited laboratory database (Foundation Medicine, Cambridge, MA). Cases were categorized as localized/locally recurrent or metastatic. All cases underwent CGP by DNA extraction from FFPE samples using a hybrid capture, adaptor ligation-based next generation sequencing assay, and all classes of genomic alterations, microsatellite instability (MSI), and tumor mutational burden (TMB) were evaluated. PD-L1 expression by IHC was measured by the DAKO 22C3 assay (scored CPS) or the Ventana SP142 assay (scored as IC). Patient

characteristics and results of CGP of MPT were summarized by either N (%) or median (range). Factors from MPT were compared to all cases of breast carcinoma in the lab database. Fisher's Exact Tests were used to test for differences between groups and analysis of variance was used to test for differences for continuous variables.

Results: Of 135 MPT cases identified; 94 (69.6%) were localized/locally recurrent (breast, chest wall, soft tissue, skin, or lymph node) and 41 (30.4%) were metastatic (73% lung, followed by bone, liver, other intraabdominal). All patients were female with a median age of 54 years (range 14-86). The median TMB across samples was 2.5 mut/Mb and only 3 were TMB-high tumors (>10mut/Mb). Over 1/3 (36.8%) of samples were PD-L1+ via Ventana SP142 assay (≥ 1) and 21.4% were PD-L1+ via Dako 22C3 assay (CPS ≥ 10). All evaluable cases (N=132) were microsatellite stable. The ten most commonly altered genes included TERT-promoter (69.7%), CDKN2A (45.9%), TP53 (37.8%), NF1 (35.6%), CDKN2B (33.3%), MED12 (28.9%), MTAP (27.7%), KMT2D (22.2%), PIK3CA (20.0%), PTEN (18.5%), and RB1 (18.5%); notably distinct in frequency from the breast carcinoma cohort (Table 1). Alterations in genes affecting cell cycle regulation (i.e. CDKN2A/B and TP53) were mutually exclusive from one another ($p < 0.001$). Several tumors harbored genomic alterations with FDA-approved indications in other tumor types were found including: NF1, PIK3CA, EGFR Exon 19/20 insertions, and BRAF V600E mutations. There were no statistically significant differences between alterations in localized/locally recurrent versus metastatic specimens.

Conclusions: In the largest genomic evaluation of localized/locally recurrent or metastatic MPTs to date, multiple clinically actionable mutations for further exploration were found. TERT-promoter was altered in the majority of cases. PDL-1 was expressed in over 1/3 of cases suggesting that clinical investigation of immunotherapeutic strategies is warranted. Routine sequencing of metastatic MPT may provide additional information to guide treatment decisions and clinical trial enrollment.

Table 1. Frequency of Genomic Alterations identified in 135 cases of Malignant Phyllodes Tumors.

Gene	Mutations in Phyllodes Cohort (N=135)	Mutations in Phyllodes Cohort (%)	Mutations in Breast Cohort (N=44,798)	Mutations in Breast Cohort (%)	p-value
<i>TERT*</i>	76	69.7%	467	1.1%	<0.001
<i>CDKN2A</i>	62	45.9%	3137	7.0%	<0.001
<i>TP53</i>	51	37.8%	23315	52.0%	<0.001
<i>NF1</i>	48	35.6%	2954	6.6%	<0.001
<i>CDKN2B</i>	45	33.3%	2258	5.0%	<0.001
<i>MED12</i>	39	28.9%	89	0.2%	<0.001
<i>MTAP**</i>	18	27.7%	1021	3.7%	<0.001
<i>KMT2D</i>	30	22.2%	943	2.1%	<0.001
<i>PIK3CA</i>	27	20.0%	16062	35.9%	<0.001
<i>PTEN</i>	25	18.5%	5735	12.8%	0.053
<i>RB1</i>	25	18.5%	3479	7.8%	<0.001
<i>EGFR</i>	23	17.0%	1117	2.5%	<0.001
<i>SETD2</i>	12	8.9%	451	1.0%	<0.001
<i>NRAS</i>	11	8.1%	272	0.6%	<0.001
<i>BRAF</i>	10	7.4%	667	1.5%	<0.001
<i>BCOR</i>	7	5.2%	232	0.5%	<0.001

* N=109 in Phyllodes Cohort, N=42,382 in Breast Carcinoma Cohort

** N=65 in Phyllodes Cohort

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Laura H. Rosenberger, MD, MS: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-23-05

Trastuzumab-Induced Tumor Microenvironment Changes in Early HER2+ Breast Cancer

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Background Trastuzumab (H) is a critical component of therapy (tx) for HER2+ breast cancers (BCs) and can induce anti-tumor immune responses that as part of its mechanism of action. Pre-clinical studies have suggested that antibody-dependent cell-mediated cytotoxicity (ADCC) through NK cells is a major driver of the immune response. However, there is also evidence that macrophages and dendritic cells (DCs) can play an important role in H immune response through antibody-dependent cellular phagocytosis (ADCP). Here, we present pre- and post-tx gene expression and immunohistochemistry (IHC) data to characterize the tumor microenvironment (TME) changes in response to a single dose of H in patients (pts) with early HER2+ BC. Methods Pts with Stage I-III HER2+ BC with minimum 1 cm tumors were eligible. Pts received 8 mg/kg IV H followed by tissue collection. There was a minimum of 14 days between (btw) H and post-tx tissue collection. Pre- and post-tx tissues were assessed for tumor-infiltrating lymphocytes (TILs), immune-related gene expression, and AE1/3, CD31, CD4, CD8, CD11b, CD68, and CD56 expression through IHC. Results Thirteen pts were enrolled and evaluable. 5/13 were estrogen-receptor positive (ER+). TILs were assessed independently by two pathologists and the results averaged. Tx with H resulted in an increase in TILs in the post-tx tissue ($p < 0.01$). Pre-tx TILs ranged from 2-80% (median 6%) and post-tx TILs ranged from 2-80% (median 20%). 6/13 pts had immune infiltration (Inf), defined as a TIL increase of greater than 1 decile btw pre- and post-tx samples. 2/6 pts with Inf were ER+. Pts with Inf had a significantly higher DC immune signature (ISS) compared to pts without Inf ($p < 0.01$, univariate analysis). No other ISS reached significance. 6 pts had paired pre- and post-tx samples evaluated by IHC. 4/6 pts had Inf per prior definition. Pts with Inf had an increase in CD11b+ (includes macrophages and some DCs) and CD56+ cells (includes NK cells) after H tx within the tumor compartment ($p < 0.05$). Pts with Inf had an increase in CD11b+, CD56+, and CD44+ cells in the stromal compartment ($p < 0.05$). Conclusions Innate immune cells such as macrophages and DCs are key players in H-induced immune response in the early HER2+ BC TME. This data is consistent with prior pre-clinical findings.

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Laura C. Kennedy, MD PhD: No financial relationships to disclose

Rebeca Alvarez, MD: No financial relationships to disclose

Suzanne Dintzis, MD PhD: No financial relationships to disclose

Vijayakrishna K. Gadi, M.D., Ph.D.: 3rdEyeBio: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Agendia Inc: Contracted Research (Ongoing); AmunBio: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); EMCIF: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Hologic: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); New Equilibrium Biosciences: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Novilla: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Phoenix Molecular Designs: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Puma: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); SEngine Precision Medicine: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Tizona Therapeutics: Contracted Research (Ongoing)

12/7/2022

7:00 AM - 8:15 AM

P2-23-06

Estrogen receptor-negative progesterone receptor-positive breast cancer is a molecularly distinct group characterized by the down-regulation of genes controlled by ESR1 and SUZ12

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Background: Single hormone receptor-positive breast cancers (BCs) display two distinct phenotypes: ER+/PgR- and ER-/PgR+ further stratified by their HER2 status. Their molecular features are not well defined. Our study aimed to identify differentially expressed genes in ER-/PgR+ BCs compared to other phenotypes. Methods: Our cohort comprised 15 ER+/PgR-/HER2-, 11 ER+/PgR-/HER2+, 17 ER-/PgR+/HER2-, 9 ER-/PgR+/HER2+, 5 ER+/PgR+/HER2-, and 5 ER-/PgR-/HER2- invasive BCs collected from 9 Polish and 2 Hungarian centers. The cases were selected from a larger cohort after being matched according to grade, HER2 status, lymph nodes, and distant metastasis status. ER-/PgR+ group was thoroughly validated via immunohistochemistry [Kunc et al. 2022]. The expression of 776 genes was profiled with nCounter® Breast Cancer 360™ Panel in archival formalin-fixed paraffin-embedded tissue samples. A gene was defined as differentially expressed between groups if it met the following criteria: the log2 fold-change in the expression of >1 or <-1 and the p-value < 0.05 (Mann-Whitney U test). Additionally, weighted correlation network analysis (WGCNA) was performed to identify modules of at least 15 highly correlated genes. Subsequently, the association between gene modules and PgR status in ER- subgroup was performed. Identified mRNAs were subjected to functional annotation analysis to determine the top enriched pathways. Results: ER-/PgR+ BCs were characterized by significantly lower expression of ESR1 compared to double-positive (p< 0.001) and ER+/PgR- tumors (p< 0.001), whereas PGR expression was higher compared to ER+/PgR- (p< 0.001), and no significantly different from ER+/PgR+ BCs (p=0.14). Triple-negative BCs had no detectable PGR mRNA. Four genes (MIA, ID4, FOXC1, CDC20) were consistently up-regulated and six genes (FAM214A, MLPH, NFKBIZ, FOS, SLC44A4, SPDEF) were down-regulated in ER-/PgR+/HER2- tumors compared to other HER2- subgroups. Compared to ER+/HER2- BCs, ER-/PgR+/HER2- cases showed up-regulation of 15 genes associated with response to vitamin D, response to ketone, and regulation of transcription, and downregulation of 33 genes

involved in response to estrogen, negative regulation of cell population proliferation, regulation of epithelial-mesenchymal transition, and controlled by ESR1 and SUZ12. In WGCNA analysis of the ER⁻ subgroup, PgR status was negatively correlated with 4 gene modules and positively correlated with 1 gene module. In line with differential gene expression analysis, genes negatively correlated with ER⁻/PgR⁺ status are regulated by ESR1 and SUZ12 and are involved in the regulation of cell proliferation, extracellular matrix organization, and NOTCH1 signaling. Genes positively correlated with ER⁻/PgR⁺ status are regulated by E2F4, FOXM1, SIN3A, NFYB, E2F1, FOS, IRF1, ZMIZ1, and UBTF and participate in cell cycle, regulation of mitosis, and microtubule cytoskeleton regulation. Conclusions: ER⁻/PgR⁺ BCs display a distinct mRNA expression profile characterized by the down-regulation of genes controlled by ESR1 and SUZ12. The latter as a part of Polycomb Repressive Complex 2 contributes to chromatin silencing, and some previous studies suggested its role in the regulation of steroid hormone receptors expression. Additionally, ER⁻/PgR⁺ BCs overexpress FOXC1 which is linked to more aggressive, high-grade, and treatment-resistant breast cancers. Our data indicate the need to unravel the mechanism of epigenetic regulation of PGR expression, especially its methylation status, in ER⁻/PgR⁺ breast cancer.

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

P2-23-07

DNA Methylation Analysis of Triple Negative Breast Cancers

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Background: Triple negative breast cancers (TNBC) are characterized by the absence of estrogen receptors, progesterone receptors, and HER2 receptors on immunohistochemical analysis (IHC). This subtype of breast cancer has been traditionally associated with unfavorable prognosis. TNBC includes morphologically diverse mammary carcinomas including apocrine, metaplastic, medullary and other less common variants with heterogeneous clinical behavior and outcome. Despite previous efforts to further characterize TNBC with genomic and transcriptomic techniques, there is no specific targeted therapy for TNBC. Cytotoxic chemotherapy remains the mainstay of systemic treatment for these patients. DNA methylation has proved to be a promising tool in classifying a variety of cancers. In this study, we aim to analyze TNBC using comprehensive DNA methylation profiling. Method: DNA methylation profiling was performed in TNBC cases from a single academic institution using Illumina Infinium MethylationEPIC Kit. The tumors were obtained from formalin-fixed paraffin-embedded tissue from surgical specimens. Unsupervised clustering analysis based on the methylation profile was performed. Clinical, pathological, and genetic features were analyzed between the clusters. Results: We analyzed 44 cases (all female; median age 61 years) with treatment naïve TNBC diagnosed from March 2011 to April 2018. Median follow-up time was 58 months. Thirty-four (77%) patients were identified as white with the remaining 10 (23%) as non-white. Thirty-four tumors (77%) were classified as invasive ductal carcinoma of no special type, six

(14%) as apocrine carcinoma, and four (9%) as metaplastic carcinoma. Six tumors (14%) were grade 2 and 38 (86%) were grade 3. Lymphovascular invasion was noted in 7 patients (16%). Tumor size ranged from 4 to 45 mm (median: 20 mm). Lymph node involvement was identified in 8 (18%) patients. Eleven (25%) patients harbored germline BRCA1/2 mutations. During the follow up period, 7 patients developed recurrent disease: 3 had local recurrences, 4 patients were found to have metastatic disease, and 1 patient had both local and distant recurrence. At last follow-up, 34 patients (77%) showed no evidence of disease, while 4 (9%) were alive with disease and 5 (11%) had died of disease. In this cohort, we identified three distinct DNA methylation clusters. In Cluster 1 (n=9), the patients were significantly older (mean age: 72 years; p=0.008) and tumors were more likely to be of apocrine morphology (56%, p= 0.001), of lower grade (55% were grade 3; p=0.009), and showed lower proliferation index (mean ki-67: 32%; p= 0.002). Cluster 3 (n=28) included younger patients (mean: 55 years) and tumors with higher grade (92% were grade 3) and proliferation index (mean ki-67: 75%). Cluster 2 (n=7) represented cases with intermediate features between Clusters 1 and 3. All patients in Cluster 1 were white, while Clusters 2 and 3 included non-white women. Cluster 1 included a significantly higher percentage of HER2-low tumors (HER2 1+ or 2+ by IHC and negative fluorescence in situ hybridization) (p=0.03; cluster 1: 89%, cluster 2: 28%, cluster 3: 46%). The vast majority of patients with germline BRCA1/2 mutation were found in Cluster 3 (67% of patients with genetic testing in Cluster 3 had germline BRCA1/2 mutation). There was no difference between the clusters in relation to stage, recurrence, and outcome. Conclusion: DNA methylation profiling is a promising tool to classify TNBC patients into clinicopathologically relevant groups, and we are continuing to expand this cohort. Classification by DNA methylation profile may result in better risk stratification for TNBC patients, which can inform their system therapy. In addition, specific methylation profiles have the potential to lead to the development of specific targeted therapies to improve the prognosis and survival for these patients.

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

P2-23-08

Concordance of Targeted Sequencing from Circulating Tumor DNA and Paired Tumor Tissue

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Purpose

In this study, we evaluated the concordance of targeted sequencing results between paired ctDNA and tumor samples from early breast cancers scheduled for curative surgery with or without adjuvant therapy. If high concordance was observed, pre-operative ctDNA testing could serve as a non-invasive surrogate for variants meant to be revealed after definite surgery. On the other hand, poor concordance may hamper wide clinical absorption of liquid biopsy early breast cancer.

Materials and Methods

The study VGH-TAYLOR: Comprehensive precision medicine research on the heterogeneity of Taiwanese breast cancer patients, consisted of three years enrollment and approximately four years follow-up after enrollment. Individual subject was assigned into Group 1 [planned to receive surgery as first-line treatment and followed by adjuvant therapy, Group 2 [planned to receive neoadjuvant therapy as the first-line treatment and followed by surgery], and Group 3 [diagnosed with de novo and treatment naïve stage IV breast cancer, or stage IV breast cancer with recurrence beyond three years after surgery]. Molecular profiling and potential biomarkers were determined using OncoPrint Comprehensive Assay v3 from FFPE tissues and OncoPrint Breast cfDNA Assay v2 from plasma. OncoPrint Comprehensive Assay is a targeted sequencing of NGS experiments were performed with TMO comprehensive using FFPE tissues, included 161 cancer-relevant genes and types of mutation detected such as frameshift, missense, synonymous, SNV, Indel, and CNV. OncoPrint Breast cfDNA Assay detects breast-derived cfDNA including hotspot genes: AKT1, EGFR, ERBB2, ERBB3, ESR1, FBXW7, KRAS, PIK3CA, SF3B1, TP53 (~152 hotspots), CNVs: CCND1, ERBB2, FGFR1, and full length TP53 (~80% coverage). Common genes interrogated by both ctDNA and TMO assay were identified, and concordance between paired targeted sequencing results from the same individuals were reported.

Results

We reported the mutational landscape of initial 612 patients interrogated with the OncoPrint Breast cfDNA assay; 239 out of 612 patients reported at least one mutation (39%). Among 246 patients assayed for both ctDNA and tumor tissue, cfDNA assay detected 73 (29.6%) and TMO comprehensive assay detected 201 (81.7%) breast cancers with at least one variant (c2 test, $p=0.001$). Sixty-seven (25.6%) were tested positive for both liquid and tissue assays, while cfDNA and TMO comprehensive assay detected additional 10 (4%) and 138 (56%) cases, which were not identified by the other platform. Table 1 details the distributions of called variants among common targeted genes.

Conclusion

In current study, we evaluated the concordance of called variants between targeted sequencing from ctDNA and tumor tissue among an early breast cancer cohort in Taiwan. Only one-quarter of patients were positive for both cfDNA and TMO comprehensive assays from the same

subject, indicating assay-specific sensitivity inevitably resulting in diagnostic discrepancy. Another plausible explanation came from the early stage nature of interrogated patients, which may inherit fewer ctDNA spillage from tumor and compromise detectability from liquid biopsy. The most prevalent mutant genes from both platforms were TP53 (68.3%) and KRAS (53.5%), both were well-known drivers in cancers. From breast cancer actionability, PIK3CA (39.4%) mutation is a biomarker for the FDA-approved PI3Ka inhibitor such as alpelisib, AKT1 (45.9%) mutation for agents such as capivasertib (AZD5363) and ipatasertib, and ERBB2 mutation for tyrosine kinase inhibitor such as neratinib. Our study showed that tumor should be the preferred source for targeted sequencing, and additional 4% of variants would be revealed from liquid biopsy.

Table 1. Distributions of variants from common targeted genes (n=6) from cfDNA and TMO comprehensive assay.

	ctDNA	Tumor tissue	Both detectable	Both non-detectable	Total affected
AKT1	1	113	1	133	113(45.9%)
ERBB2	0	42	0	204	42(17.1%)
KRAS	4	130	3	115	131(53.5%)
PIK3CA	15	93	11	149	97(39.4%)
SF3B1	3	14	1	230	16(6.5%)
TP53	65	146	43	78	168(68.3%)

Disclosure(s):

Chi-Cheng Huang, MD, PhD: No financial relationships to disclose

Ling-Ming Tseng, MD: No financial relationships to disclose

12/7/2022

7:00 AM - 8:15 AM

P2-23-09

Ultra-high Tumor Mutation Burden in Metastatic/Clinically Advanced Breast Cancer (MBC)

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Background: High (HTMB) tumor mutation burden (TMB) defined as ≥ 10 mutations/megabase (Mb) identifies breast cancer patients who could benefit from pembrolizumab. The higher the TMB the greater the likelihood of benefit. The goal of this analysis was to determine the frequency and genomic landscape of MBC with ultra-high TMB (UHTMB) defined as a TMB > 20 mutations/Mb. Design 2,049 MBC patients (pts) underwent hybrid capture based comprehensive genomic profiling for genomic alterations (GA) in at least 324 genes including determination of TMB to guide therapy decisions using the FoundationOne@CDx assay. ER, PR and HER2 expression were abstracted from submitted pathology reports. Results: 165 of 2049 MBC (8.1%) had HTMB > 10 mutations/Mb, among these 45 (2.2% of all cases) had UHTMB. When compared with the 2,004 non-UHTMB MBC pts with TMB < 20 mutations/Mb, the 45 UHTMB pts were older (mean 64.6 yrs vs 58.2 yrs; $p < .0001$), more often had lobular histology (40.00% vs 14.5%; $p < .0001$) and ER+ disease (86.6% vs 70.0%), had higher average driver GA/tumor (9.84 vs 5.7; $p < .0001$), and less often had TNBC (13.3% vs 27.0%; $p = .041$) compared to non-UHTMB high cancers. There were no significant differences in ancestry. Mutation signature analysis revealed that APOBEC was predominant in UHTMB samples (82.5%) with a minor portion with an MMR signature (10%), however, MSI-H status was significantly higher in UHTMB high cases (11.6% vs 0.40%; $p < .0001$). GA more frequently identified in UHTMB cases included CDH1 (45.50% vs 14.32%; $p < .0001$), PIK3CA (81.80% vs 37.86%; $p < .0001$), CDKN2A (11.40% vs 3.19%; $p = .017$), ARID1A (25.00% vs 5.01%; $p < .0001$) and NF1 (20.50% vs 5.94%; $p = .0014$). PD-L1 (CD274) gene amplification (2.3% vs 1.3%) or protein expression by the Ventana SP142 assay (57.14% vs 51.10%) were not significantly different. Conclusions: UHTMB MBC is a rare but clinically important subset in breast cancer that could have high response rates to single agent pembrolizumab. This phenotype is driven by APOBEC mutagenesis, more often seen in ER+ lobular cancers, and have higher frequencies of MSI-high status and mutations in CDH1 and PIK3CA.

Disclosure(s):

Kristina Fanucci, MD: No financial relationships to disclose

maryam lustberg, MD MPH: AstraZenica: Consulting Fees (e.g., advisory boards) (Ongoing); Hengrui USA: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing)

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12/7/2022

7:00 AM - 8:15 AM

P2-23-10

Gene expression and mutation profiles in HER2-mutated metastatic breast cancer

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Background: HER2 activating mutations occur in 2-5% of metastatic breast cancer (MBC) patients. These mutations cluster in the kinase domains and at amino acids 309-310 in the extracellular domain. The MutHER, SUMMIT, and PlasmaMATCH clinical trials have shown neratinib monotherapy or neratinib plus fulvestrant combination produce clinical benefit in 28% to 46% in HER2-mutated MBC patients, but median progression-free survival was only 3.6 to 5.4 months. In order to improve the knowledge and outcomes for patients with HER2-mutated MBC, we compared the mutational landscape and gene expression of HER2-mutated MBC patients to HER2-amplified and HER2-wild type MBC patients. Methods: De-identified data from a cohort of stage 4 breast cancer patients (n=1,834) sequenced with the Tempus xT (DNA-seq of 595-648 genes, whole exome-capture RNA-seq) solid tumor assay was retrospectively analyzed. The most recent sample of the patient was used for analyses. Patients were stratified by HER2 mutational status: HER2-wild type (HER2-wt), HER2-amplifications (HER2-amps), or HER2-mutants (HER2-muts). Additionally, a sub-analysis was conducted among HER2-mutants to compare kinase domain mutations to other HER2 mutations. Patient demographic characteristics were compared between groups along with the prevalence of individual gene alterations (pathogenic/likely pathogenic short variants and copy number alterations), adjusted for false-discovery. Results: Within the cohort, 62 (3.4%) patients harbored HER2-muts tumors and 125 (6.8%) patients had HER2-amps tumors. Three patients, whose tumors had both HER2 mutation and amplification, were classified among the HER2-

mutants. Relative to the HER2-wt cohort (median = 53 yo), HER2-mutants patients were older (median = 55 yo) while HER2-amps patients were younger (median = 49 yo) ($P < 0.001$). Significant differences were observed in genomic alterations co-occurring with HER2-mutants compared to HER2-wt and HER2-amps, including CDK12 (4.8% vs 0.2% vs 74%), CDH1 (44% vs 11% vs 4.8%), ESR1 (4.8% vs 21% vs 8.8%), TOP2A (3.2% vs 0.5% vs 14%), and ERBB3 (11% vs 0.9% vs 0.8%). Of note, the majority of CDK12 mutations are amplifications (96%). Median HER2 mRNA log₁₀ gene expression differed among the three cohorts (HER2-mutants (3.79), HER2-wt (3.56), HER2-amps (4.54); $P < 0.001$). Among HER2-mutants patients, 46 (74.2%) patients had HER2 kinase domain mutations (HER2-kinase). Relative to other HER2-mutants patients, HER2-kinase patients displayed a lower prevalence of CDH1 mutations (35% vs 69%; $P = 0.018$). No significant differences were noted in ERBB3 co-mutations, however all 7 were missense variants (5 of which are p.E928G variants) and occurred among HER2-kinase patients. Conclusions: Real-world data show increased HER2 mRNA expression in both HER2-mut and HER2-amps MBC patients. Co-occurring genomic alterations were different among all three groups. Notably, ERBB3 and CDH1 alterations co-occurred commonly in HER2-mut MBC patients, while ESR1 alterations co-occurred in only 4.8%. All ERBB3 co-mutations occurred with HER2 kinase domain mutations, while CDH1 co-mutations were less prevalent in the HER2-kinase group. Understanding the frequency and spectrum of HER2 mutations in MBC, as well as co-mutations, will help to guide combination treatment strategies and improve the clinical benefit of targeted therapy in HER2-mutated MBC.

Disclosure(s):

Whitney L. Hensing, MD, MSCR: No financial relationships to disclose

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regarding these tests. Did not impact clinical or research activity. (Ongoing)

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12/7/2022

7:00 AM - 8:15 AM

P2-23-11

Quantitative gene expression by RT-PCR in histologic subtypes of invasive breast carcinoma: an update in nearly one million cases

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Background: Invasive ductal carcinoma (IDC) accounts for ~80% of all invasive breast carcinomas (IBC) with several histologic subtypes comprising the remainder of cases. Some histologic subtypes of IDC (such as tubular carcinoma) have been associated with better prognosis, while other subtypes (such as metaplastic and micropapillary) have been associated with poorer prognosis. Prior studies have shown patients with early stage, hormone-receptor positive IBC that have low Recurrence Score® (RS), as measured by the 21-gene Oncotype DX® (ODX) assay, have little benefit from chemotherapy. Here, we report our experience with the histologic subtypes of IDC and associated patterns of observed gene expression using ODX.

Methods: All US samples submitted for IBC ODX between 2005 to 2021 were reviewed. Ductal carcinoma NOS (DC), tubular carcinoma (TC), cribriform carcinoma (CC), mucinous carcinoma (MUC), lobular carcinoma classic, solid or alveolar type (ILC), pleomorphic lobular carcinoma (PL), medullary/medullary-like carcinoma (MED), metaplastic carcinoma (MET), micropapillary carcinoma (MP), papillary carcinoma (PC) and solid papillary carcinoma (SPC) were included. Quantitative expression of 16 cancer-related genes was measured on a scale from 2 to 15 (relative to reference genes) where 1 unit increment is associated with ~2-fold change in expression. RS was calculated as published. Descriptive statistics for the RS, individual genes (ER, PR, HER2), and gene groups [invasion gene group (IGG) and proliferation gene group (PGG)] were obtained.

Results: A total of 957,624 samples were included in this analysis with 85.4% DC, 9.7% ILC, 2.8% MUC, 0.5% TC, 0.4% PL, 0.4% PC, 0.3% MP, 0.2% CC, 0.2% MED, 0.1% SPC, and

0.02% MET. For all types, a wide continuous range of RS was noted. MET had the highest median RS, followed in decreasing order by MED, PL, DC & ILC, TC, MUC, MP, CC, SPC, and PC. ER and PR were highest among PC and SPC. ER and PR were lowest among MED and MET. HER2 was highest among PC and TC and lowest among MED and MET. IGG was highest in MET and lowest in SPC. PGG was lowest for TC and highest for MED and MET. ER+/PR-/HER2- phenotype occurred more often in MED and PL. ER-/PR+/HER2- phenotype rarely occurred, but was most frequent in MED and MET. ER+/PR+/HER2+ accounted for 0.4% of our total sample.

Conclusions: Here, we demonstrate histologic subtypes of IDC have a wide continuous range of RS. ODX assay may be used to further stratify patients with IDC and its histologic subtypes; however, further studies are needed to better understand the predictive capability of ODX in the histologic subtypes.

Table 1. Quantitative gene expression by RT-PCR in histologic subtypes of invasive breast carcinoma

Histologic subtype	N	RS [median (IQR)]	RS<25	RS 26-100	ER [median]	PR [median]	HER2 [median]	IGG [median]	PGG [median]
Ductal carcinoma, NOS (DC)	81797	16 (0-100)	675040 (82.6%)	142757 (17.4%)	10.2	7.6	9.2	7.1	5.5
Lobular carcinoma (classic, solid or alveolar) (LC)	92472	16 (0-82)	64939 (70.1%)	7533 (8.1%)	9.8	7.2	9.3	6.5	5.1
Mucinous carcinoma (MUC)	26638	13 (0-82)	24236 (90.6%)	2302 (8.6%)	10.6	7.7	8.6	6.3	5.2
Tubular carcinoma (TC)	4509	14 (0-44)	4368 (96.9%)	141 (3.1%)	9.5	7.5	9.5	6.6	4.4
Papillary carcinoma (PC)	4046	6 (0-100)	3916 (96.8%)	470 (11.6%)	11.6	8.9	9.5	8.3	5.7
Plasmourphic lobular carcinoma (PL)	4003	18 (0-80)	3197 (79.9%)	806 (20.1%)	9.9	7.2	9.3	6.7	5.5
Micropapillary carcinoma (MP)	2487	12 (0-81)	2302 (92.9%)	185 (7.4%)	10.5	8.5	9.3	7.1	5.7
Cribiform carcinoma (CC)	2190	11 (0-76)	2012 (91.9%)	148 (6.7%)	10.8	8.4	9.4	6.5	5.3
Medullary carcinoma (MED)	2035	36 (0-81)	490 (24.1%)	1542 (75.9%)	7.8	4.4	8.0	6.2	6.4
Solid papillary carcinoma (SPC)	1215	7 (0-77)	1091 (89.8%)	114 (9.3%)	11.7	8.9	9.2	6.0	5.6
Metaplastic carcinoma (MET)	232	45 (0-76)	22 (9.5%)	210 (90.5%)	6.9	3.7	8.1	7.4	6.2

Table 2. Biomarker profile in histologic subtypes of invasive breast carcinoma

Histologic subtype	N	ER+/PR+/HER2-	ER+/PR-/HER2-	ER-/PR+/HER2-	ER+/PR+/HER2+
Ductal carcinoma, NOS (DC)	81797	668578 (81.8%)	114817 (14.0%)	904 (0.1%)	3057 (0.4%)
Lobular carcinoma (classic, solid or alveolar) (LC)	92472	75116 (81.2%)	15559 (16.8%)	65 (<0.1%)	173 (0.2%)
Mucinous carcinoma (MUC)	26638	22847 (85.8%)	3281 (12.3%)	8 (<0.1%)	61 (0.2%)
Tubular carcinoma (TC)	4509	4010 (88.9%)	461 (10.2%)	8 (0.2%)	2 (<0.1%)
Papillary carcinoma (PC)	4046	3416 (84.4%)	381 (9.4%)	5 (0.1%)	13 (0.3%)
Plasmourphic lobular carcinoma (PL)	4003	2949 (73.7%)	879 (22.0%)	4 (0.1%)	18 (0.5%)
Micropapillary carcinoma (MP)	2487	2106 (84.7%)	294 (11.8%)	0	15 (0.6%)
Cribiform carcinoma (CC)	2190	1941 (88.6%)	178 (8.1%)	1 (<0.1%)	8 (0.4%)
Medullary carcinoma (MED)	2035	684 (33.6%)	558 (27.4%)	24 (1.2%)	10 (0.5%)
Solid papillary carcinoma (SPC)	1215	1030 (84.8%)	144 (11.9%)	0	1 (<0.1%)
Metaplastic carcinoma (MET)	232	45 (19.5%)	40 (17.2%)	6 (2.6%)	0

Disclosure(s):

Nhu Thuy Can, MD: Exact Sciences: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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7:00 AM - 8:15 AM

P2-23-12

The Mutational Landscape of 1172 Patients with Hormone Receptor-Positive, HER2-negative Metastatic Breast Cancer Treated with CDK4/6 Inhibitors

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Background:

Recent studies suggest differences in outcomes among patients (pts) with metastatic breast cancer (MBC) treated with abemaciclib, ribociclib, or palbociclib, but whether these differences have a genomic basis is unknown. Here, we utilize a large real-world dataset to compare the mutational landscapes of HR+/HER2- MBC samples in which CDK4/6 inhibitor (CDK4/6i) treatment was initiated ≥ 6 months prior to biopsy to describe variations in tumor biology associated with exposure to each CDK4/6i. We also compare mutations detected by solid tumor sequencing and liquid biopsy to better understand each assay's ability to identify relevant alterations in this population.

Methods:

De-identified data from a cohort of pts with HR+/HER2- MBC (n=1172) sequenced with the Tempus xT (DNA-seq of 595-648 genes, whole exome-capture RNA-seq) solid tumor and xF (105-gene panel focused on detecting oncogenic and resistance mutations from cell-free DNA) liquid biopsy assays were retrospectively analyzed. For pts with multiple samples sequenced, the most recent sample was analyzed. Pts were selected based on receipt of CDK4/6i between metastatic diagnosis date and biopsy collection and excluded if < 6 months elapsed between CDK4/6i initiation and biopsy collection.

Demographics, clinical characteristics, and NGS findings were compared between groups by Chi-squared/Fisher's Exact tests or Kruskal-Wallis tests, as applicable. The prevalence of individual gene alterations (consisting of pathogenic/likely pathogenic SNVs/indels and copy number alterations) were compared similarly with adjustment for false-discovery.

Results:

We compared the immune biomarker and DNA mutational landscapes of 1172 samples collected after a period of treatment with abemaciclib, ribociclib, or palbociclib. Across all pts, the most commonly altered genes were TP53, PIK3CA, ESR1, CDH1, and GATA3. Abemaciclib-treated pts had the highest median TMB and MSI-high frequency (Table). Palbociclib-treated pts were less likely to have a high TMB (≥ 10 mutations/megabase) or RB1 mutations, a known biomarker of resistance to CDK4/6i (Table). We note that the total N for pts positive for TMB high or MSI-high was very low across all groups. We also compared DNA mutational landscapes between pts tested with solid tumor sequencing and liquid biopsy; the lower prevalence of RB1 mutations in palbociclib-treated pts trended towards significance in both groups (Table).

Conclusions:

Results from our real-world dataset suggest that treatment with the different CDK4/6i drugs results in unique immune biomarkers and DNA mutational profiles. Detection of relevant alterations such as RB1 by both tissue testing and liquid biopsy supports a role for either assay in identifying mutations associated with CDK4/6i. Our findings raise the possibility that unique targeted treatment strategies and combination therapies may be warranted after progression on the different CDK4/6i drugs. Additional investigation into the differences in genomic alterations and outcomes among CDK4/6i drugs is necessary to further explore the hypotheses generated by this real-world study.

Prevalence of immune biomarkers and DNA mutations in pts treated with each CDK4/6i drug

Table: Prevalence of immune biomarkers and DNA mutations in pts treated with each CDK4/6i drug

Biomarker	Abemaciclib (N=122)	Palbociclib (N=954)	Ribociclib (N=96)	p-value ¹	q-value ²
TMB, Median (IQR) ³	4.6 (3.4, 7.1)	3.1 (1.9, 5.0)	2.8 (2.0, 4.1)	0.004	N/A
High TMB ⁴	14%	5.2%	12%	0.040	N/A
MSI-high ⁵	2.5%	0.1%	1.1%	<0.001	N/A
RB1 mutation (xT or xI)	12%	4.8%	11%	<0.001	0.032
xI only (N=488)	17%	5.9%	23%	0.001	0.4
xT only (N=684)	10%	4%	7.1%	0.032	0.3

¹Pearson's Chi-squared test; Fisher's exact test; ~~Kruskal~~-Wallis rank sum test

²False discovery rate correction for multiple testing

^{3,4}N=464; 708 pts with missing data

⁵N=1163; 9 pts with missing data

1 Pearson's Chi-squared test; Fisher's exact test; Kruskal-Wallis rank sum test

2 False discovery rate correction for multiple testing

3,4 N=464; 708 pts with missing data

5 N=1163; 9 pts with missing data

Disclosure(s):

Ami N. Shah, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Terminated, March 31, 2022)

Bora Lim, MD: Astrazaneca: Consulting Fees (e.g., advisory boards) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Genentech: research funding (Ongoing); Merck: research funding (Ongoing); Natera: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Puma: Research Funding (Ongoing); Takeda Oncology: research funding (Ongoing)

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12/7/2022

7:00 AM - 8:15 AM

P2-23-13

Highly proliferative estrogen receptor-positive breast cancer is associated with better response to neoadjuvant chemotherapy but worse clinical outcome

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Introduction: Highly proliferative cancers are known to respond better to neoadjuvant chemotherapy (NAC), and pathological complete response (pCR) is a surrogate for survival benefit in breast cancer. Ki67 is the most commonly used cell proliferation marker; however, conventional immunostaining is subjected to variability by the assessor and the institution including the antibody used. To this end, we used the Ki67 gene expression to identify highly proliferative breast cancer and investigated whether it is associated with better response to NAC and survival by intrinsic subtype. Materials and Methods: Total of 6623 breast cancer patients from 11 independent cohorts with full transcriptome and clinical data were analyzed. The top 20% of Ki67 gene expression in each cohort were defined as highly proliferative group based on previous studies using immuno-staining. Results: Highly proliferative breast cancer was associated with high proliferation score, and all five cell proliferation-related gene sets in the Hallmark collection; E2F Targets, G2M Checkpoint, Mitotic Spindle, and Myc Targets v1 and v2 were enriched by gene set enrichment analysis in multiple cohorts regardless of subtype. MKI67 gene expression increased with higher grade in both ER-positive breast cancer and TNBC in multiple cohorts, but no clear association with staging was observed. Highly proliferative ER-positive breast cancer was significantly associated with worse disease-free, disease-specific, and overall survival consistently in METABRIC and GSE96058 cohorts, and showed a trend toward worse overall survival in TCGA; however, this was not the case in TNBC. Further, we found that highly proliferative tumor was significantly associated with better pathologic complete response (pCR) rate in six of the eight neoadjuvant chemotherapy cohorts of ER-positive breast cancer, but only two for TNBC. We also found that highly proliferative ER-positive breast cancer was associated with abundant silent and non-silent mutations, increased intra-tumoral heterogeneity, and homologous recombination defect scores when compared to lower proliferation groups, and this was not seen in TNBC in TCGA cohort. Although DNA

repair gene set was enriched in the highly proliferative ER-positive breast cancer, it was also associated with higher neoantigen activity, higher infiltration of tumor infiltrating lymphocytes including Th1 cells, Th2 cells, regulatory T cells, and M1 macrophages, as well as with enrichment of Interferon-gamma response gene set consistently in 3 large cohorts. In contrast, several stromal cell fractions were decreased in this group. Conclusions: Highly proliferative ER-positive breast cancer is significantly associated with pCR after NAC with increased tumor infiltrating lymphocytes, but is not a surrogate for survival, which are not the case in TNBC.

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7:00 AM - 8:15 AM

P2-23-14

Molecular characterization of HER2-low invasive breast carcinoma by quantitative RT-PCR using Oncotype DX®

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Background: The DESTINY-Breast04 clinical trial demonstrated the superiority of trastuzumab deruxtecan (T-DXd) versus physician's choice chemotherapy in HER2-low [immunohistochemistry (IHC) staining score 1+ or 2+ with no gene amplification by in-situ hybridization] metastatic breast cancer. The reproducibility of HER2 IHC category 0 versus 1+ scoring is poor in community practice. 89% of the DESTINY-04 participants were hormone receptor positive (HR+). In HR+ breast cancers, the Oncotype DX® (ODX) assay is widely used to estimate risk of recurrence and guide adjuvant chemotherapy selection. It also provides standardized quantification of HER2 mRNA expression by RT-PCR. Prior studies have demonstrated a high degree of overall concordance between central IHC and RT-PCR using ODX in HER2+ and HER2- cases. Here, we (i) compare HER2 mRNA levels quantified by ODX in HER2 IHC 0, 1+ and 2+ invasive breast carcinomas (IBC), (ii) compare the Recurrence Score® (RS) distribution across these three IHC categories and (iii) describe RS distribution and proliferation score in HER2-low IBC.

Methods: 212 patients with HER2 IHC 0, 1+ and 2+ who were negative for HER2 gene amplification by FISH and had RS results were identified in Yale Department of Pathology archives. All US samples submitted for IBC ODX testing between 2005 to 2021 were reviewed in the Exact Sciences database. RS, quantitative HER2 mRNA expression, and proliferation scores were examined. IHC results were not available. Based on quantitative RT-PCR measures of HER2 expression, cases were assigned to: HER2 positive ≥ 11.5 , equivocal ≥ 10.7 to < 11.5 , and negative < 10.7 (1 unit increment is equivalent to approximately 2-fold change). Results: In the Yale cohort, 42%, 33%, and 25% of cases were IHC 0, 1+ and 2+, respectively. There was no difference in age or tumor grade by IHC category. HER2 mRNA levels increased across IHC categories (means 9.05, 9.16, 9.39, respectively), but in group-wise comparisons, only the IHC 0 compared to IHC 2+ reached statistical significance (Mann-Whitney test, $p=0.0014$). The RS scores were also modestly, but significantly higher in IHC 2+ compared to IHC 0 cases (mean 19.5 vs 14.51, Mann-Whitney $p=0.034$). Among IHC 0 and 1+ cases, 14% had RS >25 , and among IHC 2+ cases, 32% had RS >25 . All IHC 0 and 1+ cases were HER2 negative by RT-PCR. Of the HER2 2+ cases, there was one HER2 positive and one HER2 equivocal by RT-PCR. There was substantial variation in HER2 expression by RT-PCR in all IHC groups. In the Exact Sciences cohort, a total of 957,624 samples were analyzed. 0.8% of samples were HER2 positive, 1.2% were equivocal, and 98% were negative by RT-PCR. There was a wide range of RS results. Of the HER2 positive cases, 94.7% had RS >25 . Among the HER2 equivocal cases 39.1% had RS >25 , and among the HER2 negative cases, 15.5% had RS >25 .

Conclusions: HER2 IHC 0 and HER2 low IBC have a broad and overlapping range of HER2 expression by RT-PCR. Whether RT-PCR based HER2 expression predicts benefit from T-DXd is yet to be determined. Most HER2 low cases have RS ≤ 25 , indicating no or limited benefit from adjuvant chemotherapy. Further studies are required to determine if patients with HER2 low IBC and RS ≤ 25 , particularly with high anatomical risk, could benefit from adjuvant T-DXd.

Table 1. Clinicopathologic and molecular characteristics by HER2 IHC group

HER2 IHC	n	0	1+	2+	Chi-square test p-value
Age (years)					0.466
<50	28 (13%)	9 (10%)	12 (17%)	7 (13%)	
≥ 50	184 (87%)	79 (90%)	59 (83%)	46 (87%)	
Tumor Grade					0.173
1	74 (35%)	31 (35%)	31 (44%)	12 (23%)	
2	109 (51%)	46 (52%)	32 (45%)	31 (58%)	
3	29 (13%)	11 (13%)	8 (11%)	10 (19%)	
HER2 RT-PCR					0.200
Positive (≥ 11.5)	1 (0.47%)	0	0	1 (2%)	
Equivocal (10.7-11.5)	1 (0.47%)	0	0	1 (2%)	
Negative (< 10.7)	212 (99%)	89	71	52 (98%)	
RS					0.012
≤ 25	173 (81%)	76 (86%)	61 (86%)	36 (68%)	
> 25	39 (18%)	12 (14%)	10 (14%)	17 (32%)	

Table 2. Quantitative gene expression by HER2 IHC group

HER2 IHC	0	1+	2+
HER2 RE-PCR mean	9.05	9.56	9.99
IS mean	14.51	14.85	19.50

Disclosure(s):

Mariya Rozenblit, MD: No financial relationships to disclose

Hao-Kuen Lin, n/a: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-23-15

Histologic, immunohistochemical and genomic comparison between classic Invasive lobular carcinomas and lobular-like invasive ductal carcinomas

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Background: Invasive lobular carcinomas (ILCs) are the most frequent special histologic subtype of breast cancer, accounting for up to 15% of all breast cancer cases. ILCs are characterized by a distinctive discohesive growth pattern, with cells arranged in single cell infiltrative file and dispersed throughout the stroma, which stems from the loss of E-cadherin expression due to bi-allelic inactivation of the CDH1 gene. A subset of breast cancers display a

similar single cell infiltrative growth pattern but, in contrast to classic ILC, display diffuse strong membranous E-cadherin reactivity and membranous p120 expression. We refer to such cases as “lobular-like invasive ductal carcinoma” (LLIDC), but it is unclear if this terminology is appropriate and if such cases show biallelic inactivation of CDH1, similarly to ILCs. Here, we sought to define whether LLIDCs would harbor bi-allelic alterations of CDH1 and to perform an exploratory, hypothesis generating analysis of the repertoire of somatic genetic alterations of LLIDCs and classic ILCs. Materials and methods: Representative H&Es, as well as sections subjected to E-cadherin and p120 immunohistochemistry from seven classic ILCs and seven bona fide “lobular-like invasive ductal carcinomas” were retrieved and independently reviewed by two pathologists with experience and expertise in breast pathology. DNA samples were extracted from representative sections from tumor and normal breast tissue from each patient and subjected to an FDA-approved targeted sequencing assay comprising the coding regions and selected regulatory elements of 515 genes. Somatic single nucleotide variants (SNVs) were detected with MuTect, indels with Strelka, VarScan2, Scalpel and Lancet. All mutations were manually inspected using the Integrative Genomics Viewer (IGV). The cancer cell fraction (CCF) of each mutation was inferred, as well as clonal probability, using ABSOLUTE. Copy number alterations and loss of heterozygosity were determined using FACETS. Mutational signatures were inferred using SigMA based on all synonymous and nonsynonymous somatic mutations. Results: Based on the histopathologic evaluation, of the 14 cases analyzed, seven were classified as ILC, and the other seven were classified as LLIDC. Sequencing analysis revealed that the classic ILCs harbored 16q LOH and CDH1 mutations (7/7), of which five were frameshift indel and two were splice site mutations consistently coupled with loss-of-heterozygosity (LOH) of the wild-type allele. Conversely, five of the seven LLIDCs did not harbor CDH1 mutations or genomic rearrangements. CDH1 mutations were identified in 2 LLIDCs: one harbored a subclonal CDH1 in-frame indel mutation coupled with LOH. This case displayed membranous E-cadherin and p120 expression with areas of aberrant expression. The other CDH1-mutated LLIDC harbored a complex in-frame indel with subclonal LOH. This case displayed membranous E-cadherin and p120 expression. The comparative analysis of the repertoire of somatic genetic alterations and mutational signatures present in LLIDCs and classic ILCs did not reveal any significant differences. Conclusion: Despite the histologic similarities, LLIDCs differ from classic lobular carcinomas based on the lack of CDH1 bi-allelic inactivation and the patterns of expression of E-cadherin and p120 catenin. Further whole-genome sequencing analyses are warranted to define the molecular basis of the discohesive cancer cells of LLIDC display.

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Edaise M. da Silva, MSc, PhD: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-23-16

Clinico-Pathological and Molecular Characterization of HER2-Enriched Breast Tumors Independently of HER2 Status

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INTRODUCTION

Breast cancer (BC) is a highly prevalent and heterogeneous disease, entailing different so-called intrinsic subtypes (IS) according to gene expression, namely Luminal A, Luminal B, HER2-Enriched (HER2E) and Basal-like, as well as a normal breast-like group. The HER2E is still a poorly understood entity, which needs further biologic characterization to improve

therapeutic management.

MATERIAL AND METHODS

Patients (pts) treated at Hospital Clinic (Barcelona, Spain) over 18 years with a diagnosis of metastatic BC, with available matched primary and metastatic tumor samples for gene expression analyses were retrospectively recruited. Using the nCounter® Breast Cancer 360 panel, we studied the expression of 776 genes pertaining to different tumor and immune pathway-related signatures, with a focus on HER2E vs. non-HER2E tumors. Significant changes were considered at a false discovery rate (FDR) < 5%. Main clinicopathological features were also compared. IS changes from primary to metastatic disease were assessed.

RESULTS

Ninety-one pts with paired tumor samples were included. Briefly, primary tumors were 67.0% hormone receptor-positive (HR+)/HER2-negative (HER2-), 14.8% were HER2-positive (HER2+) and 18.2% were triple-negative (TNBC). IS distribution in primary tumors was the following: 25 Luminal A (28%), 22 Luminal B (24%), 24 HER2E (26%), 12 Basal-like (13%), and 8 Normal-like (9%). In contrast, IS distribution in metastatic tumors was the following: 13 Luminal A (14%), 22 Luminal B (24%), 34 HER2-E (37%), 16 Basal-like (18%), and 6 Normal-like (7%). The HER2E disease proved to be a relatively stable subtype, with 16 (66.7%) tumors not changing IS in the transition to metastatic disease ($p=0.078$). Particularly, within HR+/HER2-, HER2+ and TNBC, 8/12 (66.7%), 8/10 (80.0%) and 1/2 (50.0%) tumors remained HER2E. Conversely, an overall significant switch from Luminal to non-Luminal tumors at the metastatic progression was observed ($p=0.031$), with 14/19 (73.7%) new non-Luminal BC being HER2E.

When considering all primary and metastatic tumors, HER2E were observed to be less frequently estrogen receptor (ER) positive than non-HER2E tumors (55.8% vs. 78.7%; $p=0.002$), with lower mean progesterone receptor (PR) levels (15.3% vs. 25.8%; $p=0.027$). Compared to the other subtypes (as a group), the PAM50 risk of recurrence score (ROR-P) was higher for HER2E tumors (59.1 vs. 41.7; $p < 0.001$), which were also more frequently HER2+ (36.5% vs. 5.8%) and less likely HR+/HER2- (50.0% vs. 73.6%) and TNBC (13.5% vs. 20.7%), compared to non-HER2E ($p < 0.001$). No significant differences in grade, TILs, Ki67 and histotype were observed. Overall, 140/776 genes were significantly downregulated in HER2E vs. non-HER2E tumors, including genes related to cell adhesion, migration, DNA damage repair, apoptosis, estrogen signalling pathway, senescence. Conversely, 178/776 genes were significantly upregulated, including the tyrosine-kinase receptor FGFR4, genes involved in nuclear activity, DNA transcription regulation, MAP-kinase signaling pathways, proliferation, cytokine response, epithelial-to-mesenchymal transition (EMT), cell cycle progression, and immune-related genes such as CD274 (PD-L1 gene).

DISCUSSION

A switch towards more aggressive IS from primary to advanced disease was observed, with an increase in HER2E prevalence. HER2E tumors, which tend to maintain their IS at the metastatic disease, showed upregulation of genes related to proliferation, survival and EMT, coherently with their well-known worse prognosis. FGFR4 and CD274 upregulation, along with downregulation of genes involved in DNA damage repair suggest these tumors might benefit from targeted therapeutic approaches. Genomic higher risk was not conveyed by consistent clinicopathological features, except for lower PR levels and HER2 overexpression at IHC. Further characterization according to primary/metastatic and HR status is ongoing.

Intrinsic subtype distribution across primary and metastatic breast tumors

INTRINSIC SUBTYPES	PRIMARY SAMPLES		METASTATIC SAMPLES	
	N	%	N	%
	91	100.00	91	100.00
<i>Luminal A</i>	25	27.47	13	14.29
<i>Luminal B</i>	22	24.18	22	24.18
<i>HER2-Enriched</i>	24	26.37	34	37.36
<i>Basal-like</i>	12	13.19	16	17.58
<i>Normal-like</i>	8	8.79	6	6.59

Disclosure(s):

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Fara Brasó-Maristany, PhD: Fundació Clínic per a la Recerca Biomèdica: Receipt of Intellectual Property Rights / Patent Holder (Ongoing)

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12/7/2022

7:00 AM - 8:15 AM

P2-23-17

Programmed death ligand-1 expression in triple-negative breast cancer from Nigeria

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Introduction: The incidence of triple negative breast cancer (TNBC) in West Africa appears to mirror the higher incidence of the disease among African American women in the United States. However, there remains a paucity of molecular data on TNBC from sub-Saharan Africa, despite the emergence of effective immunotherapies. Methods: Consecutive patients diagnosed with invasive breast cancer between March 2018-Jan 2020 were identified from a prospective clinical database and paired biobank at Obafemi Awolowo University Teaching Hospital (OAUTH). All specimens were processed and fixed in formalin within 60 minutes of excision by a trained pathologist. Tissue sections (4µm thick) representative of tumor were selected for routine evaluation of estrogen, progesterone and human epidermal growth factor receptor-2 expression by immunohistochemistry. This was performed at OAUTH with adequate controls according to the ASCO/CAP guidelines and verified at an outside institution for quality assurance. Additional sections from the FFPE blocks of TNBC specimens were further stained using the Dako PharmDx 22C3 PD-L1 commercial assay according to manufacturer protocols at Dalhousie University. External on-slide controls included tonsil, PD-L1 negative TNBC, and PD-L1 positive TNBC. PD-L1 expression was scored using the combined positive score (CPS), which is the number of 22C3 staining tumour cells, lymphocytes, and macrophages divided by

the number of viable tumour cells, multiplied by 100. The threshold for a positive result was a CPS of ≥ 10 as per manufacturer instructions and institutional protocol. Research ethics board approval as well as data and material transfer agreements between institutions was obtained for this study. Results: From 85 cases, 32 were TNBC (37.6%). The mean age and BMI were $49.6 \pm SD 7.7$ and 26.2 ± 5.7 , respectively. The majority of patients presented with locally advanced disease (64.2% Stage III, 14.2% Stage IV). Seventy-nine percent (78.5%) of patients received an average of five cycles of neoadjuvant chemotherapy (SD 2.3). From 32 TNBC specimens, 27 had available FFPE tissue blocks, and of those, 24 had interpretable PD-L1 IHC for inclusion in the analysis. A total of 37.5% (9/24) of cases demonstrated a CPS ≥ 10 . Conclusions: Over a third of breast cancer specimens in this Nigerian cohort were triple negative, 37.5% of which had PD-L1 CPS scores of ≥ 10 . These results suggest a large proportion of patients in Nigeria may benefit from access to immunotherapy. This is the first reported incidence of PD-L1 expression in breast cancer from sub-Saharan Africa.

Disclosure(s):

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7:00 AM - 8:15 AM

P2-23-18

Analysis of Serum Galectin Profiles by Breast Cancer Subtypes and Patient Characteristics

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Background:

Galectins are sugar binding proteins that play a role in adhesion, apoptosis, immune regulation, and many other cellular processes. There are three different classes of galectins, and they are all found intracellularly and secreted in serum. Galectins have an established relationship with breast cancer, and galectin-3 has been repeatedly associated with cancer cell survival and tumor progression. Most research regarding breast cancer and galectins has used immunohistochemistry (IHC) as a method for identifying galectin expression in breast cancer tissue samples. However, little research has identified a relationship between serum galectin concentrations and breast cancer subtypes. Breast cancer is characterized both by histological and molecular subtype, and this identification often directs treatment decisions. The current method for identifying breast cancer subtypes is through invasive biopsy and the subsequent use of IHC. This project characterized serum galectin concentrations in breast cancer patients to determine if they changed based on different histological and molecular subtypes, cancer stage, and other patient characteristics. Our goal was to evaluate a potential noninvasive means of breast cancer subtype identification and to identify potential therapeutic targets.

Methods:

One-hundred breast cancer patient serum samples were studied using Enzyme-linked Immunosorbent Assays (ELISAs) to determine concentrations of galectins -1, -3, -7, and -9. Results were compared using many patient characteristics, including breast cancer subtype,

stage, and patient history (smoking status and treatment). Statistical Analysis was performed using ANOVA, Student's t-test, and the Wilcoxon Method.

Results:

The concentrations of galectins -1, -3, and -9 in breast cancer patients were all significantly higher than those of healthy controls (Table 1), which is consistent with previous studies. The concentration of galectin-3 was significantly higher in invasive lobular carcinoma samples (N, 6; mean, 13.04 ng/mL) compared to invasive ductal carcinoma samples (N, 80; mean, 9.93 ng/mL; p-value, 0.0428). Galectin-3 concentrations were significantly lower in samples from breast cancer patients who received chemotherapy (N, 9; mean, 9.22 ng/mL) versus those who did not (N, 7; mean, 14.60 ng/mL; p-value, 0.0228). Concentrations of galectin-1 were found to increase by stage (p-value, 0.0031), with significant differences between samples from patients with stage I breast cancer (N, 45; mean, 19.02 ng/mL) and both stage II (N, 40; mean, 24.15 ng/mL; p-value, 0.0127) and stage III (N, 12; mean, 28.37 ng/mL; p-value, 0.0026) disease.

Conclusions:

Our findings suggest a potential use for serum galectin-3 concentrations as a non-invasive means for breast cancer histological subtype differentiation and more refined diagnosis. In addition, our results suggest a possible use of galectin-1 concentrations for more accurate cancer staging. Further research could explore the relationship of serum galectin concentrations and other breast cancer subtypes. Future studies could also analyze how galectin concentrations change with patient treatment status and determine the potential of galectins as specific targets for breast cancer treatment.

Table 1: Galectin Concentrations in Breast Cancer vs Healthy Controls

Table 1: Galectin Concentrations in Breast Cancer vs Healthy Controls						
	Galectin-1		Galectin-3		Galectin-9	
	Cancer	Healthy	Cancer	Healthy	Cancer	Healthy
N	98	16	100	15	33	36
Mean (ng/mL)	22.25	14.14	10.08	1.44	10.14	7.00
p-value	0.0015		<0.0001		0.0032	

Disclosure(s):

- Jonah Shealy, B.S.:** No financial relationships to disclose
- Alex Kesic, B.A.:** No financial relationships to disclose
- Avery Funkhouser, B.S.:** No financial relationships to disclose
- Julie Martin, DNP:** No financial relationships to disclose
- W. Larry Gluck, MD:** No financial relationships to disclose
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7:00 AM - 8:15 AM

P2-23-19

Interrogating multicellular signaling in breast cancer using a bio-orthogonal chemistry-based proteomics platform

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Tumors are multicellular ecosystems that communicate through the exchange of extracellular signaling molecules. In breast cancer, this multicellular communication can enable tumor cells to cooperate in a range of contexts, including tumor invasion and the outgrowth of distal metastases. Illuminating the mechanisms by which tumor cells communicate may reveal new therapies. To this end, three-dimensional tumor organoid models have emerged as versatile platforms for modeling multicellular behavior *ex vivo*. However, organoid culture typically requires the use of poorly defined, animal-derived extracellular matrices, such as Matrigel. These exogenous matrices contain thousands of proteins that dominate over and conceal cell-secreted factors in conventional proteomics approaches. Revealing low abundance cell-secreted factors from this complex exogenous background presents a formidable challenge. To surmount this challenge, we develop a new method to isolate the pericellular proteome in 3D organotypic culture models. This technology harnesses biorthogonal click chemistry to bypass exogenous factors, infiltrate intercellular spaces, and retrieve the endogenous intercellular proteome. This approach requires no genetic manipulation, requires only 1 million cells, and can be adapted to diverse organotypic models. These capabilities enable isolation of intercellular signaling factors in models that yield precious amounts of material and that can sustain only limited manipulation *ex vivo*, which we demonstrate using organoids established from patient-derived xenografts. To establish the generalizability of our approach, we apply this technology to a panel of breast cancer and small-cell lung cancer organoid models. Furthermore, we demonstrate that this method can be readily adapted to different extracellular matrix environments that are widely employed in organoid research, including basement membrane matrices and collagen gels. Taken together, our results establish this technology as a scalable and generalizable platform that may open opportunities for researchers investigating diverse questions in organoid models of cancer. Moving forward, we are leveraging these capabilities to investigate changes in the intercellular proteome that emerge after the acquisition of therapy resistance. We hope to uncover new mechanisms of collective signaling that may be targeted to overcome therapy resistance.

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7:00 AM - 8:15 AM

P2-24-01

The development of covalent microtubule stabilizers for drug-resistant cancers

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Microtubule targeting agents (MTAs) are some of the most commonly used and effective chemotherapeutic agents used in the treatment of breast cancer and other solid tumors. Clinically approved MTAs include microtubule destabilizers, such as the vinca alkaloids or eribulin, as well as the taxane class of microtubule stabilizers, including paclitaxel. While MTAs are effective chemotherapeutics, the development of resistance due to drug efflux or changes in β -tubulin isotype expression are major clinical limitations to each the currently approved drugs of this class. One strategy for overcoming drug resistance is the development of drugs that covalently bind to their drug target, which has been validated in the clinic with the success of irreversible EGFR inhibitors in drug resistant non-small cell lung cancer. We have identified the C22,23-epoxytaccalonolides (taccas) as a class of plant-derived microtubule stabilizers that covalently bind to β -tubulin with a high degree of specificity and retain efficacy in drug-resistant models in vitro and in vivo. Although the taccas have potent and persistent antitumor efficacy in vivo, they suffer from a narrow therapeutic index and short serum half-life that provides optimal efficacy when targeted directly to the tumor site. We are undertaking a multipronged approach to generate synthetic tacca analogs (taccalogs) that retain the efficacy of the natural product with improved pharmacokinetic properties, including improved serum binding, to increase half-life and provide better in vivo tolerability. We are also identifying strategies to improve tumor targeting of the taccas, which is being guided by determining their in vivo distribution with radiolabeled analogs. In a complementary approach, we tested the hypothesis that non-covalent microtubule stabilizers that have increased binding affinity to tubulin share properties with the taccas, such as the ability to circumvent drug resistance and provide potent and persistent in vivo efficacy with a more tolerable therapeutic window. Our data suggest that while non-covalent microtubule stabilizers with improved binding compared to paclitaxel provide improved cellular persistence after drug washout and potent antitumor efficacy, they are not able to overcome drug resistance to some degree as covalent inhibitors, demonstrating the advantage of continuing to develop irreversible drugs such as the taccalonolides for the treatment of drug resistant disease.

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7:00 AM - 8:15 AM

P2-24-02

Analyzing susceptibility to macrophage-activating immunotherapy bexmarilimab in breast cancer by using patient-derived tumor explants

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The immunosuppressive tumor microenvironment governed by tumor-associated macrophages (TAMs) remains a major obstacle to effective cancer immunotherapy. A novel humanized antibody bexmarilimab, targeting the scavenger receptor Clever-1 on TAMs, has shown clinical benefit in ~40% of patients with late-stage ER+ breast cancer (MATINS; NCT03733990). To increase response rates, a comprehensive understanding on how TAM phenotype and the tumor immune landscape affect bexmarilimab-induced immune activation is needed. Single-cell RNA sequencing analysis of breast tumor macrophages shows high phenotypic variation across pathological subtypes and Clever-1 mRNA (STAB1) expression on various immunosuppressive IL4I1+ and TREM2+ monocyte-derived TAMs. STAB1 expressing macrophages were located in both lymphocyte rich and excluded areas in the tumor stroma based on digital spatial profiling with GeoMx. Due to this diversity, we studied bexmarilimab mode-of-action in breast cancer patient-derived tumor explant cultures (PDEC) by RNA sequencing and cytokine profiling. Our results show that bexmarilimab induced TNF α and CXCL10 secretion in 30-40% of the treated explants. In depth analysis of the responsive PDECs revealed a lower baseline expression of interferon responsive genes in their tumor microenvironment. Correspondingly, in vitro assays with primary human macrophages showed that chronic IFN γ priming abolished bexmarilimab-induced immune activation, suggesting potential use of bexmarilimab in patients with immunologically cold breast tumors.

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P2-24-03

Z-Endoxifen Allosterically Inhibits PKC β I and its Paradoxical Membrane Translocation

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Z-Endoxifen Allosterically Inhibits PKC β I and its Paradoxical Membrane Translocation
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Background: Z-Endoxifen (ENDX), the active metabolite of tamoxifen (TAM) and a selective estrogen receptor modulator (SERM), exhibited high antitumor activity in endocrine-resistant hormone receptor-positive breast and other gynecologic cancer. ENDX has also been shown to be a protein kinase C (PKC) inhibitor. PKCs participate in diverse cellular functions and their activity is often elevated in breast tumors. Guided by mechanistic insights from our recently determined crystal structure of PKC β I, we sought to determine the effects of ENDX on PKC β I in a breast cancer cell line model. Methods: To determine how ENDX regulates PKC activity, we used a Z'LYTE kinase activity assay. This Fluorescence Resonance Energy Transfer (FRET) based biochemical method can detect differential sensitivity of phosphorylated and non-phosphorylated peptides to proteolytic cleavage. We probed changes in activity for conventional and novel PKCs, as well as the purified catalytic domain of conventional PKCs in vitro. Alongside, as kinase activity of PKC relies on its spatial assembly, therefore we studied its intracellular localization using live cell confocal imaging. MCF7 cells expressing YFP-tagged PKC β I were grown in a glass bottom chamber and treated with ENDX and other modulators for relevant time and doses for this study. Images were taken using Zeiss LSM 780 confocal laser scanning microscope and analyzed in Zeiss-ZEN microscope software and GraphPad Prism 9. Results: Our data from an in vitro kinase assay indicates that ENDX inhibits the kinase activity of conventional (PKC β I) and novel (PKC δ) PKC isoforms with a similar IC₅₀, however PKC β I catalytic domain is less sensitive to ENDX. We also identified a multi-domain mechanism of PKC inhibition through an allosteric inhibitory mechanism. Our live cell imaging study demonstrated that ENDX promotes the recruitment of PKC β I to the cell membrane in both a dose and time-dependent manner. Moreover, this translocation can also be mitigated by co-treatment with inhibitors of the PKC-regulator PHLPP phosphatases. Conclusion: Taken together, these results suggest the allosteric effects of ENDX trigger PKC β I recruitment to the cell membrane, yet since ENDX also inhibits kinase activity it suggests that ENDX triggers a non-productive interaction with the enzyme and "breaks" the well-known mechanism of PKC activation upon binding the cell membrane. Furthermore, ENDX is likely to trigger dephosphorylation and ultimately degradation, suggesting that ENDX represents a new mechanistic basis for targeting and downregulating PKC in cancer cells. Hence, the current study provides an integrated pattern of highly specific treatments regimen that can exploit PKC β I as a repurposing clinical target in breast cancer.

Disclosure(s):

Sayantani Sarkar Bhattacharya, Ph.D.: No financial relationships to disclose

Taylor L. Witter, B.S.: No financial relationships to disclose

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Matthew P. Goetz, M.D.: ARC Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Biotheranostics: Consulting Fees (e.g., advisory boards) (Ongoing); Biovica: Consulting Fees (e.g., advisory boards) (Ongoing); Blueprint Medicines: Consulting Fees (e.g., advisory boards) (Ongoing); Clinical Education Alliance: CME activities (Ongoing); Curio Science: Moderator (Ongoing); Eagle Pharmaceuticals: Consulting Fees (e.g., advisory boards) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Medscape: CME activities (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Research to Practice: CME activities (Ongoing); Sanofi Genzyme: Consulting Fees (e.g., advisory boards) (Ongoing); Sermonix: Consulting Fees (e.g., advisory

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7:00 AM - 8:15 AM

P2-24-04

The ER antagonist giredestrant induces profound chromatin remodeling including activation of cis-regulatory elements bound by FOXA1 and GATA3 in HR+ breast cancer models

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The progression of HR+ breast cancers is governed by ER signaling which makes the development of optimized ER-targeting agents a high priority. Among current therapeutics, selective ER antagonists and degraders (SERDs) have emerged as a particularly attractive class. Fulvestrant is the only SERD that is currently approved, but its clinical potential is hypothesized to be somewhat limited by poor physicochemical properties, dosage and exposure. We identified giredestrant as an orally bioavailable, highly potent non-steroidal ER antagonist, immobilizer and degrader with robust anti-proliferative activity. Giredestrant is currently being evaluated in phase III clinical trials for the treatment of ER+ breast cancer, after showing evidence of clinical activity in phase I and II trials. Here, we set out to investigate the impact of giredestrant on the transcriptome and chromatin landscape of ER+ breast cancer cells in vitro and in vivo. RNA-seq data from MCF-7 cells in vitro and three patient-derived xenograft (PDX) models in vivo showed that giredestrant inversely regulates the RNA levels of E2-regulated genes. Transcriptome wide, the expression of genes affected by giredestrant are strongly correlated ($r^2=0.8$) with those affected by siRNA-mediated silencing of ESR1, consistent with on-target ER antagonism. Performing ATAC-seq in the three PDX models, including one ESR1 mutant model, reveals that giredestrant reduces accessibility in up to 18,173 chromatin regions that are associated with genes induced by E2. These regions are also enriched in the ER binding motif. In addition, we found up to 17,127 chromatin regions with increased accessibility upon giredestrant treatment. These regions are associated with genes suppressed by E2, and are enriched in the FOXA1 binding motif. To probe giredestrant's role in functional modulation of cis-regulatory elements (CREs), we performed ChIP-seq targeting FOXA1 and GATA3, as key pioneer factors for ER, as well as ER itself and H3K27ac as a marker of active enhancers in MCF-7 cells. We identified 3,195 regions with significantly reduced H3K27ac signals that also exhibit significant reduction of both ER and FOXA1 binding

upon giredestrant treatment, indicating that giredestrant deactivates these CREs concomitantly with suppressing ER and FOXA1 binding. ChIP-seq analysis further revealed 2,292 regions with a significant increase in H3K27ac signals upon giredestrant treatment. Interestingly, the GATA3 motif was identified as the most enriched motif in these activated CREs. Further, GATA3 and FOXA1 ChIP-seq signals were stronger in the activated CREs compared to the deactivated ones. Similar profiling of both tamoxifen, an approved selective ER modulator (SERM), as well as GNE-858, a SERM from the same chemical series as giredestrant, showed their epigenetic effects to be highly distinct from those observed for giredestrant, suggesting that the high degree of chromatin remodeling is likely related to giredestrant's mechanism of action. Our studies here show that giredestrant profoundly alters ER binding and remodels the chromatin landscape, thus changing the transcriptional profile of cells in a manner that is associated with an anti-proliferative response. While deactivation of CREs with ER binding is perhaps in line with expectations, giredestrant treatment also leads to the activation of a number of regions associated with pioneer factors, potentially through their redistribution. This raises the question of the functional consequences of CRE activation and if this is relevant for the anti-proliferative effects of giredestrant.

Disclosure(s):

Musaddeque Ahmed, PhD: Hoffmann-La Roche Ltd: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

Jane Guan, PhD: Genentech Inc: Salary (Ongoing); Roche: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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12/7/2022

7:00 AM - 8:15 AM

P2-24-05

TAVO412 - A Novel Trispecific cMet x EGFR x VEGF Antibody for Triple Negative Breast Cancer

Presenting Author(s) and Co-Author(s):

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Novel Multispecific Antibody with Superior Activity in TNBC INTRO: TNBC (Triple Negative Breast Cancer) has a diverse etiology and high unmet need. We created a novel multispecific antibody with unique 2:1:1 ratio of EGFR:cMet:VEGF binding arms with excellent activity against TNBC. METHOD: Multiple in vitro EGFR & cMet signaling pathway inhibition, proliferation inhibition, and ADCC, ADCP, and CDC were conducted. Various in vivo studies using the TNBC cell lines (MDA-MB-468, MDA-MB-231, HCC70, BT20) with diverse levels of EGFR and cMet receptor density levels were tested. RESULTS: Strong tumor growth inhibition was found in multiple TNBC animal models (56% tumor growth inhibition (TGI) in BT20, 26% TGI in HCC70, 62% TGI in MDA-MB-231). Tavo412 demonstrated better activity than comparator molecules in several in vivo models using lung, gastric, and pancreatic cancer cell lines (data not shown). A one month GLP toxicity study in cynomolgus monkeys has been completed with well-expected tolerability and pharmacokinetic profiles. Besides shutting down three important cancer pathways, TAVO412 showed high potency because it also has strong EGFR and VEGF binding at pH 6 in the tumor microenvironment. Moreover, Tavo412 has exemplary Fc effector function engaging the innate immune responses that include ADCC, ADCP, and CDC. There is also a synergistic tumor growth inhibition in the presence of a standard of care molecule such as doxorubicin (61% in HCC70 with TAVO412 + doxorubicin, 66% TGI in BT20 with TAVO412 + doxorubicin, 71% TGI in MDA-MB-231 with TAVO412 + doxorubicin). In addition, gastric, pancreatic, and lung cancer in vivo models showed excellent TGI profiles. CONCLUSIONS: Tavo412 has the potential activity to be a superior multispecific antibody to treat patients with triple negative breast cancer. Phase 1 clinical testing in patients is anticipated in early 2023.

Disclosure(s):

Mark Chiu, Ph.D.: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-24-06

α EGFR-E-P125A ANTIBODY-ENDOSTATIN FUSION PROTEIN REDUCES VASCULOGENIC MIMICRY AND TUMOR CELL MOTILITY BY INHIBITION OF EGFR, INTEGRIN AND FAK SIGNALING

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Triple Negative Breast Cancer (TNBC) is an aggressive subtype of breast cancer with high metastatic potential and increased morbidity and mortality. Although expression of, and signaling by the epidermal growth factor receptor (EGFR) is commonly seen in TNBC, anti-EGFR antibodies such as Cetuximab have had limited therapeutic efficacy, used alone or in combination with chemotherapy. Primary TNBC tumor growth and metastases require supporting vasculature, which develops through a combination of endothelial angiogenesis and vasculogenic mimicry (VM). VM is more frequently seen in TNBC than other breast cancer subtypes, and is associated with aggressive metastatic behavior. We previously developed α EGFR-E-P125A, an antibody-endostatin fusion protein, linking an anti-EGFR antibody targeting domain to a mutated version of the anti-angiogenic protein endostatin (E-P125A). α EGFR-E-P125A delivers a dimeric E-P125A payload which inhibits TNBC angiogenesis and VM in vitro and in vivo, and markedly decreases metastasis in both the MDA-MB-231-4175 and MDA-MB-468 TNBC xenograft models. To determine the mechanism of α EGFR-E-P125A action on inhibition of VM, we studied the effects of α EGFR-E-P125A on both the transcriptome and proteome. RNA-seq was conducted on MDA-MB-231-4175 TNBC cells plated on matrigel and undergoing VM, and on TNBC cells plated in matrigel and treated with α EGFR-E-P125A.

Gene set enrichment analysis demonstrated that α EGFR-E-P125A treatment downregulated genes on the KRAS, JAK-STAT, and angiogenesis signaling pathways, including EGF, VEGFA, STAT3, PTK2, ITGB1, ITGB3, ITGAV, and ITGA5. Phospho-array analysis was used to interrogate the proteome and demonstrated downregulation of phosphorylation on multiple sites downstream of the EGFR and the α 5 β 1 integrin receptors, such as the EGFR Y1069 site, the FAK Y397 site, implicated in the regulation of endothelial and TNBC motility, and the STAT3 Y705 and S727 sites, known for their role in promoting the transcription of angiogenic genes. Since inhibition of EGFR signaling alone does not inhibit VM, we interrogated the mechanistic relationship between α EGFR-E-P125A and VM inhibition through the α 5 β 1 integrin/FAK signaling pathway. Specific inhibition of FAK at the Y397 site using the small molecule inhibitor, PF-573228 inhibited TNBC VM in vitro. Transient siRNA knockdown of FAK in MDA-MB-231-4175 cells and shRNA-mediated knockdown of FAK in MDA-MB-231 TNBC cells confirmed that downregulation of FAK inhibited VM in vitro. To understand the effect of α EGFR-E-P125A on the EGFR and α 5 β 1 integrin receptors, competition assays were conducted. α EGFR-E-P125A competed with EGF for the EGFR receptor and with the binding of fibronectin to α 5 β 1 integrin. Treatment of TNBC cells with α EGFR-E-P125A reduced total α 5 integrin protein levels and decreased co-localization of EGFR and α 5 β 1 integrin receptors. These results indicate that α EGFR-E-P125A is bound to both EGFR and α 5 β 1 integrin, simultaneously suppressing downstream EGFR and integrin signaling. Simultaneous inhibition of EGFR and α 5 β 1 integrin signaling by α EGFR-E-P125A fusion is a promising approach to inhibition of TNBC growth and metastases.

Disclosure(s):

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P2-24-07

Combination of complete estrogen receptor antagonist, OP-1250, and CDK4/6 inhibitors enhances tumor suppression and inhibition of cell cycle-related gene expression

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OP-1250, a complete estrogen receptor antagonist (CERAN) and selective estrogen receptor degrader (SERD), is currently in Phase I/II clinical trials for the treatment of estrogen receptor positive (ER+)/ human epidermal growth factor receptor 2 negative (HER2-) breast cancer. OP-1250 has previously demonstrated efficacy in both estrogen receptor 1 (ESR1) wild-type and Y537S mutant breast cancer xenograft models. Inhibitors of cyclin-dependent kinases 4 and 6 (CDK4/6) are a standard first-line treatment for ER+ advanced or metastatic breast cancer in combination with endocrine therapy. To characterize OP-1250 efficacy in this setting, we explored the combination of OP-1250 with CDK4/6 inhibitors palbociclib and ribociclib in ER+/HER2- breast cancer preclinical models, and profiled the transcriptional changes associated with single agent and combination therapy. OP-1250 and CDK4/6 inhibitors were tested alone and in combination in ESR1 wild-type MCF7 and ESR1 Y537S mutant ST941 xenograft models. Higher doses of OP-1250 and either CDK4/6 inhibitor, when given as a monotherapy, suppress tumor growth and increase animal survival, while lower doses of the compounds display a modest or minimal effect on tumor growth or survival. In combination, lower doses of OP-1250 and either CDK4/6 inhibitor result in significantly greater tumor growth suppression (both xenograft models), tumor regression (MCF7) and animal survival (ST491) than each compound individually. RNA sequencing revealed substantially more gene expression changes with combination treatment than monotherapy. In particular, pathways associated with cell cycle progression displayed greater changes with combination treatment, similar to what was observed with a much higher dose of monotherapy. This study supports the clinical evaluation of OP-1250 in combination with CDK4/6 inhibitors (palbociclib or ribociclib) and provides additional context to mechanisms of combination efficacy. OP-1250 is currently

being evaluated in a Phase Ib clinical trial in combination with palbociclib and a study including evaluation of the combination of OP-1250 with ribociclib is planned to initiate in Q3 2022.

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

P2-24-08

Altersolanol B, a fungal metabolite, induces proteasome-dependent degradation of estrogen receptor α (ER α) and inhibits downstream signaling targets in ER+ breast adenocarcinoma cells

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We recently reported the cellular signal-modulating properties of altersolanol B (AB), a minor fungal tetrahydroanthraquinone (THAQ) metabolite, in the estrogen receptor positive (ER+) human breast adenocarcinoma cell lines, MCF-7 and T47D. MCF-7 (IC₅₀ 5.5 μ M) and T47D (IC₅₀ 8.8 μ M) were observed to be 4- and 2.4-fold more sensitive to the antiproliferative effects of AB, respectively, compared to MDA-MB-231 (triple-negative, IC₅₀ 21.3 μ M). AB disrupted both AKT and ERK1/2 signaling leading to intrinsic apoptosis in MCF-7. The clinical limitations of multi-agent combination therapy that targets multiple pathways in cancer may potentially be circumvented by using a single molecule, such as AB, that inhibits both AKT and ERK1/2 signaling. The THAQ pharmacophore, with its disrupted conjugated ring system and relative redox inactivity, may possess greater mechanistic advantage against ER+ breast cancer when compared to the fully conjugated ring systems of the anthracyclines (doxorubicin) and anthraquinone (mitoxantrone) that are associated with nonselective mechanisms. The present phase of our study provides evidence that AB downregulated ER α expression at the post-translational level through the induction of proteasome-dependent degradation similar to a classical selective estrogen receptor degrader (SERD). AB dose-dependently downregulated both wild-type (WT)- and 17 β -estradiol (E2)-stimulated ER α protein expression without altering mRNA expression in ER+ cells. This was corroborated by the marked reduction in the expression of downstream ER α target genes (cathepsin D and pS2). AB also dose-dependently downregulated cyclin D1, the estrogen-independent activator of ER. Antiproliferative effects were enhanced when ER+ cells were exposed to a combination of AB and the ER α -selective antagonist, MPP dihydrochloride. The AKT activator, SC79, showed that the AB-induced ER α protein downregulation was independent of the inhibition of AKT-FOXO1 signaling. The expression of Hsp90 was not affected. Co-treatment with the protein synthesis inhibitor, cycloheximide, revealed that AB downregulated ER α expression at the post-translational level.

The proteasome inhibitor, MG-132, effectively suppressed AB-induced ER α degradation and restored cellular proliferation. In silico approaches were adopted to probe the direct binding of AB to ER α . AB demonstrated significant binding affinity with human ER α (PDB ID - 3ert) compared to the binding of the standard SERD, fulvestrant. Non-covalent bonding interaction analysis further revealed that, much like fulvestrant, AB successfully interacted with 5 major amino acid residues (i.e., Ala350, Asp351, Leu525, Leu536 and Trp383) at the ligand-binding domain of ER α which is stabilized by 7 non-bonding interactions. Principal component analysis indicated that binding with AB improved the compactness of 3ert folding. Molecular dynamics simulation indicated that the 3ert-AB interaction was stable even in the 100 ns simulated physiological environment.

Disclosure(s):

Md Afjalus Siraj, n/a: No financial relationships to disclose

Md Sajjadur Rahman, PhD: No financial relationships to disclose

Aaron T. Jacobs, PhD: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

P2-25-01

TRPS1 Regulates angiogenesis via JAG1 and TYMP in Triple-Negative Breast Cancer

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Background: Triple-negative breast cancer (TNBC), the most difficult subtype to treat, is defined as estrogen receptor (ER), HER2, and progesterone receptor (PR) negative and comprises roughly 15-20% of all breast cancers. Patients with a TNBC diagnosis have worse outcomes and poorer survival rates when compared to women with other breast cancers, despite adjuvant chemotherapy. One of the factors contributing to its metastatic ability is the angiogenic process it undergoes. Clinical trials with anti-angiogenic therapeutics showed to be inadequate, with moderate response rates and insignificant survival gains for patients. TRPS1, a GATA and GATA-like transcription factor, has been proven to play a role in the epithelial to mesenchymal transition (EMT) which ultimately promotes tumor growth and metastasis. It has previously been shown that TRPS1 regulates angiogenesis via the expression of VEGF proteins in breast cancer. Our purpose in this study was to further investigate the functional role of TRPS1-regulated genes involved in TNBC angiogenic pathways. Methods: Sleeping-Beauty (SB) transposons help detect cancer progression genes which participate in tumorigenesis and metastasis, not easily identified with current sequencing technology. Using the SB transposon methodology, several candidate trunk drivers were elucidated using Pten mutant mice. Validation studies further showed TRPS1 as one of the eight TNBC tumor suppressor genes discovered by this technology. Then, ChIP-seq array studies were performed which showed that TRPS1 regulates expression of genes involved in the angiogenesis pathway. To corroborate the functional role of TRPS1 in angiogenesis, tube formation and sprouting assays were performed using overexpression and inactivation of TRPS1 in MDA-MD-231 and HCC70 cells, respectively. Furthermore, we performed a ChIP qPCR human angiogenesis array to determine TRPS1-regulated angiogenic genes. A luciferase reporter assay was performed to determine whether TRPS1 is a direct transcriptional regulator of these genes. Results: Inactivation of TRPS1 expression allowed tube formation and cell branching in the sprouting assays. Tumor xenografts overexpressing TRPS1 were analyzed by immunohistochemistry, showed a significant reduction of angiogenic vasculature when stained with CD31; and a substantial increase in blood vessels when TRPS1 was shRNA inactivated. Furthermore, human ChIP qPCR angiogenesis array identified 10 top candidate genes potentially regulated by TRPS1 transcription factor. Of these candidates, JAG1 and TYMP showed to have a higher fold enrichment compared to other angiogenic related genes. Finally, we validated its direct functional binding by using luciferase reporter assay, such demonstrated that TRPS1 is a direct transcriptional regulator of JAG1 and TYMP. Discussion: It has been previously established that

the NOTCH ligand, JAG1 and the thymidine phosphorylase enzyme, TYMP are powerful genes participating in angiogenesis. Furthermore, elevated expression of JAG1 mRNA and protein has been associated with poor patient outcomes in breast cancer. Similarly, TYMP activity has been shown to be higher in triple-negative breast tumors, leading to poor outcomes as well. Although several anti-angiogenic drugs have been approved, tumor-acquired resistance to therapy limit their effectiveness. An increased understanding of tumor vessel mechanisms involved in tumorigenesis and metastasis is necessary to overcome the obstacles that prevent successful control of the angiogenic response in tumors. This would require as many paths as can be unraveled regarding the angiogenic mechanisms driving TNBC. Understanding the relationship between the function of TRPS1 in regulating the expression of important genes such as JAG1 and TYMP lays a better foundation for new drugs and drug targets that control and inhibit tumor angiogenesis.

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Roberto Rosato, PhD: No financial relationships to disclose

12/7/2022

7:00 AM - 8:15 AM

P2-25-03

β -arrestin1, a potential tumour suppressor in breast cancer is downregulated in PERK/ATF4-dependent manner

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Introduction: β -Arrestin1 (ARRB1) belongs to the arrestin family originally identified as a multifunctional adaptor protein that negatively regulates the desensitization and internalization of G-protein-coupled receptors. Recent studies have indicated that ARRB1 can form multiprotein complexes with transcription regulators, thereby indirectly inhibiting the function of some transcription factors, e.g., NF- κ B, and promoting the activity of others, e.g., p53. Further, arrestins function as multifunctional adaptors in many signalling pathways, such as the Hedgehog (Hh), Wnt, Notch, and transforming growth factor- β (TGF- β) pathways. Expression of ARRB1 is downregulated in TNBC patients and ARRB1 expression level is inversely correlated with the histological grade of the breast cancer and positively associated with TNBC patient survival, suggestive of a tumour-suppressive function of ARRB1 in breast cancer. Loss of ARRB1 expression is associated with a poor prognosis for non-small cell lung cancer patients. However, the mechanisms regulating the expression of ARRB1 in human cancers remain unclear. We hypothesized that metabolic endoplasmic reticulum (EnR) stressors including low glucose and hypoxia that activate an unfolded protein response (UPR) in tumour cells might regulate the expression of ARRB1 in human cancers. Methods: Expression of ARRB1 was determined by a combination of real-time RT-PCR, western blotting along with promoter reporter assays. Computational target prediction analysis was done to identify miRNAs targeting ARRB1 as well as transcription factors regulating ARRB1 expression. ARRB1 overexpressing breast cancer clones were generated by lentiviral transduction to investigate its functional role in tumour progression and drug sensitivity. Results: We observed that ARRB1 expression was significantly reduced in several cancers including breast tumours as compared to normal tissue and decreased expression of ARRB1 was associated with poor prognosis in Luminal A subtype. We found significant downregulation of ARRB1 mRNA and protein during conditions of EnR stress in multiple ER-positive breast cancer cell lines. Using PERK, ATF6 and XBP1 knockdown sub-clones of MCF7 we observed that PERK signalling was required for the downregulation of ARRB1. ATF4 and miR-204/211 downstream of PERK were identified as key regulators of ARRB1 expression. Conclusion: Our results show that

ATF4 and miR-204/211 downstream of the PERK signalling pathway repress ARRB1 expression in breast cancer cells. Our results suggest that the downregulation of ARRB1 by EnR stressors in the tumour microenvironment may contribute to breast cancer progression.

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Ananya Gupta, n/a: No financial relationships to disclose

Sanjeev Gupta, Principal Investigator: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-25-04

Granzyme B expression in tumor microenvironment as a biomarker for prognosis of triple-negative breast cancer

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Background: Many analyzes on tumor microenvironment has made it clear that tumor infiltrating lymphocytes (TILs) plays an important role in treating cancers with high tumor mutation burden such as triple-negative breast cancer (TNBC). We reported that the relationship between TILs and PD-L1 expression (Oncotarget 2017) and revealed that high-TILs/positive-PD-L1 expression population in TNBC was associated with better prognosis. However, its molecular mechanism is still unclear. Meanwhile, it was well-known that activated T-cells work as antitumor lymphocytes by enhancing the apoptosis by granzyme B (GZMB) and perforin, and then production of cytokines such as INF γ . We focused on GZMB and examined the function of activated T-cells. Patients and Methods: This study included 230 patients with primary TNBC who underwent resection without neoadjuvant chemotherapy at our three hospitals between January 2004 and December 2014. The immunohistochemistry (IHC) scoring for GZMB expression on TILs was defined as 1 or 5%. PD-L1 positivity was defined as ≥ 10 Combined Positive Score (CPS) based on tumor and immune cells staining positive for PD-L1. Results: Of the 230 TNBC, GZMB on TILs was expressed as more than 1% and 5% positive in 181 (79%) and 50 (22%) tumors, respectively, and PD-L1 and CD8 on TILs was expressed as positive in 99 (43%) and 127 (55%) tumors, respectively. GZMB expression (more than 5%) was significantly correlated with PD-L1 expression ($P=0.0048$) and CD8 expression ($P=0.0156$). There was no significant difference in recurrence free survival (RFS) and overall survival (OS) regardless of CD8 or PD-L1 expression level. Meanwhile, the patients with GZMB-positive tumors had a longer OS, compared to the patients with GZMB-negative tumors ($P = 0.0155$ in RFS and $P = 0.0202$ in OS) when PD-L1 expression on TILs was high, but not when it was low. Conclusion: OS was significantly longer among patients with high GZMB expressing TNBC. These results may validate the significance of GZMB as a biomarker for various immunotherapies in TNBC.

Disclosure(s):

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Masafumi Nakamura, Prof: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-26-01

Prospective breast biopsy collection at an urban safety-net hospital serving a diverse patient population

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Background: Despite advances in breast cancer imaging, research and treatment, higher mortality among racial/ethnic minority and low-income populations persists. Consent and enrollment of diverse and vulnerable patients into breast cancer research is critical. Given this urgent need for diversity in breast cancer research, successful collection and banking of fresh biospecimens from diverse patients is key to ameliorating some of the cancer disparities. Given our access to a unique and vulnerable patient population, we developed and implemented a clinical information and biospecimen repository for patients evaluated in the breast radiology and breast oncology outpatient clinics at Boston Medical Center (BMC). Our goal was to consent patients for donation of percutaneous breast biopsy samples, surgical tissue, and blood to develop a breast cancer biospecimen bank. Our long-term goal is to provide high-yield human samples for translational research studies in breast cancer from a diverse and vulnerable patient population. Methods: We designed a multi-disciplinary team of clinical providers and basic science researchers to envision a breast cancer biospecimen bank for research. Key stakeholders were identified, workflow was arranged, IRB obtained, and research staff trained. Patients presenting with suspicious mass on breast imaging (BI-RADS 4C and 5 categories) were eligible to enroll. Two percutaneous biopsy cores were obtained for research at the time of ultrasound guided biopsy. We leveraged the Hematology Oncology translational research program at Boston Medical Center and pilot finding to launch the project. Results: Since initiation in April 2021, we approached 68 patients and consented 44, for a successful consent rate of 64.7%. Of the 44 patients consented, 22 (50.0%) identified themselves as Black/African American, 11 (25.0%) as White/Caucasian, 10 (22.73%) as Hispanic and 1 (2.27%) as Asian. Of all patients enrolled, 41 (93.2%) had a breast malignancy, of which 27 (70.7%) were hormone-sensitive and 7 (17.1%) were TNBC. Additionally, of the 44 patients on study, only 9 (20.4%) had commercial insurance or managed care plan on the day of the consent. In total, 84 percutaneous biopsy cores were collected from 42 patients. Corresponding surgical tissue, plasma, serum and PBMCs were also obtained. Conclusion: Our program demonstrates that the enrollment of diverse and vulnerable breast cancer patients onto cancer research is achievable. We successfully created a breast biopsy program to provide access to diverse human samples for breast cancer translational research studies. Currently this repository serves to address many ongoing translational projects to understand:

1) the gap in knowledge of inherent differences in tumor biology and tumor environment, 2) metabolic regulation in the breast cancer microenvironment, and 3) heterogeneity of tumors and its effects on clinical outcomes and microenvironment interactions.

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Michael Fishman, MD: No financial relationships to disclose

Michael Cassidy, MD: No financial relationships to disclose

Naomi Ko, MD MPH: Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing)

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P2-26-02

Valproic acid induces apoptosis and mitochondrial perturbations in breast cancer cells

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Introduction: Breast cancer is the second leading cause of death among women after lung cancer. Despite the increase and improvement in preventive screening, breast cancer still remains a threat, both for pre- and postmenopausal women, due to the rapid development of resistance to drug treatments, which recalls the complicity of multiple factors. Breast cancer prognosis can be correlated with specific histological subtypes and their receptor status. Depending on stage and invasiveness, ER + and PR + breast cancers are treated with surgery and adjuvant chemotherapy, which includes endocrine-based agents, such as SERMS (Tamoxifen), SERDs (Fulvestrant) and aromatase inhibitors (Letrozole and Anastrozole). Resistance to endocrine therapy can be explained by various mechanisms, such as mutations of the estrogen receptor, epigenetic modifications of the same receptor, alterations in hormone synthesis and metabolism, aberrant activation of signaling transduction pathways (up-regulation of PI3K, MAPK, CDKs). To reduce pharmacological resistance, it is possible to use histone deacetylase inhibitors, such as valproic acid, as the epigenetic alterations play an important role in the oncogenesis of breast cancer. Epigenetic modifications of genes are a mechanism used by cancer cells to silence the expression of tumor suppressor genes, driven by epigenetic mutations of regulator factors. The valproic acid, used as an antiepileptic drug and for the treatment of bipolar disorders, is also a selective inhibitor of class I and class II HDAC isoforms, involved in the progression of different types of tumors. In this study, we tested the effects of valproic acid on the signaling involved in apoptosis and in the generation of Reactive Oxygen Species (ROS) in MCF-7 breast cancer cells. Methods: MTT assay was performed to evaluate cell proliferation. Cell cycle, ROS levels and apoptosis were analyzed by flow cytometry, while protein levels were detected by Western Blotting (WB). Results: Cell treatment with valproic acid reduced cell proliferation and induced G0/G1 cell cycle arrest. In addition, the drug enhanced the generation of ROS by the mitochondria and addressed breast cell death by

apoptosis. Indeed, the valproic acid was found to downregulate the anti-apoptotic marker Bcl-2 and to upregulate the expression of pro-apoptotic markers, such as Bax and Bad, leading to release of cytochrome C into the cytosol and PARP cleavage. The drastic reduction in mitochondrial membrane potential and in mitochondrial mass was observed following treatment with valproic acid, indeed the ratio between the two parameters, index of functionality per mitochondrion, resulted to be lowered, thus emphasizing the metabolic perturbation in the cells. Conclusion: In summary, our results have demonstrated that in estrogen receptor positive breast cancer cells the valproic acid is a suitable drug to arrest cell growth, to address apoptosis and mitochondrial perturbations, all factors that are important in determining cell fate and health. This study encourages that valproic acid, as an epigenetic drug, is a promising class of antineoplastic agent to be further explored also in combination with other classical chemotherapeutics in breast tumors.

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Maria Luisa Panno, Professor: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-26-03

TRAF3 as a regulator of breast cancer aggressiveness

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TRAF3 (TNF Receptor Associated Factor 3) is a regulator of NF- κ B signaling, acting mainly as an inhibitor of the alternative NF- κ B pathway through the interaction with other TRAF molecules and the downregulation of NIK (MAP3K14) kinase. While NF- κ B has a well-established role in breast cancer development and progression, TRAF3 which acts as a ubiquitin-ligase in the NF- κ B cascade has never been studied in mammary carcinomas. Here by employing breast cancer cell lines in invasion and colony formation assays, we show that TRAF3 forced expression inhibits aggressive traits of breast cancer cells. In addition, immunohistochemistry (IHC) for TRAF3 protein in breast cancer FFPE samples and analysis of TRAF3 gene expression from publicly available data sets, indicates that TRAF3 mRNA and protein expression in breast cancer tissue correlates with Recurrence Free Survival (RFS), Overall Survival (OS) and other clinicopathological parameters such as Histological Grade and proliferation index (ki-67). To our knowledge this is the first report on TRAF3 protein in breast cancer providing preliminary evidence for an inhibitory role of this protein in breast cancer development and progression.

Disclosure(s):

Anastasios Papanastasiou, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-26-04

Human papillomavirus protein E6 regulates Toll like receptor-9 expression in breast cancer cells

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Toll like receptor-9 (TLR9) is an innate immunity DNA-receptor, which is widely expressed in various cancers, including breast cancer. Low TLR9 expression in cancer cells was initially associated with poor prognosis among patients with triple negative breast cancer. We have now discovered a similar association also among other breast cancer subtypes. The mechanism for TLR9-associated poor prognosis is not currently known, but our ongoing studies suggest that it may be due to poor chemotherapy responses. Regulation of TLR9 expression in breast cancer is poorly understood. It has been demonstrated that in cervical cancers, TLR9 expression is suppressed by human papillomavirus (HPV) infections. Although breast cancer is not typically considered HPV-associated, there are reports of HPV in breast cancer. The aim here was to test the hypothesis, that HPV-infections suppress TLR9 expression also in breast cancer. To study this, human breast cancer cells were infected with HPV16 E6-oncoprotein, followed by measurement of TLR9 mRNA and protein in vitro. We also aimed to compare the presence of HPV DNA with TLR9 protein expression in clinical breast cancer specimens. We further studied E6-infection effects on breast cancer proliferation, migration, and invasion. E6-infection decreased TLR9 protein expression in TNBC but not in estrogen receptor expressing (ER+) cells. E6-overexpression significantly altered breast cancer proliferation, but the impact was opposite in TNBC and ER+ cells. No effect on migration and invasion was observed. E6-transfected breast cancer cells were significantly less sensitive in vitro to chemotherapies typically used for the treatment of breast cancer in the adjuvant setting. In vivo studies are pending. HPV DNA was not detected in a pilot cohort of clinical breast cancer specimens (n=37) among Northern Finnish breast cancer specimens. These results indicate that HPV may affect breast cancer TLR9 expression and thereby breast cancer prognosis, through treatment

responses. Although HPV was not detected in the small pilot set of our clinical samples, this issue needs to be further studied in larger data sets.

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Katri S. Selander, MD, PhD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-26-06

Association between CK+/CD45+ circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA) alterations in advanced breast cancer patients

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Background: Circulating tumor cells (CTCs) in breast cancer (BC) are commonly defined as epithelial cells (EPCAM and cytokeratin (CK) positive), lacking the universal blood cell marker CD45. Nonetheless, CTCs expressing both CK and CD45 (= dual-positive, DP cells) can be observed in the blood of cancer patients. Early evidence suggests that DP cells might derive from the fusion of tumor cells and macrophages, and we have previously demonstrated that they present aberrant genomes and are associated with worse prognosis in BC [1,2]. Here, to further investigate the mechanisms/pathways underlying their presence, we analyzed the association between DP cells and circulating tumor DNA (ctDNA) alterations. Methods: Blood

samples were collected from patients with advanced BC (aBC), before starting a new line of therapy. All patients were enrolled in a prospective clinical trial. For CTC and DP cells analysis, 7.5 ml of blood collected in CellSave® tubes was processed with the FDA-approved CellSearch® platform (positivity cutoffs were ≥ 1 cell for DPcells and ≥ 5 cells for CTCs). For ctDNA analysis, plasma was collected from Streck stabilizing tubes and analyzed with the Guardant360™ NGS platform for the detection of somatic single nucleotide variants (SNVs), insertions/deletions (indels), gene fusions/rearrangements and copy number variations (CNVs), which were then classified into pathways based on previously defined profiles generated on the Cancer Genome Atlas database (RTK, RAS, RAF, MEK, NRF2, ER, WNT, MYC, P53, cell cycle, notch, PI3K). Associations between ctDNA-detected gene alterations and circulating cell types were analyzed through chi square test, while mutant allele frequency (MAF) and number of detected alterations (NDA) were tested by Mann Whitney test. Results: We analyzed blood samples from 169 patients with luminal-like (n=80), HER2+ (n=34) and triple-negative (n=52) aBC. DPcells were detected in 85 patients (50.3 %, range 0-53), of which 40 (47 %) were CTC-positive and 45 (53%) CTC-negative. Somatic ctDNA alterations were detected in all analyzed samples. In the overall population, the presence of ≥ 1 DPcell was associated with SNVs in the cell cycle pathway ($p = 0.043$), a numerically higher incidence was also observed for CNVs in this pathway. SNVs and CNVs in the cell cycle pathway were associated with CTCs ≥ 5 as well ($p = 0.005$ and $p = 0.003$, respectively). Moreover, associations with CTCs ≥ 5 were observed for RTK SNVs and CNVs ($p = 0.041$ and $p = 0.046$, respectively), PI3K SNVs and CNVs ($p = 0.006$ and $p = 0.007$, respectively), MYC SNVs and CNVs ($p = 0.042$). No associations were observed in terms of MAF and NDA. In the luminal-like subgroup an association was highlighted for CNVs in the cell cycle pathway, $p = 0.038$. CTCs ≥ 5 were associated with PI3K SNVs ($p = 0.031$). In the triple-negative subgroup DPcells were associated with SNVs in the RAF pathway ($p = 0.041$), whereas CTCs ≥ 5 were associated with PI3K SNVs and CNVs ($p = 0.044$ and $p = 0.024$, respectively) and RTK SNVs ($p = 0.008$). In the HER2 positive subgroup, a higher MAF and number of detected SNVs was observed for samples with ≥ 1 DPcell ($p = 0.0286$ and $p = 0.0099$, respectively). Conclusions: The study analyzed ctDNA features associated with canonical and CK+/CD45+ CTCs, showing differential gene alteration profiles. Cell cycle pathway SNVs were common in both CTC populations, while other pathways (RTK, PI3K, MYC and RAF) were significantly altered in a mutually exclusive pattern. These results suggest that DPcells might have a different biological meaning compared to canonical CTCs. More studies need to be conducted to better characterize this understudied CTC subpopulation and understand their specific contribution to cancer progression. References: 1) Reduzzi C. et al., Semin Cancer Biol. 2020;60:344-350. DOI:10.1016/j.semcancer.2019.10.008 2) Reduzzi C. et al., Journal of Clinical Oncology 40, no. 16_suppl (June 01, 2022) 1093-1093. DOI: 10.1200/JCO.2022.40.16_suppl.1093

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Carolina REDUZZI, Ph.D: Menarini Silicon Biosystems: Research funding (Ongoing)

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Massimo Cristofanilli, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Celcuity: Consulting Fees (e.g., advisory boards) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing),

Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Ellipses: Consulting Fees (e.g., advisory boards) (Ongoing); Foundation Medicine: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Guardent: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Menarini: Consulting Fees (e.g., advisory boards) (Ongoing); Olaris: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Semonix: Consulting Fees (e.g., advisory boards) (Ongoing)

12/7/2022

7:00 AM - 8:15 AM

P2-26-07

Alteration of gut microbiota signatures and its association with diarrhea during abemaciclib treatment: A multicenter prospective cohort study (KBCRN-A002 study)

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Background: Abemaciclib is a selective CDK4 and CDK6 inhibitor with demonstrated efficacy in hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer. The most common adverse event across previous trials was early-onset diarrhea, affecting the patients' quality of life and necessitating dose reductions. However, the exact mechanism for the lower rate of diarrhea in the other CDK4 and CDK6 inhibitors

compared with abemaciclib is unknown. Ample evidence indicates that the gut microbiome is a tumor-extrinsic factor associated with the anti-tumor response; however, reported microbial signatures associated with adverse events by anti-cancer agent are inconsistent. To determine the underlying mechanism, we evaluated the correlation between diarrhea with abemaciclib and microbiota signatures in a metastatic breast cancer cohort.

Methods: The KBCRN-A002 study is a multicenter, prospective cohort study, which aims to evaluate the association between gut microbiota signatures and abemaciclib-induced diarrhea in breast cancer patients. Patients with metastatic breast cancer who were receiving abemaciclib were eligible. The primary objective of this study is the correlation between diarrhea and the microbiota signatures and immune profile. Incidence and severity of diarrhea were evaluated by the Bristol stool scale at baseline, from day 1 to day 14, and at day 90 of treatment. Stool samples were collected at baseline and at day 90 after the start of abemaciclib treatment. The gut microbiota signature was evaluated by 16S rRNA analysis. Blood samples were collected at baseline and at days 14 and 90 after starting abemaciclib to evaluate the correlation between the gut microbiota signatures and the systemic immune profile in peripheral blood mononuclear cells (PBMCs). The immune profile was evaluated by mass cytometry, multi-plex cytokines assay, and RNA-sequencing of bulk PBMCs. We characterized the gut microbiota signatures, immune cell composition, immune cell signature, comprehensive cytokines, and severity of diarrhea in all patients.

Results: We analyzed 39 patients, 77 stool samples, and 117 blood samples. In the preplanned interim analysis, among the 39 patients, 90% experienced diarrhea. Depleted gut microbiome α -diversity was positively associated with abemaciclib treatment and the severity of diarrhea. The relative abundances of 10 intestinal bacteria species increased and those of 18 intestinal bacteria decreased significantly after abemaciclib treatment, including bacteria known to be involved in diarrhea severity and anti-tumor immunity, such as *Faecalibacterium* (Table). The immune cell and cytokine profiles in PBMCs were also associated with the gut microbiota signatures.

Conclusions: Gut microbiota signatures are associated with abemaciclib-induced diarrhea and the immune profile in metastatic breast cancer patients. These findings can help to elucidate the mechanism of diarrhea caused by abemaciclib and offer strategies for its management and prevention.

Intestinal Microbiota Altered by Abemaciclib

Decreased by Abemaciclib	p value
Lachnoclostridium	<0.0001
Fusobacterium	0.007
[Ruminococcus] gnavus group	0.014
Tyzzarella 4	0.019
Eggerthella	0.022
Parabacteroides	0.023
Bilophila	0.023
Klebsiella	0.034
Blautia	0.036
Phascolarctobacterium	0.046
Increased by Abemaciclib	p value
Faecalibacterium	<0.0001
Roseburia	0.001
Subdoligranulum	0.002
Ruminiclostridium 5	0.003
Agathobacter	0.004
Clostridium sensu stricto 1	0.008
Bifidobacterium	0.011
Oscillospira	0.012
[Eubacterium] coprostanoligenes group	0.014
Olsenella	0.018
GCA-900066225	0.021
Christensenellaceae R-7 group	0.022
Adlercreutzia	0.035
DTU089	0.036
Lachnospiraceae NK4A136 group	0.036
Slackia	0.043
Lachnospiraceae UCG-001	0.043
Ruminococcaceae UCG-002	0.047

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12/7/2022

7:00 AM - 8:15 AM

P2-26-08

Influence of genetic ancestry on breast stromal cells provides biologic basis for increased incidence of metaplastic breast cancer in women of African descent

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The biologic basis of genetic ancestry-dependent variability in disease incidence and outcome is just beginning to be explored. We recently reported enrichment of a population of ZEB1-expressing cells located adjacent to the ductal epithelial cells in the normal breast of women of African Ancestry (AA) compared to European Ancestry (EA). By establishing and characterizing cell lines corresponding to these cells and validating in vitro findings with tissue microarrays of healthy breast tissue from AA, EA and Latina Ancestry (LA) women, we demonstrate that these cells have the properties of fibroadipogenic/mesenchymal stromal cells that express PROCR and PDGFR α . PROCR+/ZEB1+/PDGFR α + cells, hence renamed as PZP cells, are enriched in the normal breast tissues of AA compared to EA or LA women. In vitro, PZP cells trans-differentiated into adipocytes or osteocytes. In co-culture conditions, PZP:epithelial cell communication resulted in luminal epithelial cells acquiring basal/stem cell characteristics and increased expression of IL-6 suggesting the impact of this communication on the microenvironment and breast epithelial hierarchy. Consistent with this possibility, the level of phospho-STAT3, which is a downstream target of IL-6, was higher in the normal and cancerous breast tissues of AA compared to EA women. PZP cells transformed with HRasG12V \pm SV40-T/t antigens generated metaplastic carcinoma in NSG mice suggesting that these cells could be the cell-of-origin of metaplastic breast cancers. Collectively, these results identify a stromal cell component that could influence the biology of breast cancer in AA women.

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12/7/2022

7:00 AM - 8:15 AM

P2-26-09

Synergistic activity of PI3K inhibitor in combination with AZD6738, ATR inhibitor in breast cancer preclinical model via DNA damage response pathway

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Background: The PI3K inhibition has been an appealing approach for anticancer therapy due to its crucial role in cell growth, proliferation, and survival in various cancers. Emerging data suggest the PI3K pathway is also involved in DNA replication and genome stability, making DNA damage response (DDR) inhibitors as an attractive combination treatment for PI3K pathway blockades. Here, to enhance the efficacy of PI3K inhibitors, we investigated the novel approach combining PI3K inhibitors (alpelisib, AZD8835, AZD8186, NVP-BKM120) with DDR blockade using ATR inhibitor (AZD6738) in breast cancer preclinical models. Methods: Hormone receptor-positive breast cancer cells, MCF7 (PIK3CA E545K mutation) and T47D (PIK3CA H1047R mutation) were used. First, cell viability and the synergistic effect of combination drug was carried out by MTT assay. Next, western blot, cell cycle analysis, apoptosis assay, and immunocytochemistry were conducted to validate the hypothesis. Finally, tumor xenograft experiments were conducted using BALB/c nude mice to validate the in vitro data. Results: A synergistic antiproliferative effect was observed over a wide range of combination (PI3K inhibitor + ATR inhibitor) concentrations (even in a lower concentration as 1/10 x IC50) in vitro, suggesting that when alpelisib is combined with an ATR inhibitor, there may be possibility of lowering the effective dosage of alpelisib. After confirmation of the strong synergistic effect in sub-G1/G0-G1 arrest-mediated apoptosis by the combination treatment, we demonstrated that expressions of phospho ATR, ATM, and CHK1 were suppressed but γ -H2AX markedly increased by combination treatment as compared to PI3K inhibitors and ATR inhibitor alone. This suggests that combination treatment activates apoptotic pathway through enhanced DNA double strand breaks. Finally, the in vivo study showed that the combination treatment group tended to show a greater tumor growth inhibition compared with PI3K inhibitor or ATR inhibitor alone. Conclusion: The combined inhibition of PI3K and ATR showed a synergistic anticancer effect in vitro and in vivo. ATR inhibitor in combination with PI3K inhibitor merits further clinical investigation to enhance the activity of PI3K inhibitor for the treatment of PIK3CA mutated breast cancer patients.

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12/7/2022

7:00 AM - 8:15 AM

P2-26-10

Statins exhibit an anti-tumor effect by attenuating PD-L1 in breast cancer cells and macrophages and reducing breast tumor progression in xenograft mouse model

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Background: Statins were suggested for repurposed drugs, having multifaceted effects which include anti-tumor activities by modulating the immune response. Here, we aimed to demonstrate the effect of statins on programmed death-ligand 1 (PD-L1) expression in triple-negative breast cancer (TNBC) cells. Methods: Thirteen human TNBC cell lines, mouse macrophage cell line (RAW 264.7), cholesterol and 27-hydroxycholesterol, and clinically approved lovastatin and simvastatin were used. Flow cytometry, Annexin V/propidium iodide assay, western blot, qRT-PCR, transwell migration assay, and immunohistochemistry were employed. A co-culture of macrophages with various breast cancer cells was performed. An orthotopic breast tumor mouse model and metastasis model by injection of GFP-tagged MDA-MB-231 cells into mammary gland fat pad and the tail vein injection were produced. In tumor model mice, lovastatin(10mg/kg) was daily injected intraperitoneally. In vivo fluorescent imaging was used to identify primary tumor development and lung metastasis. Results: Among thirteen TNBC cell lines, MDA-MB-231, HCC38, and HCC70 highly expressed endogenous/constitutive PD-L1. Statins reduced PD-L1 expression and exerted anti-proliferative and apoptotic effects in MDA-MB-231, HCC38, HCC70, and Raw264.7 in a dose- and time-dependent manner ($p < 0.05$). Meanwhile, statins increased the expression of PD-L1 in Hs578T and MDA-MB-468. STAT3 phosphorylation was inhibited in MDA-MB-231 and HCC70, but not in Hs578T, while AKT phosphorylation was reduced in MDA-MB-231, HCC70, Hs578T, and MDA-MB-468 when statins were treated. The migration of MDA-MB-231 and Raw264.7 in statin-treated conditioned media was decreased ($p < 0.05$). Cholesterol and 27-hydroxy cholesterol did not restore PD-L1 expression in statin-treated MDA-MB-231. Statins suppressed the expression of M2 markers

(PD-L1, CD206, YM-1, Fizz1, arginase-1) in RAW26437 stimulated by a conditioned medium of MDA-MB-231. Lovastatin suppressed the primary tumor growth and metastasis in xenograft tumor mice. Conclusions: Our findings show that statins have an anti-tumor effect, which kills breast cancer cells and triggers macrophage reprogramming by reducing PD-L1 expression, impairing the AKT, ERK, and STAT3 signal pathways, and decreasing M2 markers. Further study is needed to investigate an in-depth molecular mechanism study by which statins regulate PD-L1 expression in TNBC and to confirm the safe and effective use of statins as adjuvant therapy in TNBC.

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7:00 AM - 8:15 AM

P2-26-11

Protein phosphatase 1 catalytic units, PPP1CA, PPP1CB and PPP1CC in breast cancer

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Introduction. Protein phosphatase-1 (PP1) belongs to the Serine/threonine-protein phosphatase family and is known to participate in multiple functions in the cells including glycogen metabolism, cellular proliferation and cell receptor regulations. Protein phosphatase-1 has three catalytic units, namely PPP1CA, PPP1CB and PPP1CC. A PP1 protein complex is composed of one of the catalytic units and at least of one the various phosphatase regulatory units (PPP1Rs). The regulatory units of the phosphatase, abundant in numbers, also influence the functions of the protein phosphatase within cells. PP1 has been indicated to have a role in certain clinical conditions such as the Alzheimer's and certain viral infections. The value of the PP1 catalytic units in clinical cancers including breast cancer is not well established, therefore this current study aimed to examine the expression profile of the three PP1 catalytic units in human breast cancer and attempted to establish the clinical relevance of the catalytic units in the disease progression of breast cancer. Methods. Fresh frozen normal mammary tissues and breast cancer tissues were investigated for the levels of gene transcripts of the three PP1 catalytic units were quantified and corrected with an epithelial cell marker. The expression and integrated expression profile of PPP1A, PPP1B and PPP1C in the tissues were assessed against the pathological, clinical and outcome of the patients as well as the hormone receptor status. Results. All three catalytic units of PP1 were positively expressed in normal and tumour breast tissues, with PPP1A at significantly higher levels in normal mammary tissues than tumours ($p=0.01$) and PPP1B and PPP1C showing no significant difference. Expression of PPP1B in breast cancer was significantly lower in high grade breast cancers ($p < 0.05$ vs low grade), in tumours from patients who died of breast cancer ($p=0.047$ vs those who survived) and with breast cancer related incidence ($p=0.048$ vs incidence free). The most significant finding of the present study was a correlation between high levels of all three catalytic units and favourable overall survival of the patients. Those patients with high levels of PPP1A, PPP1B and PPP1C in breast tumours had a mean survival time of 142.6, 141.6 and 140.3 months compared with those with low levels respectively at 111.8, 115.8 and 117.6 months. When the expression profiles of the three units were integrated, the integrated profile formed a highly valuable and independent indicator for both overall survival ($p=0.008$, HR=0.694) and for disease free survival ($p=0.004$, HR=0.702). The predictive value of PPP1A/PPP1B/PPP1C for survival was more significant for ER negative tumours than ER positive tumours ($p=0.003$), but

appeared to be indifferent for Her2 status. Finally, our data indicated that the integrated expression of the three catalytic units had a significant predictive value in bone metastasis of the patients ($p=0.008$, $HR=0.546$). Discussion. Protein phosphatase-1 catalytic units, PPP1CA, PPP1CB and PPP1CC are expressed in human mammary tissues; raised levels of the catalytic units are a favourable clinical indicator for the survival of patients and for a decreased tendency to develop bone metastasis.

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7:00 AM - 8:15 AM

P2-26-12

Interaction between CTCs and platelets complicate their detection by masking surface epitopes

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1) Background: It is well known that solid tumors have the ability to form metastases. The development of distant metastases is due to the primary tumor shedding cells that travel to distant sites via the blood vessels. Platelets specifically promote tumor cells survival in the bloodstream. To investigate the interplay between platelets and circulating tumor cells, we implemented our approach to label simultaneously circulating epithelial tumor cells and platelets. 2) Methods: 40 breast cancer patients were enrolled into the study. Blood samples were collected in EDTA tubes without fixatives and processed at 3 timepoints (0h, 24h and 48h) using the maintrac® approach. In order to visualize platelets we used anti-CD36 antibody staining. 3) Results: We observed at 0h post-blood draw platelet aggregates strictly attached to single cells that did not stain with anti-EpCAM antibody. After keeping blood samples at room temperature for 24h platelet aggregates could still be detected, but the anti-EpCAM antibody became accessible to the underlying cells. CTCs were detected in 94% of patients on day 1 post-blood draw. At 48h following initial blood drawing, platelets had almost completely disappeared from the cell surface and the number of detected CTCs remains stable between 24h and 48h. Furthermore, the number of CTCs correlates with clinical stage of disease. Patients with stage I/II have significantly less CTCs as compared to patients with stage III/IV (median 5 vs. 19 CTCs/100µl cell suspension, $p < 0.05$). 4) Conclusion: Our results suggest that platelets play a key role in masking circulating tumor cells. Masking may explain the difficulties in detection of these cells and prevention of their elimination by the immune system.

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Dorothea Schott, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-26-13

Gene deletion of insulin receptor in MCF-7L breast cancer cells by CRISPR gene editing

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The type I insulin-like Growth Factor Receptor (IGF-IR) plays important roles in breast cancer cell proliferation and metastasis. However, preclinical and clinical research targeting IGF-IR also revealed the potential for insulin receptor (IR) to compensate for IGF-1R inhibition. IR is expressed as two isoforms (IRA and IRB) through alternative splicing. The IRB is expressed in adult tissues and thought responsible for cell metabolism while IRA is expressed in fetal development to enhance cell growth. Since breast cancer cells usually express both IGF-IR and IRA/IRB, differential signaling by IRA and IRB has not been clearly demonstrated. To further define the role for IR, we used CRISPR technology for gene editing in exon 2 of IR in MCF-7L cells to delete IR. Cells were selected for absent IR expression by flow cytometry and Sanger sequencing confirmed that one of the clones (CL35) had the targeted 4 base pair deletions in exon 2. Immunoblotting using an antibody to the α subunit of IR showed no expression in CL35. Unexpectedly, 10 nM insulin exposure resulted in downstream AKT and Erk1,2 phosphorylation. Immunoprecipitation showed that IGF-IR was activated by the insulin in CL35 cells. Insulin signaling in CL35 through IGF-IR was inhibited by huEM164, an anti IGF-IR monoclonal antibody. Compared to MCF-7L parental cells, CL35 was more sensitive to IGF-I and less sensitive to insulin as demonstrated by downstream AKT phosphorylation and MTT monolayer growth assay. Insulin stimulated monolayer growth of CL35 measured by MTT was not affected in testing serum free media (SFM) unless transferrin was deleted from the media. These data suggest IGF-IR can function to activate signaling in response to insulin. To ensure that our clone does not contain alternate splicing products resulting in aberrant IR proteins, we are further sequencing IR mRNA in CL35. In conclusion, we have established an IR null breast cancer cell line with reduced sensitivity to insulin and increased sensitivity to IGF-I. This cell line can be used to express the IRA and IRB isoforms to characterize their function in breast cancer cells.

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Marvis Monteiro, n/a: No financial relationships to disclose

Douglas Yee, MD: Boehringer Ingelheim: Contracted Research (Ongoing); Martell Diagnostics: Consulting Fees (e.g., advisory boards) (Ongoing)

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7:00 AM - 8:15 AM

P2-26-14

CDK4/6 inhibitors modulate the ubiquitin–proteasome pathway in ER+ breast cancer by downregulation of UBE2C/S/T

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Despite significant improvement in therapeutic development in the past decades, breast cancer remains a formidable cause of death for women worldwide. The hormone positive subtype (HR(+)) (also known as luminal type) is the most prevalent category of breast cancer, comprising ~70% of patients. The clinical success of the three CDK4/6 inhibitors palbociclib, ribociclib, and abemaciclib has revolutionized the treatment of choice for metastatic HR(+) breast cancer. Accumulating evidence demonstrate that the properties of CDK4/6 inhibitors extend beyond inhibition of the cell cycle, including modulation of immune function, sensitizing PI3K inhibitors, metabolism reprogramming, kinome rewiring, modulation of the proteasome, and many others. The ubiquitin–proteasome pathway (UPP) is a crucial cellular proteolytic system that maintains the homeostasis and turnover of proteins. By transcriptional profiling of the HR(+) breast cancer cell lines MCF7 and T47D treated with Palbociclib, we have uncovered a novel mechanism that demonstrate the CDK4/6 inhibitors suppress the expression of three ubiquitin conjugating enzymes UBE2C, UBE2S, UBE2T. Further validation in the HR(+) cell lines show that Palbociclib and ribociclib decrease UBE2C at both the mRNA and protein level, but this phenomenon was not shared with abemaciclib. These three E2 enzymes modulate several E3 ubiquitin ligases, including the APC/C complex which plays a role in G1/S progression. We further demonstrate the UBE2C/UBE2T expression levels are associated with breast cancer survival, and HR(+) breast cancer cells demonstrate dependence on the UBE2C. Our study suggests a novel link between CDK4/6 inhibitor and UPP pathway, adding to the potential mechanisms of their clinical efficacy in cancer.

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P2-26-15

CCR7 expression in Inflammatory breast cancer.

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Background: Inflammatory breast cancer is an aggressive breast cancer characterized by florid congestion of lymphovascular spaces by tumor emboli. CCR7 is an immune cell receptor that mediates traffic of immune cells into lymphatics that can be expressed on tumor cells. An RNA-seq screen of tumor promoting mammary glands in mice identified CCR7 as an upregulated signal in mammary glands that promoted IBC-like skin invasion. We examined the expression of CCR7 in IBC cell lines and patients to determine the prevalence of this receptor in IBC. Methods: Protein lysates from IBC and non-IBC cell lines were subjected to immunoblotting using anti CCR7 (R&D systems). An IBC tissue microarray from post-chemotherapy mastectomy specimens of 39 patients, each with three replicates was subjected to immunohistochemical staining for CCR7 (Invitrogen, catalog number MA5-31992) performed using a Leica Bond RX autostainer with an incubation time of 60 minutes at 1:15,000 after 20 minutes of heat-induced antigen retrieval at pH 6.0. In 15 cases there were no tumor cells observed in the cores. Staining was scored by an expert breast pathologist for intensity and percent tumor stained. Staining patterns were scored. Descriptive statistics were examined for

representation by receptor subtype. Results: CCR7 staining was strong in all lines examined including MCF7, SUM149, SUM190, MDA-IBC, and SUM159. Among 24 IBC patient cores with tumor in the tissue, 23 (96%) expressed CCR7 in tumor, 15 with complete membranous staining and 9 with incomplete membranous staining. In one case with LVSI the emboli were CCR7 positive. Among the 24 positive cases, 22 were 3+ intensity while two were 2+. Nine CCR7+ cases were estrogen receptor (ER) ER+, 8 ER-, and 6 unknown. HER2 status is pending. Conclusions: CCR7 expression is present across tumor subtypes in IBC cell lines and in both ER+ and ER- patient tumors. Given developing novel pharmacologic targeting of CCR7, this target warrants further investigation in IBC and other breast cancers.

Disclosure(s):

Wintana Balema, B.A.: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-26-17

Establishment of an in vitro preclinical platform: A living biobank of patient-derived organoids with ER+ breast cancer

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Introduction and objectives Estrogen receptor positive (ER+) tumors are the most common form of breast cancer and are responsible for most of the deaths from the disease. Treatment of ER+ breast cancer comprises interventions that suppress estrogen production and/or target the ER directly. While endocrine therapy has considerably reduced recurrence and mortality from breast cancer, de novo and acquired resistance to this treatment remains a major challenge. In this context, patient-derived organoids (PDOs), 3D structures composed of epithelial cells, are changing our understanding of cancer heterogeneity and its implications for personalized medicine. Our aim was to establish and characterize a PDO platform of ER+ breast cancer as preclinical tool to decipher and target this heterogeneity in order to tailor effective treatments based on the precise molecular makeup of the tumor. **Material and Methods** Surgical resections were collected from patients diagnosed with ER+ breast cancer. Organoid generation from patient material were divided in three main steps: 1) mechanical fragmentation of tissue pieces; 2) digestion of fragments into single-cell suspension; and 3) plating of cell preparations into matrigel domes to mimic the extracellular matrix. Organoids were passaged every 7–21 days based on confluency. Each newly organoid line was cryopreserved for further expansion. **Results** We have successfully achieved an outgrowth efficiency of almost 50% for PDOs from patients diagnosed with breast cancer. Characterization of PDO cultures is essential to validate its predictive potential. To asses that PDOs represent the tumor of the patient, for each organoid line, expression levels of the main histological markers (ER, PR, HER2, Ki67) were evaluated and correlated with the tissue of origin. In parallel, we have performed immunofluorescence on paraffin-embedded organoid samples with routinely used cancer stem

cell markers. Potential contamination with normal cells (present in the resection used to establish the culture) should be considered. To address the tumor purity of the culture we have performed targeted DNA sequencing in both the original tissue and established PDOs. Conclusions PDOs represent a superior preclinical system compared to previous models due to their inherent heterogeneity, long-term stability, applicability for high-throughput screens and enhanced capacity to capture tumor characteristics. Therefore, the implementation of a well-annotated patient-derived organoid biobank will be of great interest for drug discovery and personalized therapy. Understanding the sources and implications of tumor heterogeneity will undoubtedly improve our evolving definition of cancer and aid in the design of effective patient-specific treatment strategies.

Disclosure(s):

Maria A Dominguez-Cejudo, PhD: No financial relationships to disclose

Raquel Chapresto, n/a: No financial relationships to disclose

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P2-26-18

Adiponectin regulates stem cell activity in tamoxifen-resistant breast cancer cells

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Introduction: Breast cancer is the most diagnosed neoplasia and the second leading cause of malignancy death in women. Drug resistance is still the major challenge in the clinical management of breast cancer patients. Indeed, despite the improvements in the early diagnosis and in the therapeutic approaches, many breast cancer patients experience disease relapse due to de novo or acquired drug resistance. Growing evidence recognized a small population of breast cancer cells, named Breast Cancer Stem Cells (BCSCs), as the leading cause of tumor progression, metastasis formation and resistance against conventional therapy. BCSCs have some specific properties such as self-renewal, differentiation into different cell types, migration, tumorsphere formation, antioxidative activity, that make tumors more aggressive. Tumor microenvironment plays a crucial role in the regulation of stem cell proliferation and resistance to apoptosis through the secretion of cytokines and growth factors. Adipocytes represent the most abundant cellular component of mammary microenvironment. The excessive fat accumulation in obesity leads to the development of a dysfunctional adipose tissue, producing an unbalance in adipokines secretion. Among the secreted factors, adiponectin plays a crucial role in breast cancer development and progression. The aim of the present study was to investigate the effects of low adiponectin level (5 µl/ml), hallmark of obese status, on BCSCs activity in hormone-resistant cells. Methods: We tested the ability of MCF-7 wild type (WT) and tamoxifen-resistant (TR) to grow as mammospheres (Mammospheres Forming Efficiency, MFE), measuring the ability to maintain cell viability (self-renewal) upon serial non-adherent passages. mRNA levels of stemness, EMT and cell cycle markers were

evaluated by qRT-PCR. CD44⁺/CD24⁻ cell ratio, ALDH expression, ROS production, cell cycle, were analyzed by flow cytometry. Results: Adiponectin treatment significantly enhanced MFE and self-renewal capacity in TR-MCF-7 cells compared to MCF-7 WT cells. To identify the presence of BCSCs into mammospheres it has been evaluated the CD44⁺/CD24⁻ biomarker signature. Flow cytometry revealed an enrichment of CD44, a trans-membrane glycoprotein which regulates growth signals in stem cells, in TR-MCF-7 mammospheres, whereas expression levels of the differentiation marker CD24 were decreased. The gene expression of these biomarkers was also analyzed by qRT-PCR. The increased BCSCs subpopulation in adiponectin-treated TR-MCF-7 mammospheres was also confirmed by the enhanced ALDH-expressing cells. qRT-PCR revealed that adiponectin increased the mRNA levels of stemness and EMT markers in TR-MCF-7 cells mammospheres. Interestingly, cell cycle analysis showed in adiponectin-treated TR-MCF-7 mammospheres a reduction of apoptosis. Moreover, flow cytometry analysis displayed a reduction of ROS levels, which generally are assumed as cues determining DNA damage-induced cell death, in adiponectin-treated TR-MCF-7 mammospheres. Conclusions: Our results demonstrated that low adiponectin level, as it occurs in obese breast cancer microenvironment, driving EMT, enhances stem-like features in TR-MCF-7 cells to sustain tumor progression.

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P2-26-19

Slc26a9 cooperates with HER2 to regulate the progression and development of HER2-positive breast cancer

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significantly inhibited after silencing Slc26a9, and tumorigenesis and metastasis were significantly inhibited in vivo. On the contrary, overexpression of Slc26a9 resulted in the opposite result. Mechanistically, overexpression of Slc26a9 activated the PI3K/AKT/mTOR signaling pathway, the key signaling pathway implicated in HER2-positive breast carcinogenesis, and promoted the expression of downstream proliferation related genes CCND1 (Cyclin D1) and c-Myc, and downregulated the expression of apoptosis related genes Caspase9, apoptosis-inducing factor (AIF) and endonuclease G (Endo G), indicating the simultaneous inhibition of caspase dependent and independent apoptosis pathway. At the same time, accompanied by changes in markers of epithelial-mesenchymal transition (EMT), including downregulation of E-cadherin and ZO-1, and upregulation of N-cadherin and Fibronectin, and SKBR3 cells changed from epithelioid morphology to mesenchymal morphology. In addition, immunofluorescence and protein nucleoplasm separation experiments showed that Slc26a9 upregulated the expression of HER2 and co-localized with HER2 in the nucleus. Co-immunoprecipitation experiments proved that Slc26a9 interacted with HER2. Furthermore, trastuzumab downregulated the expression of Slc26a9 by targeting HER2 in SKBR3 cells. Moreover, when Slc26a9 was overexpressed, the inhibitory effect of trastuzumab on HER2 was partially reversed, and we also verified the PI3K/AKT/mTOR signaling pathway. Not only that, we found that Slc26a9 was significantly upregulated in drug-resistant cell lines relative to parental cells by constructing SKBR3 drug-resistant cell lines, indicating that Slc26a9 expression was significantly correlated with chemotherapy resistance in HER2-positive BC. Conclusion(s): Slc26a9 may interact with HER2 in the form of molecular chaperones to activate PI3K/AKT/mTOR signaling pathway to promote the progression and development of HER2-positive BC and be associated with chemotherapy resistance, but the precise molecular mechanism needs further exploration. Conflict of Interest: No significant relationships.

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7:00 AM - 8:15 AM

P2-26-20

Marvel D3 and its associated junctional proteins in breast cancer

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Marvel D3 and its associated junctional proteins in breast cancer Wenxiao Ji, Wen G. Jiang, Tracey A. Martin CCMRC, Cardiff University School of Medicine, Cardiff, Wales, UK
Introduction. Marvel (Membrane Associated Domain Containing) proteins are a small family of proteins that are concentrated at the tight junction (TJ) region of epithelial and endothelial cells. They are important players in the formation and regulation of TJs. The Marvel protein family has three members, Marvel-D1, Marvel-D2 and Marvel-D3, all known to be TJ components. Marvel-D3 is more prominent in TJ regulation, by interacting widely with other proteins that co-localised at TJs. In the present study, we have examined the expression of Marvel-D3 and its splicing variants, their relationship with other known interactive TJ partners in breast cancer and in disease progression and clinical outcome. Methods. Marvel-D3 and its variants were quantified in a breast cancer cohort that contained both normal and tumour tissues. The expression was analysed together with the known Marvel-D3 interactive molecules available in our database of the same cohort. The profile of the expression of the molecules was also integrated to search for a pattern of the expression that may have clinical significance including the survival of the patients. Results. Marvel-D3 had significantly high levels in breast cancer tissues than normal tissues ($p=0.011$). The difference between normal and tumour tissues for two Marvel-D3 variants were not statistically significant. Of all the known Marvel-D3 interactive proteins that were available for analyses, we identified thirteen with viability in integrated analyses; they include the JAM family members, Marvel-D2, occludin, the zonula occluden family members, small number of the claudin family members and cingulin, all being important TJ components. The integrated expression of these Marvel-D3 partners presented a highly significant predictive power for the overall survival of the patients ($RUC=0.821$, $p < 0.0001$). Stratifying the patients based on the profile has a significant value in evaluating survival (survival rate 95.7% with favourable expression versus 57.1% unfavourable, during the followup period). This predictive power is independent of other clinical and hormonal receptor status ($p < 0.001$, $HR=1.226$ (95% CI 1.094-1.373)). We have also noted that this predictive value is applicable to subtypes of the breast cancer and hormone receptor status with similar predictive power. Conclusion. Expression of Marvel-D3, a TJ component, together with its interactive TJ partners, including both transmembrane and intracellular subcoat proteins, form an important clinical indicator for clinical progression of breast cancer.

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P2-26-21

The Principal Factors Associated with Engraftment Success of Patient-Derived Xenograft of Breast Cancer

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Background: Patient-derived xenografts (PDXs) are increasingly used in cancer research as tools for studying cancer biology and personalized immunotherapy response. However, a comprehensive evaluation of patient-derived breast cancer xenograft generation rates in various settings is understudied. Methods: We conducted a prospective study of breast cancer patients treated with surgery to generate PDXs. PDXs were characterized by molecular subtypes, specific diagnostic entities, modified Bloom-Richardson system nuclear and histologic grades, treatment with neoadjuvant chemotherapy (NAC), Miller Payne grade, residual cancer burden class, invasive tumor size, lymphovascular invasion status, number of positive lymph nodes, and the percentage of tumor infiltrating lymphocytes in the implanted tumors. Results: Three hundred and seventy-two (157 post-chemotherapy, 215 chemo-naïve) patient-derived tumors were implanted and 63 PDXs were established (17.0%). PDX engraftment was higher in the patients with higher nuclear and histologic grades using the modified Bloom-Richardson system (27.6% vs. 3.2%, $p = 0.003$) and triple negative breast cancer (TNBC) than in those with hormone receptor-positive cancer (36.4% vs. 3.2%, $p = 0.02$). Tumors from patients who received NAC (30.0% vs. 7.4%, $p = 0.05$) were also close to being statistically significant for successful PDX generation. Conclusions: PDXs can be established from clinically aggressive breast cancers, especially in patients with high nuclear and histologic grade TNBC treated with NAC. The prediction of engraftment success using these factors would establish cost-effective immunotherapy trials employing PDXs.

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7:00 AM - 8:15 AM

P2-26-22

Elevated Expression of High Mannose Glycans in Tissue and Serum Samples of Breast Cancer Patients

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Glycobiology has proved to be a new frontier in oncology research in recent years. One sector of glycobiology involves examining glycan expression of cancerous cells. Glycans are complex carbohydrates found on cell surfaces, and patterns of aberrant glycan expression, such as increased sialylation and fucosylation, have been proposed as potential novel biomarkers of cancer tumorigenesis and metastasis. However, to our knowledge, there is little literature examining the differences in expression of high mannose glycans, a subtype of N-linked glycans, which is the focus of this study. Thirty-nine samples of malignant and surrounding benign tissue from breast cancer patients were collected from the Prisma Health Cancer Institute Biorepository. Additionally, forty malignant serum samples were collected—ten of these samples were from the same patients included in the tissue samples. Serum samples from ten healthy volunteers were also obtained as controls. The malignant samples included specimens from breast cancer staged I through IV at the time of the patients' diagnosis. Samples were analyzed using MALDI-TOF mass spectroscopy for the presence of glycans by Emory Glycomics and Molecular Interactions Core. The known masses of sixty-one unique glycans were then compared to the spectra of the samples analyzed to determine the type of glycans present, and the relative amount of each glycan present was determined using the area under the curve in the spectral data. Data analysis revealed the means of the area under the curve for high mannose glycans in the malignant and normal tissue samples to be 247.18 and 163.6 respectively; the t-test established the difference in these means to be statistically significant (p-value, 0.0138). This finding was consistent in serum samples; the mean area under the curve for malignant and normal serum was 1650.34 and 376.26 respectively (p-value, >.0001). Furthermore, there were differences in expression of high mannose glycans between stages of breast cancer, with expression in stage III being significantly greater than expression

in stage II in both serum (p-value, .0097) and tissue (p-value, .0003) samples. The results of this analysis suggest a higher expression of high mannose glycans to be a promising biomarker for breast cancer. This could lead to important clinical applications such as being a helpful distinction in obtaining negative margins during tumor resection, as well as providing a non-invasive diagnostic method. Future research could include expanding the sample size and comparing the glycan composition of the samples to a library specific for high-mannose type glycans, with the goal of establishing a signature high-mannose expression pattern in each stage of cancer.

Disclosure(s):

Alex Kesic, B.A.: No financial relationships to disclose

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7:00 AM - 8:15 AM

P2-26-23

Transcriptomic modification induced by the first cycle of neoadjuvant chemotherapy impacts response to treatment in triple negative breast cancer (TNBC)

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Background Despite adequate neoadjuvant chemotherapy, TNBC remains poor prognosis. Non-responding patient have 25-40% risk of relapse at 5 years. pCR is therefore currently considered as a major goal in TNBC and new tools of early prediction of residual disease should be identified. TransTep is a phase 2 monocentric clinical trial which aims to identify transcriptomic profile of triple-negative cancer cells associated with early tumor chemoresistance, as identified by FDG PET after the first course of neoadjuvant chemotherapy. Twenty patients were included between January 2015 and October 2017, with stage II or III of the UICC classification (except stage T4d). All patients received neoadjuvant chemotherapy with anthracyclines and taxanes sequentially, none of them had a dose-dense chemotherapy. Six patients obtained metabolic response (Delta SUV < -30%) after one cycle of anthracycline. Methods Total RNA was extracted from biopsies (HES > 30%) and used to prepare libraries thanks to TruSeq RNA library Prep kit (Illumina) and sequenced on NextSeq500 device. Results Transcriptomic expression analysis between tumors before chemotherapy and tumors after one course of chemotherapy showed that tumors showing a significant decrease of their Delta SUV (<-30%) had a much higher gene expression variation than tumors with a Delta SUV >-30%. These tumors presented, after one course of chemotherapy, a decrease of cell cycle, DNA replication and Fanconi anemia pathway related genes, while they harbored an increase of genes belonging to immunity related pathways such as natural killer cell mediated toxicity, TH17 cell differentiation, or chemokine signaling pathway. As patients had a surgery after neoadjuvant chemotherapy, we had Chevalier tumor response. As observed with FDG PET data, patients with a good response according to Chevalier (class 1) criteria presented a much higher transcriptomic modification after one course of chemotherapy. Patients with a little gene

expression modification were classified as Chevalier 3. When we focused on pathways impacted by chemotherapy in tumors classified as Chevalier 1, we observed a significant decrease of cell cycle, DNA replication and DNA repair pathways related gene after one course of chemotherapy, whereas a high number of genes belonging to immunity related genes (NK cells, antigen processing and presentation, or chemokine signaling pathway) were increased. Conclusion Our results tend to indicate that transcriptomic tumor response after one course of chemotherapy could forecast final response to treatment. Moreover, it seems that one cycle of anthracycline-based chemotherapy is able to get hot some breast tumors, and that this tumor warming could be a marker of good response to the full treatment. In the following months, we will test whether transcriptomic could predict progression free survival and/or overall survival of patients. We will also look for the best early marker of response between PET FDG and tumor transcriptomic modifications. Based on these results, a new trial will be organized. A therapeutic adaptation depending on the transcriptomic or metabolic data will be proposed to increase pCR rate and prognosis of patients. Moreover, with years and therapeutic innovations, patient management obviously evolves. This was recently the case with a new standard of care in triple negative breast cancer with combination of platinum salt and immunotherapy. Therefore, a new trial, similar to TRANSTEP, will be carried out with this new standard of care.

12/7/2022

7:00 AM - 8:15 AM

P3-01-01

Unicentric experience with icdk4/6 in metastatic breast cancer

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Currently, the standard of care for luminal metastatic breast cancer is the combination of cyclin inhibitors with hormone therapy. Palbociclib and Ribociclib have been approved for marketing since 2017 and Abemaciclib since 2019 in Spain. In our center we have experience with the three cdk 4/6 inhibitors in different lines of treatment and patient profiles. We gather in the present work the unicentric experience with the three icdk 4/6. We have collected a total of 152 patients treated with the different cyclin inhibitors, achieving median PFS of 32.1 months for Palbociclib, 28.6 months for Ribociclib and 18.4 months for Abemaciclib. Overall survival data is still immature. The context of the patient and the disease has a significant impact on the results, as well as the line of treatment used. The toxicity profile of the three drugs does not differ from what the registry trials describe, with neutropenia being the most common side effect. We also describe dose reductions produced by the three icdk4/6. Conclusions: This is a real-life study with experience in a single center with the three icdk4/6 currently marketed with a cohort of more than 150 patients. We present data that conform to what was reported by the clinical trials PALOMA, MONALEESA and MONARCH. The data will be updated on the date of the congress for its presentation.

Disclosure(s):

Fernando Henao, MD: Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing)

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12/7/2022

7:00 AM - 8:15 AM

Discussion 1 + Q&A: Single Cell Genomics for Breast Cancer Outcomes

Presenting Author(s) and Co-Author(s):

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PD4-05, PD4-06, PD4-08 & PD4-09

Disclosure(s):

Christine Desmedt, PhD, Prof.: No financial relationships to disclose

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7:00 AM - 8:15 AM

Discussion 2 + Q&A: Special Imaging and the Importance of Localization

Presenting Author(s) and Co-Author(s):

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PD4-01, PD4-02, PD4-03, PD4-04 & PD4-07

Disclosure(s):

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7:00 AM - 8:15 AM

Poster Spotlight Discussion 4: Single Cell Approaches for Translational Research and Biomarker Discovery

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Disclosure(s):

Charles M. Perou, PhD: BioClassifier LLC: equity stock holder and consultant (Ongoing);

Breast PAM50 Subtyping assay: Receipt of Intellectual Property Rights / Patent Holder (Ongoing)

12/7/2022

7:00 AM - 8:15 AM

PD4-01

PD4-01 Spatial transcriptomics reveals a substantial heterogeneity in TNBC tumor and stroma compartments with potential clinical implications

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Background Triple negative breast cancer (TNBC) is a heterogeneous disease characterized by at least five molecular subtypes, namely basal like (BL), immunomodulatory (IM), luminal androgen receptor (LAR), mesenchymal (M) and mesenchymal stem like (MSL), associated with distinct gene expression, genomic and tumor microenvironment (TME) profiles. Recent technological advances allow to investigate intratumor geographic heterogeneity ignored by

bulk tumor analyses. Here, we deployed spatial transcriptomics (ST) to interrogate tumor and stroma compartments heterogeneity and assess its association with clinical outcome. Methods Spatial transcriptomics (Visium® Spatial Gene Expression, 10X Genomics) was performed on a retrospective series of 94 case-control TNBC samples matched for known clinic-pathological parameters with available long term outcome. Detailed morphological annotations spanning 11 histomorphological categories were performed by a breast dedicated pathologist assisted by the automated QuPath digital pathology software. Bioinformatic analyses were performed using in house pipelines. Results We investigated the distribution of each morphological category across the five TNBC molecular subtypes. We found that LAR, M and MSL, even though they had less tumor cells, had more patches of very small size ($p < 0.0001$). On the other hand, BL and IM had few large and dense patches. Stroma had an opposite distribution compared to tumor, with LAR and MSL being enriched with stroma ($p < 0.0001$). Tumor infiltrating lymphocytes were specific of the IM ($p < 0.0001$) and to a lesser extent the BL subtype. Normal structures, like fat tissue ($p < 0.008$), lactiferous ducts ($p < 0.03$) and vessels ($p < 0.02$), were more present in MSL and LAR. The differences between the molecular subtypes are mirrored at the level of their cell composition and tumor organization, suggesting the possibility to assess TNBC molecular subtypes from imaging data alone. At the gene expression level, spatial deconvolution analyses revealed the co-existence of tumor and stroma compartments from different TNBC subtypes within a tumor sample of a given subtype as defined by bulk tumor analysis. Interestingly, these different tumor-stroma combinations were associated with prognosis. For example, M tumors associated with MSL stroma seem to have a better prognosis than M tumors with an M stroma ($p = 0.001$). Furthermore, spatial resolution of the gene expression identified 418 individual clusters (median 4 clusters per sample) associated with specific molecular and cellular features highlighting a substantial intra-patient heterogeneity. These clusters were further grouped into 11 ecotypes associated with distinct hallmarks and pathways, including EMT, angiogenesis, DNA repair and immune profiles revealing an important inter-patient heterogeneity beyond TNBC classification. Interestingly, 2 ecotypes were identified within the IM subtype associated with distinct clinical outcome, with ecotype 6 characterized by high EMT, mesenchymal stroma and worse prognosis ($p = 0,021$). Conclusion To our knowledge, this is the largest study demonstrating the substantial intra- and inter-patient heterogeneity characterizing TNBC at an unprecedented level, with differences both in tumor and stroma composition as well as spatial organization and clinical outcome. Our results highlight the need to consider TNBC heterogeneity for patient care and future clinical development including immunotherapy.

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Xiaoxiao Wang, MD: No financial relationships to disclose

David Venet, PhD: No financial relationships to disclose

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advisory boards) (Ongoing); Eisai: participation in company sponsored speaker's bureau

(Ongoing); Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing), participation in

company sponsored speaker's bureau (Ongoing); Foundation Medicine: participation in company sponsored speaker's bureau (Ongoing); Genentech: travel, accommodation expenses (Ongoing); Pfizer: travel, accommodation expenses (Ongoing); Prime Oncology: participation in company sponsored speaker's bureau (Ongoing); Puma: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: travel, accommodation expenses (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing); Teva: participation in company sponsored speaker's bureau (Ongoing); Vertex: Consulting Fees (e.g., advisory boards) (Ongoing)

12/7/2022

7:00 AM - 8:15 AM

PD4-02

PD4-02 Spatial and temporal heterogeneity of predictive and prognostic signatures in triple-negative breast cancer treated with neoadjuvant combination immune-chemotherapy

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Background: It is well known that immunological pathways are relevant for response to classical neoadjuvant chemotherapy as well as combined chemo-immunotherapy. In addition, it has been shown that combined chemo-immunotherapy significantly improves survival, even in the context of only moderate effects on pCR. Due to the window therapy with durvalumab-alone and the option to analyze multiple consecutive biopsies, the GeparNuevo trial offers the opportunity to 1) determine gene expression patterns for pCR and DDFS endpoints 2) identify pathways most relevant for pCR and DDFS 3) identify genes specifically regulated by immunotherapy (comparison of samples pre-and post-window) 4) identify genes specifically regulated by chemotherapy (comparison of samples pre-Tx and after 4 cycles of chemotherapy) 5) identify longitudinal patterns of gene expression by comparison of up to four time points and

6) identify changes in the tumor microenvironment by spatial sequencing of tumor cell and stroma areas. Methods: 292 tumor samples were evaluated by gene expression analysis: 162 pretherapeutic core biopsies, 79 post-window biopsies, 32 biopsies during chemotherapy and 19 biopsies of the residual tumor after therapy. These samples were analyzed by HTG OBP panel targeting 2549 genes which are assigned to 25 different biological mechanisms or cellular pathways. In addition, spatial profiling was compared in a subset of pre-and post-window samples using Nanostring GeoMx spatial profiling system. Endpoints were pCR and DDFS. Results: A total of more than 600 genes were significantly associated with either the pCR or the DDFS endpoint in either the complete GeparNuevo cohort or one of the two therapy arms. Interestingly, there was a large number of predictive or prognostic genes (n=247 for pCR and n=179 for DDFS) in the durvalumab arm, while the number of genes in the placebo arm was considerably lower (n=113 for pCR and n=61 for DDFS). We used existing pathway information for HTG OBP panel to analyze the contribution of different cellular processes to pCR and DDFS signatures in different therapy arms. Immune pathways were particularly relevant for durvalumab signatures (pCR and DDFS), while cell cycle related gene expression patterns were particularly involved in signatures predictive of pCR in both therapy arms. To further assign genes to the cellular response to durvalumab-alone or chemotherapy-alone, we compared gene expression patterns in durvalumab arm before and after the window phase (gene expression patterns induced by one dose of durvalumab) with gene expression patterns in placebo arm before and after 4 cycles of chemotherapy. Further longitudinal alterations were analyzed by comparison of longitudinal samples for 4 different time-points (a: before NACT, n=162; b: after window phase, n=79; c: after 4 cycles, n=31 and d: at surgery, n=19). Using the Nanostring GeoMx spatial RNA profiling system guided by cytokeratine immunofluorescence, we compared areas with high tumor cell content with stromal areas with or without TILs. In combination with the HTG gene expression data, we were able to allocate the changes induced by durvalumab vs chemotherapy to the stromal cell and tumor cell compartment, indicating a re-organization of the tumor-microenvironment. Conclusions: In our analysis, we show that immune gene signatures are particularly relevant for neoadjuvant response to durvalumab as well as prognosis after durvalumab treatment, while proliferation signatures are involved in pCR-signatures after durvalumab as well as chemotherapy. The spatial analysis showed that relevant changes occur in the stromal compartment, indicating a re-organization of the tumor microenvironment. The parallel targeting of immune- and proliferation pathways might explain why a combined immunotherapy-chemotherapy approach is more successful than each single therapy strategy alone.

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7:00 AM - 8:15 AM

PD4-03

PD4-03 Pelareorep primes the tumor for checkpoint inhibition therapy by activating the interferon-gamma signaling pathway and tumor inflammation signature in early breast cancer patients - results of the AWARE-1 trial

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Background The status of the tumor microenvironment (TME) can profoundly affect the response to immune-based therapies for the treatment of cancer. Results previously reported from the AWARE-1 study in early breast cancer patients demonstrated that pelareorep (pela, an oncolytic reovirus), alone or in combination with checkpoint inhibitor (CPI) therapy, modified the inflammatory state of the TME. We also showed that many of pela's effects on the TME were enhanced by the addition of checkpoint blockade. Here, we report the effect of treatment with pela on selected molecular markers associated with enhanced anti-tumor immunity. **Methods** Newly diagnosed HR+/HER2- early BC patients were enrolled into two cohorts: Cohort 1 (C1): pela + letrozole (n=10); and Cohort 2 (C2): pela + letrozole + atezolizumab (n=10). Pela was intravenously administered on days 1, 2 and 8, 9, and atezolizumab was given on day 3. For this analysis, tumor biopsies (FFPE samples) collected pre-treatment (D1) and on days 3 (D3, prior to the atezolizumab administration) were examined by GeoMx digital spatial profiling (DSP, using Nanostring's Cancer Transcriptome Atlas [CTA]). Moreover, the expression of 770 immune-related genes was analyzed using a specific immune panel (n=20). Gene Set

Enrichment Analysis (GSEA) (version 4.1.0) was used to assess pela-induced activation pathways. Results GeoMx DSP showed that pela therapy significantly activated IFN-gamma signaling and associated interferon response genes from D1 to D3 (Normalized Enrichment Score [NES] = 3.3, p-values < 0.02) in the cytokeratin-positive subset of the tumor samples. GSEA of the immune dataset (730 immune genes + 30 housekeeping genes) from the whole tissue also showed a significant upregulation of IFN-gamma signaling pathway genes (FDR < 25%, p-value < 0.001). Increases were also observed in genes reported to be associated with an enhanced tumor inflammatory signal (TIS) including PD-L1, IDO1, HLA-E and STAT1 (p-values < 0.005). Conclusions These results demonstrate that treatment with pela alters the TME to induce and enhance anti-tumor immunity. This enhancement of anti-tumor immunity may potentiate the TME for CPI therapy.

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

PD4-04

PD4-04 A quantitative spatial analysis of microenvironmental biomarkers for breast cancer outcome

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Background: Understanding breast cancer progression and the relationships among biomarkers in the tumor and tumor microenvironment could go beyond established prognostic markers of breast cancer. Poor response and recurrence may indeed be a consequence of the highly heterogeneous spatial distribution of biomarkers within cancers, and/or the synergistic and antagonistic relationship between co-localized biomarkers. Recently, mechanical and physical microenvironmental signatures have emerged as relevant in determining cancer aggressiveness and invasiveness. This suggests that physical structures in the tumor tissue may drive favorable immune-tumor-stroma cell patterns. However, current assessment of tumor biopsies is limited in the ability to quantify and spatially resolve several different subtypes of cells and biomarkers within tumors. Methods: We developed a 60-marker imaging mass cytometry panel to resolve high-plex spatial patterns of cells, signaling, and microenvironmental biomarkers within tumor tissues. Our panel includes 16 tumor markers, 20 immune markers and 24 microenvironmental markers. We built an innovative computational tool to identify recurring spatial patterns of these markers within the tumor microenvironment, and define the spatial scale of heterogeneity of such patterns. We correlated the results from this spatial analysis to prospectively collected long term clinical outcome variables (e.g. 10 year survival, local and distant recurrence) in primary breast cancers sampled at baseline. Our patient cohort comprised 287 samples of patients treated with surgery and a radiation, chemotherapy, endocrine therapy, or combinations of these post-surgery. Of these, 174 were from patients alive 5 years post diagnosis, and 113 from patients lost to breast cancer deaths. Living patients were evaluated for recurrence, and of these 94% were disease free at the end of the study, while 4% had local recurrence and 2% distant metastasis. Of the dead patients, 59% had local recurrence while 27% had distant metastasis. Results: We investigated first all patients independent of tumor subtype; in this analysis the presence of both endothelial (CD31+) or HLADR+ cells were consistently associated with long term survival. We further investigated the distribution of all 60 markers in Lum A, Lum B, Lum like, Her2+ and triple negative subtypes. Among the results we confirmed the prognostic role of known biomarkers such as p53+ as a biomarker for poor survival in Luminal B. We also identified complex microenvironmental patterns associated with outcome. For example, the presence of PD1+ cells in collagen rich environments were generally associated with long terms survival in Luminal B patients. With our spatial analysis tool we further investigated intra-patient and inter-patient spatial distribution and classified clusters predictive of outcome beyond heterogeneity. We found that beyond the mere positivity of each marker, the spatial distribution and co-localization of different immune, tumor and mechanical markers determines long term outcome in different subtypes. Specifically, we investigated the role of vimentin within different microenvironments and tumor subtypes. We identified the co-localization of hCa9 and vimentin as strongly associated with poor 5 year outcome, independent of tumor subtype. Moreover, in Luminal A patients while the presence of clusters exclusively positive for vimentin was associated with poor survival, vimentin co-expression with β actin and co-localization of XBP1+ cancer cells and immune cells in a collagen matrix was associated with longer survival. Conclusion: These results suggest the importance of mechanics and physics in determining spatial distribution of tumor-promoting and tumor-inhibiting immune cells, offering new avenues of physics-based therapeutic targets.

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

PD4-05

PD4-05 Integrated multi-cohort profiling identifies CCL19+ dendritic cells to potentiate immunotherapy efficacy in triple-negative breast cancer

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Background: Immune checkpoint inhibitors (ICIs) targeting the PD-1/PD-L1 axis have emerged as constituting a new pillar for breast cancer; however, they benefit only a subset of patients, and predictive biomarkers are urgently needed. While dendritic cells (DCs) are essential for the orchestration of antitumor immune response, the clinical value of DCs in breast cancer immunotherapy remains unclear. An improved understanding of the functional diversity of DC subsets, as well as their relationship with ICI response, would eventually improve the efficacy of ICIs in breast cancer patients. Objective: We sought to comprehensively characterize DC heterogeneity within the tumor microenvironment, identify distinct DC subsets associated with the response to ICIs, and define clinically applicable predictive biomarkers for ICI therapy. Methods: We performed a comprehensive single-cell RNA sequencing (scRNA-seq) analysis of 53 breast tumors receiving ICIs or chemotherapy in two retrospective studies (NCT03197389 and GSE169246) to identify specific DC populations associated with ICI responsiveness. Next, we harnessed multiplex immunohistochemistry (n = 186), multiparametric flow cytometry of fresh tissues (n = 87), large consecutive transcriptomic datasets (The Cancer Genome Atlas [TCGA] and Fudan University Shanghai Cancer Center [FUSCC]), and in vivo experiments to illustrate the molecular portraits and clinical relevance of the identified DC subsets. Additionally, except for the two scRNA-seq datasets, we leveraged another four independent cohorts (NCT03805399, NCT04613674, NCT04129996, GSE124821) and assessed the clinical utility of the established clinically applicable biomarkers derived from prior analyses to predict response following treatment with ICIs or chemotherapy. Results: By obtaining single-cell transcriptome data of 1,955 high-quality DCs, we identified five distinct DC subpopulations (CLEC9A+, CD1A+, CLEC10A+, CCL19+, and LILRA4+). We then illustrated that a specific CCL19+ DC population, but not whole DCs or other subsets, was associated with ICI responsiveness, particularly in triple-negative breast cancer (TNBC). Mechanistically, a potent CD8+ T-cell response was unleashed, rendering tumors susceptible to PD-1 blockade in vivo and confirming their putative immunomodulatory capacity. This phenomenon was only

observed in CCL19+ DCs but not in CCL19- DCs, indicating CCL19 as a specific marker and could reflect the infiltration and functional phenotype of CCL19+ DCs in breast tumors. Finally, by integrating six independent ICI therapy cohorts, we demonstrated that baseline CCL19 in both tumor and blood could predict better response and survival in TNBC patients receiving ICIs, but not so for chemotherapy. Conclusions: Our results provide important insights into the relationship between the clinical outcome of ICIs and DC heterogeneity at single-cell resolution, support the development of therapies modulating CCL19+ DCs to trigger antitumor CD8+ T-cell immunity, and suggest baseline CCL19 levels as a noninvasive predictive biomarker for patients receiving ICIs, that are potentially applicable in the clinic. In light of these results, we suggest CCL19+ DC modulation as a possible precision immunotherapy approach for cancer patients.

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Ding Ma, M.D.: No financial relationships to disclose

Xi Jin, M.D.: No financial relationships to disclose

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PD4-06

PD4-06 Obesity-associated changes in transcriptomic profile and immune landscape of primary breast cancer revealed by bulk and single-cell gene expression data

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Background: Breast cancer (BC) is one of the cancer types recognized as an obesity-associated disease. Current understandings of molecular mechanisms underlying the BC-obesity connection however largely came from experimental models while systematic investigation of the impact of obesity on BC biology in large patient series is still lacking. The purpose of this study is to discover changes in the transcriptomic profile of primary BC according to patients' body mass index (BMI). Data and Methods: Bulk and single-cell gene expression data from treatment-naïve primary breast tumors from non-underweight patients were retrieved from the MINDACT trial (NCT00433589; N = 1481) and the pre-treatment cohort of the BioKey trial (NCT03197389, N = 36), respectively. Three categories were considered for BMI: lean, overweight and obese. The main analyses focused on the invasive carcinoma of no special type (NST) estrogen receptor-positive/HER2-negative (ER+/HER2-, N_bulk = 735, N_single-cell(sc) = 10) and NST ER-/HER2- (N_bulk = 118, N_sc = 15) subgroups. The bulk expression data was subjected to differential gene expression analyses according to BMI which was adjusted for menopausal status and tumor grade, then followed by gene set enrichment analyses. Clustering and cluster annotation were performed on the single-cell profiling data before differentially expressed genes according to BMI were identified for each of the present cell types. Results: Obesity-associated differences in the transcriptomic profile of breast tumors, which were subtle but potentially indicative of a biological relationship, were revealed by the bulk data. In both investigated subgroups, tumors from obese patients were shown to be enriched in cell cycle hallmarks. In ER-/HER2- tumors, adiposity further increased MYC signaling. We also observed different obesity-associated changes according to the ER status. Among ER+/HER2- tumors, those from obese patients were enriched in hallmarks related to inflammatory response compared to those from lean patients. In contrast, these hallmarks appeared to be enriched in the ER-/HER2- tumors from lean patients. Our investigation of the single-cell data further revealed shifts in the cell composition of tumor tissue and cell type-specific transcriptomic differences according to BMI which were more pronounced than those detected from the bulk data. ER+/HER2- tumors from obese patients have a higher frequency of immunosuppressive and pro-tumoral cell subpopulations such as dendritic cells (DC) enriched in immunoregulatory molecules ($p = .03$), LYVE1+ macrophages ($p = .02$) and myofibroblasts ($p = .03$) than those from lean patients. Overexpression of Cyclin D1 and CD24 was found in cancer cells in ER+/HER2- tumors from obese patients. A reduction in anti-tumor immune responses was evident with downregulation of multiple interferons in CD8+ and CD4+ T cells as well as B cells. We observed in the ER-/HER2- subgroup increased infiltration of plasmacytoid DC ($p = .01$), CCL2+ macrophages ($p = .01$) in tumors from obese versus lean patients, while fibroblasts showed an opposite tendency. Additionally, significant obesity-associated downregulation of major histocompatibility complex (MHC) molecules class I in cancer cells and MHC class II molecules in B cells could be suggestive of deficient antigen presentation and activation of cytotoxic and helper T cells. Conclusion: We highlighted the impact of obesity on the remodeling of tumor and tumor microenvironment which might generally lead to a suppression of anti-tumor immune responses, albeit potentially via diverse

axes according to the ER status. Although investigation on a larger cohort is warranted, our current results suggest that obesity-associated transcriptomic changes in BC could be highly cell type-specific, hence we recommend single-cell approaches in addition to spatial multi-omics analysis to further elucidate the interplay between obesity and BC.

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12/7/2022

7:00 AM - 8:15 AM

PD4-07

PD4-07 Uncovering molecular heterogeneity of mixed ductal and lobular carcinoma using digital spatial profiling

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Background Mixed invasive ductal and lobular carcinoma (mDLC) is a rare special subtype (3-6%, ~10,000 cases/annually in US) of invasive breast cancer with elusive pathophysiology. This entity exhibits a mix of ductal-like and lobular-like tumor sub-components within the same tumor. With few seminal studies, mDLC remains poorly understood with little molecular

understanding of its sub-components including their origin and implications on disease evolution, prognosis, and treatment response. With increasing recognition of no special type (NST) and invasive lobular carcinoma (ILC) as distinct diseases with unique biology, it is important to understand whether this mixed entity, and its sub-components are like NST and ILC subtypes or a distinct disease. **Methods** We identified mDLC cases from the UPMC cancer registry. These underwent comprehensive evaluation by a panel of expert pathologists. Three cases (each with a ductal and lobular sub-component on the same FFPE block) were shortlisted. These cases underwent digital spatial profiling (DSP) using Nanostring GeoMX Human Whole Transcriptome Atlas. Briefly, 5um slides were stained using RNAscope morphology marker probes (E-cadherin and PanCK) and GeoMX DSP oligo-conjugated RNA detection probes. Between 3-6 ductal and lobular regions of interest (ROI) per tumor were selected by pathologists. DSP barcodes were cleaved off using UV light and collected into 96-well plate. These underwent library preparation and sequencing. Raw reads were aligned to reference probes to quantify RNA counts. Q3 normalized counts were used in downstream analyses using R version 4.1. Linear modeling was used to assess differentially expressed genes (DEGs). Hypergeometric enrichment tests were used for geneset enrichment. T-tests was used to compare gene expression between two groups. **Results** In total 26 ROIs (14 ductal and 15 lobular) were profiled across the three mDLC FFPE slides. Overall data quality was excellent with > 90% sequencing saturation across profiled ROIs. Principle component analysis and consensus clustering showed that lobular and ductal ROIs clustered separately indicating distinct molecular profiles. Similarly, PAM50 analysis showed that ductal and lobular ROIs within each patient tumor had distinct PAM50 subtypes. To further investigate the molecular differences between ductal vs lobular ROIs, we performed differential gene expression analysis. We identified 38 up-regulated and 78 down-regulated genes in lobular compared to ductal ROIs. To assess whether mDLC sub-components share any molecular similarities to pure counterparts i.e., ILC and NST, we compared mDLC lobular vs ductal DEGs with those from TCGA ILC vs NST comparison. SHROOM1, KLK10 and KLK11 were up-regulated while CDH1, DCD, and CPB1 were down-regulated in both mDLC lobular ROIs and ILC vs mDLC ductal ROIs and NST, respectively. Pathway analysis revealed estrogen response, adhesion, and metabolism related differences between mDLC lobular vs ductal ROIs. Furthermore, key transcription factor signatures enriched in the up-regulated genes in lobular vs ductal ROIs included ESR1, FOXA2, GATA1/2 and AR signatures while those enriched in the down-regulated genes in lobular vs ductal ROIs included RCOR1, MYC, ZBTB7A, NELFE, and SPI1 signatures. **Conclusion and Future Work** Using DSP, we uncovered the molecular heterogeneity of mDLC. We revealed that lobular and ductal sub-components have distinct biology with differences in transcriptional signatures and hormone signaling, adhesion and metabolism related pathways. Our pilot study is the first to shed light on this elusive mixed entity using spatial profiling. Our future work will focus on DNA sequencing of mDLC sub-components to identify sub-component specific driver mutations. Our findings will need further investigation in larger mDLC cohorts to better understand their clinical implications in terms of evolution of this disease and its prognosis.

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

PD4-08

PD4-08 A Novel Single Cell Model of Tamoxifen Response in Primary Human Breast Tumors

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A Novel Single Cell Model of Tamoxifen Response in Primary Human Breast Tumors Austin Whitman, Hyunsoo Kim, Kamila Wisniewska, Rasha Kakati, Susana Garcia Recio, Hector Franco, Charles Perou, Philip Spanheimer Background: Resistance to endocrine therapy is a primary cause of treatment failure and death in patients with estrogen receptor (ER)-positive breast cancer. Intratumor heterogeneity is associated with resistance to therapy across tumors, and specifically in ER+/HER2- breast cancer, heterogeneity in ER and PR expression is associated with a worse response to endocrine therapy. We hypothesize that subpopulations within and across ER+/HER2- human breast tumors have distinct responses to tamoxifen and that discerning heterogeneity in response will improve understanding of inherent and emerging resistance to endocrine therapy. Methods: We developed an operating room-to-laboratory pipeline immediately after surgical resection for studies using alive tissue. Tissue samples were obtained and single cell suspensions created using physical and enzymatic dissociation. Cells were treated with tamoxifen (10 μ M) or control media for 12 hours in suspension and single cell RNA libraries generated using the 10X Genomics droplet-based kit and sequenced using the

Illumina NextSeq2000. Results: We obtained normal breast tissue from 2 women undergoing reduction mammoplasty and tumor tissue from 10 women with ER+/HER2- invasive breast carcinoma. In tamoxifen treated and control matched pairs, a total of 22,195 cells from normal breast and 94,558 cells from tumor samples were sequenced. Computational analysis using consensus clustering was performed and cell types assigned using canonical correlation. Both tumor and normal samples identified clustering by cell type and not by patient revealing significant variability in cell type abundance between samples. In the normal breast samples, we performed differentially expressed genes (DEG) analysis comparing tamoxifen treatment to control for each cell type (Immune cells, fibroblasts, basal epithelial cells, luminal progenitor cells, and mature luminal cells) and enrichment analysis of up- and down-regulated genes performed. Strong depletion of estrogen induced genes was observed in tamoxifen-treated normal luminal progenitor and mature luminal cells, but not in basal epithelial cells or fibroblasts, demonstrating distinct, subpopulation-specific response to tamoxifen. In the 10 tumor matched pairs, 4 had a high epithelial proportion and tumor cells identified using inferred copy number variation. Tumor cells in 3 of these 4 samples showed significant down regulation of estrogen response genes with tamoxifen treatment. Using scBCSubtype to assign PAM50 subtype to individual tumor cells, the 3 responsive tumors were comprised primarily of LumA cells while the unresponsive tumor was predominantly LumB. Finally, we developed a novel score to quantify responsiveness at the single cell level based on downregulation of estrogen response genes with tamoxifen treatment relative to matched cluster-specific untreated expression. This analysis demonstrated heterogeneity in response to tamoxifen in tumor cells and identified distinct subpopulations of responsive and unresponsive tumor cells to tamoxifen treatment. Conclusion: We developed a novel ex vivo model to determine heterogeneity in therapeutic response to tamoxifen in normal human breast tissue and primary human breast tumors. We demonstrate differences in tamoxifen response by cell type and identify distinctly responsive and resistant subpopulations within human tumors. This provides a foundation to define features of responsive and resistant populations on the individual cell and specimen basis, and should allow us to develop precise, single cell-based predictors of response to endocrine therapy, and to identify genes and pathways driving resistance to therapy.

Disclosure(s):

Hyunsoo Kim, Ph.D.: No financial relationships to disclose

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Charles M. Perou, PhD: Bioclassifier LLC: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds)

(Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Royalty (Ongoing)

Philip Spanheimer, M.D.: No financial relationships to disclose

12/7/2022

7:00 AM - 8:15 AM

PD4-09

PD4-09 Single cell RNA-sequencing identifies intra-tumoral cellular heterogeneity and drug-induced subpopulation shifts in Triple Negative Breast Cancer mouse models

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Introduction: Triple Negative Breast Cancer (TNBC) is an aggressive disease with a poor prognosis that accounts for 10-20% of breast cancer cases worldwide. Intra-tumoral heterogeneity and tumor cell plasticity are thought to contribute to drug resistance in TNBCs. Our work aims to: 1) precisely identify the intra-tumoral heterogeneity in cellular states present within TNBC, and 2) test whether drugs can block or initiate plasticity between subpopulations to improve drug sensitivity. We hypothesize that treatment(s) induce cellular plasticity, thus causing cells to shift into resistant states that persist until treatment is removed. We further hypothesize that these resistant subpopulations give rise to new tumor outgrowths once the treatment stops. Methods: To test this, we are treating TP53^{-/-} Genetically Engineered Mouse Model (GEMM) syngeneic transplant tumors of the basal-like TNBC phenotype with the chemotherapeutic doublet of carboplatin/paclitaxel, and targeted agents implicated in plasticity including the MEK inhibitor trametinib, a chromatin remodeling inhibitor I-BET151, and the

dihydroorotate dehydrogenase inhibitor brequinar. To identify cellular subpopulations and examine their response to treatment, we performed both in vivo and in vitro drug sensitivity testing, as well as gene expression profiling using single cell RNA-sequencing (scRNAseq). Results: We have identified clear intra-tumoral heterogeneity with at least 6 distinct cell states present, including basal, mesenchymal/claudin-low, and proliferative subpopulations in vivo in most TNBC GEMM models. We performed 18 individual scRNAseq experiments on the TP53-/- 2225L GEMM transplant line with the aforementioned treatments and untreated controls in triplicate and compared subpopulation frequencies in treated versus untreated tumors. Notably, treatment with trametinib and brequinar caused the rise of two rare subpopulations (i.e. 1% to 3-4% of total tumor cells) that express genes consistent with previously described drug-tolerant persisters (DTP), which we have called "Epithelial-DTP" (Tacstd2, Krt6a, and Cryab enriched) and "Mesenchymal-DTP" (Snai2 and Sca-1 enriched). A gene signature generated from the Epithelial-DTP subpopulation predicted poor patient outcomes in neoadjuvant chemotherapy treated TNBC patients. Further, in TNBC patient-derived xenografts (PDX), these two DTP subpopulations are also present and induced by treatment to an even greater frequency. Ongoing experiments include the use of fluorescence-activated cell sorting to isolate and functionally test the tumor-initiating capabilities of these two rare cell subpopulations. In addition, many experiments are underway to identify means to therapeutically target these DTP cells, with these results to be presented. Ultimately, identifying these rare drug resistant subpopulations, and identifying means to eradicate them, could vastly improve therapeutic regimens and outcomes for patients with TNBCs.

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Cherise R. Glodowski, MPhil: No financial relationships to disclose

Kevin R. Mott, n/a: No financial relationships to disclose

Denis Okumu, PhD: No financial relationships to disclose

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Breast PAM50 Subtyping assay: Receipt of Intellectual Property Rights / Patent Holder (Ongoing)

12/7/2022

7:00 AM - 8:15 AM

Discussion 1 + Q&A: PD5-01, PD5-02, PD5-03 & PD5-04

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12/7/2022

7:00 AM - 8:15 AM

Discussion 2 + Q&A: PD5-05, PD5-06, PD5-07, PD5-08, PD5-09 & PD5-10

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12/7/2022

7:00 AM - 8:15 AM

Poster Spotlight Discussion 5: Advances in TNBC Biology

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12/7/2022

7:00 AM - 8:15 AM

PD5-01

PD5-01 Genomic and epigenomic BRCA alterations predict adaptive resistance and response to platinum-based therapy in triple negative breast cancer and ovarian carcinoma

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Background. Homologous recombination deficiency (HRD), induced by germline and somatic BRCA1 or BRCA2 gene mutations (BRCAmut) and by BRCA1 promoter methylation (BRCA1meth), has been associated with better response to platinum agents in both triple negative breast cancer (TNBC) and ovarian carcinoma (OvCa). A major conundrum arising from recent studies is why patients with BRCA1meth cancers do more poorly compared to those with BRCAmut cancers given the biologically equivalent HRD in both states. Here, we address this question by performing detailed genomic analyses of primary TNBC and OvCa cohorts and through patient-derived xenografts (PDXs) and their derivative cell lines. **Methods.** Both new and publicly available cohorts of primary TNBC and OvCa encompassing 499 individuals treated with a combination of platinum and taxane chemotherapy were analyzed by whole genome and transcriptome sequencing as well as limited epigenetic analyses. A cohort of 43 PDX models of TNBC was genomically characterized and responses to both single agent platinum and docetaxel were evaluated in vivo. PDX longitudinal studies were performed to assess the dynamics of BRCA1 methylation following treatment. **Results.** Genomic analyses revealed that BRCA1mut and BRCA1meth cancers share the same pattern of BRCA1-linked genomic rearrangements. Nonetheless, in all four primary cancer cohorts examined we found that patients with BRCAmut cancers, but not those with BRCA1meth cancers, had significantly better response outcomes compared to those with BRCA proficient cancers. A separate analysis of PDX TNBCs with BRCA1 promoter methylation showed that PDXs derived from treatment naïve cancers had complete methylation of the BRCA1 promoter, whereas those derived from post-treatment cancers invariably had only partial methylation. Compared to PDXs with complete methylation, those with partial methylation had a lower response rate to in vivo platinum-based therapy, but not to docetaxel. Using single cell clonal expansions from BRCA1meth PDX models, we confirmed that partial methylation was the result of demethylation of one of the BRCA1 promoter alleles and not of the outgrowth of a non-methylated clone. Exposure of TNBC PDXs with complete methylation to a single course of platinum therapy resulted in the emergence of an unmethylated BRCA1 promoter allele, which associated with an increase in BRCA1 expression. We confirmed that platinum treatment results in progressive loss of BRCA1 methylation and restoration of BRCA1 expression in the clinical setting, by studying the BRCA1 status of a longitudinal series of four TNBC PDX models established from the same patient at different stages of her clinical history. Differential gene expression analysis revealed an increased immune transcriptional signal, especially an elevated M1 macrophage signature, associated with enhanced response to platinum therapy only in patients with BRCA proficient cancers, in both TNBC and OvCa. Integrating both the strength of this cancer immune signature and the presence of BRCA mutations resulted in more accurate predictions of response when compared to either HRD or BRCA status alone. **Conclusions.** These results suggest that unlike BRCAmut cancers, where BRCA deficiency is more genetically stable, BRCA1meth cancers are highly adaptive to genotoxin exposure resulting in demethylation of one allele, recovery of BRCA1 expression and acquired insensitivity to platinum. On the other end, a high immune transcriptional signature identifies patients with BRCA proficient cancers that are more likely to benefit from platinum therapy. Taken together, our study underscores the importance of characterizing molecular heterogeneity to optimize predictive precision in assigning response probabilities in TNBC and OvCa.

Disclosure(s):

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Kalyan Banda, MD: No financial relationships to disclose

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12/7/2022

7:00 AM - 8:15 AM

PD5-02

PD5-02 An Organoid Model System to Study Resistance Mechanisms, Predictive Biomarkers, and New Strategies to Overcome Therapeutic Resistance in Early-Stage Triple-Negative Breast Cancer

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Background: While new treatments and improved subtyping schemas are anticipated to improve treatment response in triple-negative breast cancer (TNBC) patients, therapeutic resistance remains a significant challenge. Moreover, there is an urgent need for additional research model systems to study resistance and residual disease in breast cancer, including aggressive subtypes of breast cancer. Organoid culture is a promising technology used for growing breast cancer cells with high efficiency; however, the extent to which treatment resistance can be modeled using this system is unknown. This research used patient-derived organoid cultures in the context of computational analyses of large molecular and clinical datasets to study resistance mechanisms, biomarkers, and alternative treatment strategies to overcome drug resistance in early-stage TNBC. Methods: Organoid cultures were derived from breast tumor samples (taken from lumpectomy, mastectomy, or core biopsy samples), digested to the organoid level using collagenase, and grown in three dimensional cultures using a basement membrane extract and a fully-defined organoid medium (Dekkers et al. Nat Protoc 2021). An evaluation of all available I-SPY2 biomarker data (Wolf et al. Cancer Cell 2022) was performed focusing on genes, proteins, and pathways associated with resistance. These were then used to study whether resistance biomarkers identified in patient tumors are also present in organoids propagated from breast cancer post-treatment residual disease. To this end, bulk RNA sequencing data of organoids were normalized and merged with the TCGA dataset (Hoadley et al. Cell 2018) to enable analysis in a larger context, and immunofluorescence staining of organoids was performed. A high-throughput 386 anti-cancer drug compound screen and subsequent synergy testing with the most promising compounds were performed to identify and predict alternative treatment strategies. Additional assays to explore kinome activity in this organoid model are in progress. Results: A TNBC organoid biobank was established (n=31), which was enriched for inflammatory breast cancer (IBC; n=15), an aggressive form of breast cancer. Most organoids were derived from residual disease after neoadjuvant therapy. Bulk RNA sequencing analysis performed on 10 TNBC organoids revealed 3 subsets that were characterized predominantly by either normal-like/luminal androgen receptor or basal-like features or expressed distinct gene expression profiles, with IBC cases present in all 3 subsets. Intriguingly, the IBC organoids were characterized by higher expression of a number of immune-related signatures, despite an absence of clear immune cells in culture. A residual disease IBC/TNBC organoid resistant to chemotherapy was used to perform the 386-drug compound screen. The organoid model showed resistance to veliparib-cisplatin, consistent with

the expression of gene/protein biomarkers predictive of drug resistance found in I-SPY2 (low PARPi7 levels and high pFOXO1 and pMEK1/2 expression). In addition, the screen identified multiple classes of inhibitors as promising synergistic/additive candidates for overcoming resistance to cisplatin. Conclusion: In this proof-of-principle study, we demonstrated the utility of matching I-SPY2 resistance biomarkers and signatures to residual disease tumor organoid cultures. We show that tumor organoid cultures modeling drug resistance states are a useful complement to existing research models of breast cancer and can be used for compound testing. We have developed a pipeline to propagate residual tumors from patients enrolled in I-SPY2 into organoid cultures to create a broader platform for preclinical drug testing informed by tumor biology with the ultimate goal of enabling faster, more successful translational studies and increased treatment options for resistant disease.

Disclosure(s):

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7:00 AM - 8:15 AM

PD5-03

PD5-03 Comparison of a personalized sequencing assay and digital PCR for circulating tumor DNA based Molecular Residual Disease detection in early-stage triple negative breast cancer in the cTRAK-TN trial

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Background: Detection of circulating tumour DNA (ctDNA) in patients (pts) who have completed treatment for early-stage breast cancer is associated with a high risk of future relapse. Identifying those at high risk of subsequent relapse may allow tailoring of further therapy to delay or prevent recurrence. Previous analysis of this cohort showed that tools capable of detecting ctDNA at lower concentrations are needed to increase sensitivity and lengthen the lead time between ctDNA detection and relapse. We compared ctDNA detection via a personalised sequencing assay to dPCR in patients from the cTRAK TN clinical trial. Methods: The cTRAK-TN trial recruited 161 pts into prospective ctDNA surveillance with dPCR, with ctDNA positive pts randomised to 1) CT staging plus pembrolizumab therapy for patients

without relapse or 2) observation. Pts had serial post-treatment surveillance plasma samples collected every 3 months for up to 2 years. Whole exome sequencing (WES) was performed on tumor DNA from FFPE samples to design personalised Residual Disease and Recurrence (RaDaR®) multiplex PCR based NGS assays. Retrospectively, plasma DNA extracted from a minimum of 2mls banked plasma, was sequenced with personalised RaDaR assays, and ctDNA detection identified with a proprietary algorithm. dPCR assays tracked 1-2 mutations, as previously described. Primary endpoint was rate of positive ctDNA detection by 12 months from start of surveillance in both assays. Secondary endpoints were agreement in ctDNA detection between RaDaR and dPCR assays and lead-time between ctDNA detection and disease recurrence. Results: Overall, 147 pts and 241 tissue samples were subject to WES, and RaDaR assays were developed for 142 pts with sufficient plasma for testing. RaDaR assays tracked a median of 47 variants (range 33-56) per patient, and a total of 907 timepoints were analysed (median 6 timepoints per pt, range 1-11). With RaDaR, 39.4% (56/142) patients tested ctDNA positive during follow-up, with a median ctDNA detected level of 0.081% estimated variant allele fraction (eVAF). With dPCR, 35.2% (50/142) pts tested ctDNA positive. The ctDNA detection rate by 12 months from the start of ctDNA surveillance was 36.2% (95% CI; 27.6% – 43.7%) with RaDaR and 29.9% (95%CI; 21.6% – 37.3%) with dPCR. The overall test agreement between RaDaR and dPCR assays was 92.7% (95%CI; 90.7% – 94.4%). From a patient perspective, 58.7% pts were ctDNA negative for both assays, 32.9% ctDNA were positive for both assays and 8.6% presented discrepancies. ctDNA was detected by RaDaR but not by dPCR in 9 pts and it was detected by dPCR but not by RaDaR in 3 pts. Among ctDNA positive pts, 55.2% were first detected positive by RaDaR, 5.2% by dPCR, and 39.6% were detected at the same time-point (test of proportions, $p < 0.001$). The median lead time from ctDNA detection to relapse was 7.1 months (95% CI 5.9 – 15.9%) with RaDaR and 5.7 months (95% CI 3.2% – 7.4%) with dPCR. Conclusion: The RaDaR personalised multi-mutation sequencing assay detected MRD with a longer median lead time prior to relapse, and with higher sensitivity, than dPCR mutation tracking assays. These findings have implications for the choice of ctDNA assay in clinical trials designed to treat patients at the point of MRD detection.

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12/7/2022

7:00 AM - 8:15 AM

PD5-04

PD5-04 Characterizing the HER2-/Immune-/DNA repair (DRD-) response predictive breast cancer subtype: the hunt for new protein targets in a high-needs population with low response to all I-SPY2 agents

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Background: In previous work we leveraged the I-SPY2 trial to create treatment response predictive subtypes (RPS) incorporating tumor biology beyond clinical HR/HER2, to better predict drug responses in an expanded treatment landscape that includes platinum agents, dual HER2-targeting regimens and immunotherapy [1]. We showed that best performing schemas incorporate Immune, DRD and HER2/Luminal phenotypes, and that treatment allocation based on these would increase the overall pCR rate to 63% from 51% using HR/HER2-based treatment selection. The RPS schema has been selected for prospective evaluation in I-SPY2. Using the RPS, one would prioritize platinum-based therapy for HER2-/Immune-/DRD+, immunotherapy for HER2-/Immune+, and dual-anti-HER2 for HER2+ that are not luminal. HER2+/Luminal patients have low response rates to dual-anti-HER2 therapy but may respond better to anti-AKT. However, there is still a considerable 'biomarker-negative' group of resistant cancers (HER2-/Immune-/DRD-) with very low pCR rates to all tested agents, that require a new therapeutic approach. Here we characterize the protein signaling architecture of these tumors to identify new target candidates. Methods: 987 I-SPY 2 patients from 10 arms of the trial were considered for this analysis. All have gene expression, pCR and RPS; 944 have distant recurrence free survival (DRFS) data; and 736 have reverse phase protein array (RPPA) data from laser capture microdissected tumor epithelium. These data – known collectively as the I-SPY2-990 mRNA/RPPA Data Resource - were recently made public on NCBI's Gene Expression Omnibus [GEO: GSE196096]. We focus on HER2-/Immune-/DRD- tumors, applying Wilcoxon and t-tests to identify phosphoproteins that differ between HR+HER2-/Immune-/DRD- and other HR+HER2- tumors; and between TN/Immune-/DRD- and other TNs. The Benjamini-Hochberg (BH) method is used to adjust p-values for multiple hypothesis testing. In addition, the Kaplan-Meier method is used to estimate DRFS. Results: 201/736 I-SPY 2 patients with RPPA data are classified HER2-/Immune-/DRD- (HR+HER2-:

n=138; TN: n=63). Of these, 8.5% (17/201) achieved pCR. Non-responding HER2-/Immune-DRD- had worse outcomes than responders (~75% vs. ~95% DRFS at 5 years). 60/139 phospho-proteins differ significantly between HR+HER2-/Immune-/DRD- and other HR+HER2-tumors (n=122). These tumors are relatively 'cold', in that 90% (54/60) of the phosphoprotein activities characterizing this group are at lower levels than in the overall HR+HER2- population; including immune (e.g. pPDL1, pJAK/STAT) and proliferation (e.g., Ki67, CyclinB1, pAURK) endpoints. Phosphoproteins showing higher levels in this subset include ERBB2 (BH p=1.7E-06), Cyclin D1 (BH p=1.4E-05), pAR (BH p=1.4E-05), and ER (BH p=3E-04). Within the TN subset, only 3/139 phospho-proteins differed significantly between TN/Immune-/DRD- and other TN tumors (n=189). These were all immune-related (pPDL1, pSTAT1, and HLA DR), with lower expression in the TN/Immune-/DRD- group. Conclusion: HR+HER2- and TN patients who are Immune-Low and DRD-Low have very low pCR rates to all tested therapeutics in I-SPY2 including standard chemotherapy, platinum, and immunotherapy. Senolytics (possibly targeting Cyclin D1), HER2low agents, and AR modulators may overcome resistance in HR+HER2-/Immune-/DRD-, whereas an immune activator beyond checkpoint inhibition is suggested for TN/Immune-/DRD- patients. [1] Wolf et. al., Redefining Breast Cancer Subtypes to Guide Treatment Prioritization and Maximize Response: Predictive Biomarkers across 10 Cancer Therapies. Cancer Cell 2022

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12/7/2022

7:00 AM - 8:15 AM

PD5-05

PD5-05 DAPK3 modulates migration and invasion of triple negative breast cancers

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Triple negative breast cancer (TNBC) is associated with poorer prognosis compared to other subtypes of breast cancer due to aggressive metastatic behavior and lack of targeted therapies. Human kinases are a large family of proteins that play critical roles in multiple biological pathways, and aberrant expression or mutations of kinases drive cancer progression and metastasis. Therefore, we applied Mass Spectrometry (MS)-based Kinase-inhibitor pulldown (KiP) technology to profile unique kinase signatures associated with TNBC and prioritize novel regulators for this subtype. Human kinases were captured by a mixture of nine FDA-approved kinase inhibitors, each conjugated separately to sepharose beads to profile all the major branches of the kinome tree. We performed KiP assay in 16 patient-derived xenografts (PDXs) [PMC5379071] consisting of different molecular subtypes of breast cancers. Differential expression analysis identified Death Associated Protein Kinase 3 (DAPK3) as a significantly upregulated kinase in TNBC PDXs which somehow remains understudied. Furthermore, RNA-seq and proteomics data with the same set of PDXs revealed that the upregulation of DAPK3 expression in TNBC was exclusively at protein levels, not RNA levels. Consistently, DAPK3 protein levels were significantly elevated in TNBC cell lines in DepMap dataset. Genomic knockout of DAPK3 in SUM159 and MDA-MB-231 cells dramatically inhibited migration and invasion measured by the transwell assay. We also observed that DAPK3 knockout reduced

the phosphorylation of Myosin Light Chain 2 (MLC2) at T18/S19 site, which was shown to regulate cancer cell invasion [PMC4195943]. DAPK3 belong to DAPK family protein, and has an N-terminus kinase domain with high homology to its family proteins, and a C-terminus leucine-zipper domain. While re-expression of wild-type (WT) DAPK3 cDNA can rescue the migration and invasion phenotype caused by DAPK3 knockout, kinase-dead mutant (D161N) and leucine-zipper-domain-deleted mutant (Δ LZ) cannot rescue the phenotype. Moreover, not only D161N, but also Δ LZ mutant cannot restore the phosphorylation level of MLC2 as DAPK3 WT does. Therefore, both kinase activity and leucin-zipper domain of DAPK3 are critical for the phosphorylation of its substrate MLC2 and thus migration and invasion phenotype. By unbiased Immunoprecipitation-Mass Spectrometry (IP-MS) method, we identified Leucine-Zipper Protein 1 (LUZP1) as one of the strongest interactors of DAPK3. Interestingly, LUZP1 also has a leucine-zipper domain on its N-terminus. Further study showed that DAPK3 binds to LUZP1 via its leucine-zipper domain as expected. Moreover, we observed a tight correlation between DAPK3 and LUZP1 protein expressions in the proteomics data of PDXs and DepMap cell lines (Pearson correlation coefficient is 0.90 and 0.81, respectively). However, the correlation at RNA levels is not significant. Besides, we found that DAPK3 protein stability, but not RNA, is dependent on LUZP1 presence in TNBC cells, strongly implying the roles of LUZP1 on the post-transcriptional regulation of DAPK3. To summarize, we demonstrated that DAPK3, as a novel TNBC-enriched protein, modulates migration and invasion possibly via MLC2 phosphorylation. Both kinase activity and leucine-zipper domain of DAPK3 is necessary for its functionality. We also found LUZP1 is a strong interactor and a potential regulator of DAPK3 in TNBC biology.

Disclosure(s):

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7:00 AM - 8:15 AM

PD5-06

PD5-06 CCN6 suppresses spindle metaplastic breast carcinoma in part via antagonizing Wnt/ β -catenin signaling

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Background: Metaplastic breast carcinomas (mBrCAs) are a rare and highly aggressive subtype of triple negative breast cancer, with histological evidence of non-glandular differentiation and frequent activation of the canonical (β -catenin-dependent) Wnt pathway. Our laboratory has reported that CCN6 is expressed in normal mammary epithelium, but CCN6 expression is lost in 68% of spindle mBrCAs. We found mice with mammary epithelial cell-specific conditional deletion of *Ccn6* (MMTV-Cre; *Ccn6*^{fl/fl} mice) develop mammary tumors that recapitulate human spindle mBrCAs, including upregulation of Wnt pathway genes. We investigated if and how secreted CCN6 protein functions in tumor suppression in spindle mBrCA via effects on the canonical Wnt pathway. Methods: To investigate CCN6 binding to the Wnt co-receptors LRP6 and FZD8 proteins, we performed Flag-IPs on MDA-MB231 mesenchymal-like breast cancer cells expressing Flag-CCN6 or vector. Effects of CCN6 on β -catenin subcellular localization and gene and protein expression were studied by IHC, IF, qRT-PCR and immunoblot in human cell lines and MMTV-Cre;*Ccn6*^{fl/fl} tumors. To test effects of recombinant CCN6 on canonical Wnt signaling, we used the Leading-Light Wnt Reporter Assay and also tested CCN6 effects in WNT3A- and WNT10B-mediated Wnt signaling activation and on MDA-MB231 cell invasion. To study β -catenin/TCF function in invasive growth of CCN6-deficient cancer cells, we employed two independent approaches: i) expression of a dominant-negative Tcf4 (dnTcf4) versus control vector in MMTV-Cre; *Ccn6*^{fl/fl} tumor-derived cells; and ii) expression of a constitutively active mutant (S33Y) β -catenin in concert with treatment with recombinant human CCN6 (rhCCN6; 500 ug/ml) versus BSA control. Syngeneic orthotopic mammary tumor transplants of MMTV-Cre;*Ccn6*^{fl/fl} were used in vivo for rescue experiments with i.p. injections of rhCCN6 or BSA. We monitored tumor growth and morphology, and performed IHC to determine β -catenin localization and expression. Results: We found in co-IPs that CCN6 interacts with LRP6 and FZD8 to form a complex that antagonizes canonical Wnt signaling. CCN6 ectopic expression in MDA-MB231 cells led to reduced nuclear and increased membrane localization of β -catenin and decreased invasive growth in vitro. In vivo, CCN6 protein administration to MMTV-Cre; *Ccn6*^{fl/fl} mice reduced tumor growth and was linked to decreased nuclear β -catenin in the tumors. Conclusion: CCN6 antagonizes canonical Wnt/ β -catenin in part by binding Wnt ligands, leading to reduced active β -catenin in the cytoplasm and nucleus. Our data indicate a critical role for β -catenin activation for CCN6-deficient mBrCA tumor phenotypes. In vivo, rhCCN6 protein reduces tumorigenesis in MMTV-Cre; *Ccn6*^{fl/fl} mBrCA tumors, highlighting how CCN6 restoration or β -catenin inhibition could be new therapeutic approaches for mBrCAs.

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Maria E. Gonzalez, MS: No financial relationships to disclose

Eric R. Fearon, MD: No financial relationships to disclose

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7:00 AM - 8:15 AM

PD5-07

PD5-07 Hepatic Leukemia Factor (HLF), a potential therapeutic target in triple negative breast cancer

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The importance of the antitumor immune response in triple negative breast cancer (TNBC) is well established. We showed previously that the extent of tumor-infiltrating lymphocytes (TILs) in the residual disease after neoadjuvant chemotherapy is associated with a better prognosis. By analyzing 99 pretreatment samples we discovered that the expression of the transcription factor Hepatic Leukemia Factor (HLF) in tumor cells is associated with lower infiltration of immune cells, leading to bad prognosis. Thereby, the aim of our project is to investigate the cellular and molecular mechanism regulated by HLF to better understand the tumor immune microenvironment, so we can develop better treatment options for patients with TNBC. Analysis of publicly available datasets of TNBC (METABRIC and TCGA) showed that tumors with low levels of HLF correlate with the upregulation of genes involved in biological processes associated with the regulation of immune response and in particular with neutrophils activation. Analysis of HLF expression patterns in these patients indicate that tumors presenting a mesenchymal profile exhibited higher HLF levels than the other TNBC subtypes. To elucidate the mechanism of this phenomenon regulated by HLF and his implication in anti-tumoral immune response, we developed several human TNBC cell lines knock-out or knock-down for our target gene using CRISPR/Cas9 editing technology. Comparison of the transcriptomes showed that the silencing of HLF in some mesenchymal TNBC cell lines lead to the upregulation of components involved in the attraction and activation of neutrophils, including CXCL8 (Neutrophil-activating peptide 1), a major cytokine directly responsible for the attraction of neutrophils in the tumor site. In vitro migration experiments supported these observations since purified blood circulating neutrophils have defective migration capacity that depends on the presence or absence of HLF. Finally, the co-culture of neutrophils with tumor cells silenced for HLF showed us, using a large panel of antibodies by spectral flow cytometry, an activated state of mature neutrophils. In conclusion, our study suggest that HLF plays a fundamental role in the regulation of genes involved in the control of tumoral immune microenvironment through the attraction and the activation of mature neutrophils. These findings have the potential for important implications since they suggest that HLF can be a potential target in treating TNBC.

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PD5-08

PD5-08 Drug target activation mapping of matched triple negative primary and axillary lymph node metastases identifies and links the ER-AR-GR steroid hormone receptor axis with downstream AKT activation

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Title: Drug target activation mapping of matched triple negative primary and axillary LN metastases identifies and links the ER-AR-GR steroid hormone receptor axis with downstream AKT activation Background: Triple negative breast cancer (TNBC) is comprised of heterogeneous subtypes that arise from various molecular alterations that result in TNBC having the poorest overall prognosis. There is growing interest in more sensitive ways to measure estrogen receptor (ER) and HER2 levels in the ER “negative” and HER2 “low/negative” settings, as there are patients with TNBC whose tumors are actually ER and/or HER2 “expressing/active”, and who may benefit from ER- and/or HER2-targeted therapies. Given the limitations of IHC in reliably quantitating ER and HER2 in low (0-1+) expressing tumors, we utilized highly sensitive reverse phase protein array (RPPA) to quantitate expression of these therapeutic targets along with downstream signaling activation mapping in

a unique pilot set of patient-matched primary (P) and axillary lymph node (LN) metastases obtained synchronously. The quantitative expression of steroid hormone receptor expression/activation (ER, glucocorticoid receptor (GR), androgen receptor (AR)) along with their signaling architecture and dynamics were analyzed. Methods: A 12 P-LN paired tumor set was chosen for analysis (N=24). Manual macrodissection was used to enrich for tumor epithelium prior to RPPA analysis that quantitatively measured 155 proteins/phosphoprotein drug targets in key signaling pathways known to be involved in steroid hormone receptor biology and tumorigenesis. Statistical analysis using paired sample t-testing or Wilcoxon rank testing was performed ($p < 0.05$ uncorrected). Results: Protein pathway activation mapping and unsupervised clustering analysis revealed a subset of TNBCs from 3 of the 12 (25%) patients (N=4: 1 LN and 1 P, and one patient-matched LN and P) that was characterized by high relative levels of total ER. Interestingly, these same tumors also had amongst the highest relative levels of both total AR and activated (phosphorylated) GR compared to the rest of the 20 tumor samples. Downstream signaling analysis found significant ($p < 0.05$) activation/phosphorylation of AKT (S473 and/or T308) associated with the ER-AR-GR/steroid hormone activated/"high" TNBC signature compared to the 20 tumors that were steroid hormone "low". Conclusions: Functional protein pathway activation mapping of a unique study set of synchronously obtained TNBC primary and LN metastasis revealed a steroid hormone receptor expression/activation signature of co-incidentally activated/expressed ER, GR and AR, that was also characterized by increased AKT activation ($p < 0.05$). This steroid hormone receptor "activated" signature was not observed to be significantly differentially expressed in LN compared to P tissues in cohort or matched pair analysis, suggesting that this signature may be present as an intrinsic event in the P, and not acquired in LN metastases. Recent data from stage I-III TNBC patients treated in the neoadjuvant setting with an AKT inhibitor¹ revealed that responding TNBC patients had pre-treatment tumor biopsies that were enriched for both high AR expression and high phosphoAKT (S473 and/or T308) levels. If these observations that a subset of TNBCs are steroid hormone receptor "activated" despite being ER "negative" are confirmed in larger study sets, we hypothesize that this subgroup, identified by RPPA analysis of both P and LN metastases, could be potentially sensitive to AKT inhibition in combination with agents that target steroid hormone receptors. 1Shi Z, et al. Functional Mapping of AKT Signaling and Biomarkers of Response from the FAIRLANE Trial of Neoadjuvant Ipatasertib plus Paclitaxel for Triple-Negative Breast Cancer. Clin Cancer Res. 2022 Mar 1;28(5):993-1003

Disclosure(s):

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7:00 AM - 8:15 AM

PD5-09

PD5-09 Oncogenic Pathways of Tumor Cells Signal to Stem-ness in TNBC: Relationship between Stem Cell Markers and PI3K-DDR Pathway Targeted Drugs

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Background: The interest in cancer stem cells in TNBC is encouraged by the finding that CD44+ /CD24- and ALDH1+ breast cancer stem cells (CSC) are enriched in TNBC and contribute to chemotherapy resistance and aggressive tumor progression (O'Connor et al., 2018; Ma et al. 2014). CD44+ CD24- phenotype can be utilized to determine TNBC patients' prognosis (Shadbad et al., 2021; Wang et al., 2017). CD44 has also been known for its tumor-intrinsic function in TNBC (Kong et al., Cancer Res. 2020). We have reported a functional correlation between CD44+/CD24- cancer stem cells and 3D clonogenic growth in testing rational combinations of PI3K pathway inhibitors and Wnt-beta-catenin pathway inhibitors in TNBC (Aske et al., 2016; 2017). We also reported that doubling down on the PI3K pathway enhances the anti-tumor efficacy of PARP inhibitor in TNBC (De et al., 2014). Hypothesis: We hypothesized that the anti-tumor effect of PI3K pathway targeted drugs in combination with PARP inhibitor will regulate the expression of CSC in TNBC. Methods: To test our hypothesis, we examined the expression of stem cell markers CD44, CD44v6, and CD24 in MDA-MB-231, SUM149, and MDA-MB-468 TNBC cells in vitro and in vivo. IHC for CD44 and CD44v6 was standardized using tumor controls and identified in (1) BC TMAs, (2) TNBC cell lines, and (3) patients from our Avera cohort. FFPE sections of tumors from athymic mice (bearing xenograft tumors) treated with a combination of Apatolisib with Veliparib plus carboplatin were used to test stem cell markers by IHC. Staining was evaluated independently by a pathologist who was unaware of the study design. Mechanism-based in vitro studies were conducted to understand the mode of action of the drugs using flow cytometry and qRT-PCR. Results: CD44 was identified primarily in the membrane and to a lesser extent in the cytosol of tumor cells of BC patients (TMA and Avera cohort), TNBC cell lines, and xenograft-tumors. Apatolisib, in combination with Veliparib plus carboplatin, blocked the growth of established xenograft tumors by 80-90%, with a concomitant decrease in Ki67 levels. Membrane expression of CD44 inversely correlated to tumor sizes which significantly reduced in response to drug combinations. The relationship between the expression of CD44 and CD44v6 is being worked out, which will be presented at the meeting. Significance: Our findings showed that the anti-tumor effect of Veliparib plus carboplatin and Apatolisib effectively blocked the specific CD44v6 CSC population in TNBC xenograft tumors. Our results demonstrate the integral role of the

PI3K-mTOR and the DDR pathways in the control of stem-ness orchestrating anti-tumor actions of PARP inhibitor and mTOR-PI3K dual inhibitors in TNBC.

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

PD5-10

PD5-10 Dual therapeutic targeting of CDK8/19 and mTOR in triple negative breast cancer

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Triple negative breast cancer (TNBC) is the most aggressive subtype of all breast cancers. However, unlike other breast cancer subtypes, current treatments for TNBC are restricted and this scarcity of viable options is the key contributor to the poorer prognosis. Despite early response, almost all the targeted drugs tested in TNBC eventually fail due to the development of resistance. Patients' data have shown that the expression level of Mediator kinases CDK8 and CDK19 are elevated in TNBC, and that

higher expression of CDK8/19 is correlated with more advanced diseases and worse prognosis. Selective CDK8/19 inhibitor SNX631, when used as a single agent, inhibited the growth of several TNBC cell lines in vitro, cell-derived xenografts (CDXs) as well as patient derived xenografts (PDXs) in vivo, suggesting the potential of targeting CDK8/19 in treating TNBC. We also analyzed the effect of CDK8/19 inhibition on the outcome of treatment with mTORC1 inhibitor everolimus (RAD001), an approved drug for several cancers with mutations of PTEN or PI3KCA. SNX631 exhibited a synergistic effect in combination with everolimus on suppressing TNBC cell growth in vitro. In vivo treatment with everolimus alone achieved a strong tumor growth inhibition in TNBC xenograft models but all the tumors eventually resumed growth, indicated the development of resistance. Significantly, the addition of a CDK8/19 inhibitor prevented the emergence of in vivo everolimus resistance both in CDX and PDX tumors upon treatment for up to 150 days, suggesting a potential for extending remission or even achieving cures in TNBC. Transcriptomic analysis demonstrated that this effect was due to the prevention of transcriptional reprogramming associated with everolimus resistance in tumor cells.

Disclosure(s):

Xiaokai Ding, PhD: No financial relationships to disclose

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Amanda C. Sharko, PhD: No financial relationships to disclose

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7:00 AM - 8:15 AM

Discussion 1 + Q&A: Geriatric Breast Cancer

Presenting Author(s) and Co-Author(s):

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PD6-01, PD6-02, PD6-03, PD6-04, PD6-05 & PD6-06

Disclosure(s):

Rachel Freedman, MD, MPH: Puma Biotechnology: Contracted Research (Ongoing), I have received no direct funding for this study. Only institutional funding was provided to conduct the study. (Ongoing)

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7:00 AM - 8:15 AM

Discussion 2 + Q&A: Male Breast Cancer

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PD6-08, PD6-10 & PD6-11

Disclosure(s):

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12/7/2022

7:00 AM - 8:15 AM

Poster Spotlight Discussion 6: Special Populations: Male Breast Cancer/ Geriatrics

Presenting Author(s) and Co-Author(s):

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12/7/2022

7:00 AM - 8:15 AM

PD6-01

PD6-01 Association between the CARG-BC score and clinical decline after adjuvant chemotherapy in fit older adults with breast cancer: Results from the Hurria Older PatiEnts (HOPE) Prospective Study

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Association between the CARG-BC score and clinical decline after adjuvant chemotherapy in fit older adults with breast cancer: Results from the Hurria Older PatiEnts (HOPE) Prospective Study

Background: We previously developed and validated a risk prediction model for grade 3-5 chemotherapy toxicity in patients age ≥ 65 with early breast cancer, known as the Cancer and Aging Research Group-Breast Cancer (CARG-BC) score. The CARG-BC score is calculated by combining eight clinical variables that classify patients as low, intermediate, and high risk for grade 3-5 chemotherapy toxicity. However, whether this score can also identify individuals most likely to experience a clinical decline after chemotherapy remains unknown. Here, we evaluated the association between the CARG-BC score and decline in health status.

Methods: This is a pre-specified secondary analysis of the Hurria Older PatiEnts (HOPE) with Breast Cancer Study (NCT01472094). This multicenter, prospective cohort study gathered biological and clinical data from women ≥ 65 with stage I-III breast cancer scheduled to receive neo/adjuvant chemotherapy. Health status was measured pre- (≤ 14 days) and post-chemotherapy (≤ 30 days) using a Deficit Accumulation Index (DAI), derived from geriatric assessment data (Cohen et al Cancer 2017). The DAI categorized patients as robust ($0.0 < 0.2$), prefrail ($0.2 < 0.35$), or frail (≥ 0.35). Baseline clinical characteristics, blood biomarkers of inflammation (interleukin-6 [IL-6] and C-reactive protein [CRP]), and CARG-BC scores (classified as low [0-5], intermediate [6-11] or high [≥ 12]) were collected pre-chemotherapy. The population of interest was older women who were clinically fit (defined as robust per the DAI) pre-chemotherapy. The primary outcome was chemotherapy-induced decline in health status, a dichotomized (yes/no) variable defined as a decline in DAI from robust pre-chemotherapy to pre-frail or frail post-chemotherapy. Multivariable logistic regression was used to examine the association between baseline CARG-BC score and chemotherapy-induced decline in health status.

Results: Of 392 women included in this analysis, 316 (80.6%) were clinically fit based on DAI assessment pre-chemotherapy. The median age was 70 (range 65-86), 61.7% had stage II or

III disease, 31% had HR+/HER2+ disease, 22% had HR-/HER2- disease, 36% received an anthracycline, and 74% received prophylactic WBC growth factors. At baseline, 38.7% had low, 53.4% had intermediate, and 7.9% had high CARG-BC scores. Among the 316 clinically fit patients, 80 (25.3%) experienced a decline in health status at the end of chemotherapy. In univariate analysis, we observed that patients with high IL-6 (odds ratio [OR]=2.24, 95% CI: 1.32-3.79, p=0.003), high CRP (OR=1.84, 95% CI 1.10-3.09, p=0.02), and intermediate (OR=3.29, 95% CI 1.72-6.29, p< 0.001) or high (OR=6.29, 95% CI 2.36-16.71, p< 0.001) CARG-BC scores were more likely to experience chemotherapy-induced decline in health status. After adjusting for IL-6 and CRP, patients with both intermediate (OR=3.25, 95% CI 1.68-6.27, p< 0.001) and high (OR=5.17, 95% CI 1.90-14.02, p=0.001) CARG-BC scores had significantly higher odds of experiencing chemotherapy-induced clinical decline as compared to patients with low CARG-BC scores.

Conclusions: In this cohort of older women with early breast cancer who were clinically fit pre-chemotherapy, 25% experienced a decline in health status after neo/adjuvant chemotherapy. Women with an intermediate/high CARG-BC score prior to chemotherapy had 3-5-fold increased odds of experiencing chemotherapy-induced decline in health status independent of baseline clinical characteristics and biomarkers of inflammation. These findings may be useful to clinicians for predicting individual probability of chemotherapy-induced clinical decline and informing treatment decisions in older adults with early breast cancer.

Table 1. Univariate and multivariable association of the CARG-BC score with chemotherapy-induced decline in health status.

	Chemotherapy-Induced Clinical Decline		Univariate		Multivariable	
	Yes (N=80)	No (N=236)	OR (95% CI)	p-value	OR (95% CI)	p-value
CARG-BC score*						
Low (0-5)	14 (19%)	104 (45%)	1.00		1.00	
Intermediate (6-11)	50 (67%)	113 (49%)	3.29 (1.72-6.29)	<0.001	3.25 (1.68-6.27)	<0.001
High (≥12)	11 (14%)	13 (6%)	6.29 (2.36-16.71)	<0.001	5.17 (1.90-14.02)	0.001

Multivariable analysis adjusted for baseline demographic, clinical, and inflammatory levels (IL-6 and CRP); *CARG-BC score is calculated using 8 independent predictors (each assigned weighted points): anthracycline use (1 point), stage II or III (3 points), planned treatment duration > 3 months (4 points), abnormal liver function (3 points), low hemoglobin (3 points), falls (4 points), limited walking (3 points), and lack of social support (3 points). The total CARG-BC risk score is the sum of each point derived from these 8 predictors. Each patient's total CARG-BC score can then be classified into three risk groups: low (0-5 points), intermediate (6-11 points), or high (≥ 12 points).

Disclosure(s):

Jingran Ji, MD: No financial relationships to disclose

Canlan Sun, PhD: No financial relationships to disclose

Hyman B. Muss, MD: No financial relationships to disclose

Harvey J. Cohen, MD: No financial relationships to disclose

Mina S. Sedrak, MD, MS: No financial relationships to disclose

12/7/2022

7:00 AM - 8:15 AM

PD6-02

PD6-02 Health-Related Quality of Life Trajectories and Predictors among Older Breast Cancer Survivors: A SEER-MHOS analysis

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Health-related quality of life (HRQOL) is an important issue for breast cancer patients and clinicians in the treatment decision process. In addition, older women are more vulnerable due to pre-existing comorbidities and socioeconomic status. This study explored 10-year trajectories of HRQoL in older breast cancer survivors and their predictors using patient-reported outcomes data queried from the Surveillance, Epidemiology and End Results - Medicare Health Outcomes Survey (SEER-MHOS) data resources among Medicare beneficiaries. Older women diagnosed with breast cancer in 1998-2012 and who participated in the surveys before and at least once after diagnosis were included in the analysis. HRQOL was measured using SF-36/VR-12 questionnaire and summarized as Physical Component Summary (PCS) Score and Mental Component Summary (MCS) Score. Latent Class Growth Mixture Modeling was conducted to identify distinct groups of women with a similar trajectory of HRQOL. A total of 1089 women with breast cancer completed surveys an average of 2.6 times (range 2 - 19). The results showed that there were three latent classes of PCS trajectory: high-declining (46% of the sample), mid-declining (37%), and low-improving (17%). Two latent classes of MCS trajectory were identified: high-stable (76%) and low-declining (24%). The univariate analysis showed that age at diagnosis, body mass index, level of education, geographic region, tumor grade, tumor size, and the number of comorbidities were related to PCS and MCS scores. Multivariable multinomial logistic regression analysis identified the number of comorbidities as the most significant predictor for PCS score and level of education as the most significant predictor for MCS score. Future research needs to identify the most common comorbidities that influence HRQOL deterioration in older breast cancer survivors to develop interventions that better the physical HRQOL in patients. Also, interventions that target less educated, underserved patients to improve mental HRQOL.

Disclosure(s):

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Sushantti Rupesh, BS: No financial relationships to disclose

Katia Ferdowsi, MD, MPH: No financial relationships to disclose

Robert Hines, PhD, MPH: No financial relationships to disclose

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7:00 AM - 8:15 AM

PD6-03

PD6-03 Serum methylmalonic acid concentrations at breast cancer diagnosis strongly correlate with frailty: a retrospective cross-sectional study

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Introduction: Frailty commonly occurs in older persons, including those with breast cancer diagnoses. Methylmalonic acid (MMA), a metabolite and by-product of propionate metabolism, is known to increase significantly with aging. The relation between MMA concentrations and frailty is currently unknown. Objectives: A cross-sectional study was performed to study the association between baseline serum MMA concentrations and clinical frailty (estimated by G8 screening) in older patients with newly diagnosed breast cancer. Methods: 163 patients ≥ 70 years old with early-stage breast cancer were included (median age 76y). G8 screening and serum sample collection were performed at breast cancer diagnosis before any therapy was administered. MMA concentrations were measured via liquid chromatography with tandem

mass spectrometry (LC-MS-MS). Results: MMA concentrations significantly increased with age ($r_s=0.3$, $p<.0001$) and serum creatinine levels ($r_s=0.5$, $p<.0001$) in this older population. The group with an abnormal G8 ($\leq 14/17$ = 'frail', 48% of patients) had significantly higher MMA levels than the group with normal G8 ($>14/17$ = 'fit', 52%): 250nM vs. 189 nM, respectively ($p=.0002$). Higher MMA concentrations were independently associated with abnormal G8 (Odds ratio, 1.003, 95%CI 1.0 to 1.006, $p=.04$) after adjusting for age and serum creatinine levels. Among the different components of G8, MMA concentrations correlated most with weight loss ($r_s= -0.18$, $p=.02$), mobility ($r_s= -0.23$, $p=.002$), and polypharmacy ($r_s= -0.22$, $p=.005$). Conclusion: Elevated serum MMA concentrations at breast cancer diagnosis are significantly associated, not only with age but also independently with clinical frailty in older patients with early-stage breast cancer. MMA may be further evaluated as a biomarker of frailty in older persons with breast cancer.

Disclosure(s):

Qi Wu, MD, Ph.D. candidate: No financial relationships to disclose

Sigrid Hatse, PhD: No financial relationships to disclose

Cindy Kenis, PhD: No financial relationships to disclose

Yentl Lambrechts, n/a: No financial relationships to disclose

Kevin Punie, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), travel support (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); FocusPatient: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Medscape: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), travel support (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), travel support (Ongoing); PharmaMar: travel support (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), travel support (Ongoing); Sanofi: Contracted Research (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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12/7/2022

7:00 AM - 8:15 AM

PD6-04

PD6-04 Baseline Insurance and Unplanned Emergency Room Use and Hospitalizations Among Elderly Breast Cancer Patients Participating in Clinical Trials

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Background Reducing acute care use is an important strategy for improving value in cancer care. Patients with cancer are at risk for unplanned Emergency Room (ER) visits and hospitalizations during treatment which can increase the cost of care. Patients enrolled in clinical trials have equal access to supportive care and are treated uniformly according to protocol. While demographic factors such as age, race and number of comorbidities have been associated with increased healthcare utilization, less is known about insurance status, which may be a proxy for structural barriers to outpatient quality care, especially since many unplanned ER visits and hospitalizations are preventable. **Methods** We conducted a retrospective analysis among breast cancer patients over the age of 65 treated on SWOG clinical trials from 2001 to 2019 with trial data linked to Medicare claims. Patients were included if they were enrolled in Medicare for at least 12 continuous months after trial registration. Type of insurance at trial enrollment was classified as Medicare alone, Medicare + Commercial or Medicare + Medicaid. The outcomes – derived from Medicare claims – were healthcare utilization ER visits, hospital stays, and healthcare costs in the first year. Demographic, clinical, and prognostic factors were captured from clinical trial records. Logistic regression was used to examine utilization outcomes and linear regression was used to examine healthcare costs. Regression models were adjusted for age, race, and a study-specific prognostic risk score, and stratified by study and treatment. Costs were analyzed in 2021 US dollars. **Results** In total, N = 1,067 patients were analyzed. Median age was 70 years, 32% of patients had Medicare alone, 64% had Medicare + Commercial, and 4% had Medicare + Medicaid. Overall 29% had one or more ER visits and 22% had one or more hospital stays. There were no differences in outcomes between patients with Medicare alone vs. Medicare + Commercial; these groups were combined. In adjusted analyses, patients on Medicare + Medicaid were statistically significantly more likely to have a hospital stay or ER visit (combined outcome) within 12 months of trial registration (58% vs 34%; OR [95% CI], 2.13 [1.05-4.31], p=.04). Separately, patients on Medicare + Medicaid were statistically significantly more likely to have ER visits (51% vs 27.7%, OR [95% CI], 2.09 [1.05-4.19], p=.04), but not hospitalizations (34.9% vs

20.7%, OR [95% CI], 1.55 [0.74-3.24], $p=.25$) compared to the others combined. Mean costs were higher for patients who had Medicare + Medicaid compared to the others combined, but the differences were not statistically significant (\$43,150 vs. \$37,259, $p = 0.55$), possibly due to the small Medicare + Medicaid sample size. Conclusion Despite participation in a BC clinical trial, patients with Medicare + Medicaid had a two-fold increased risk of unplanned ER visits despite controlling for clinical, demographic and prognostic factors. These findings suggest that access and structural factors may adversely influence utilization outcomes for socioeconomically vulnerable older patients with breast cancer. In conjunction with reducing insurance related barriers to clinical trials, efforts are needed to ensure adequate clinical resources to prevent unplanned use of acute care.

Disclosure(s):

Dawn L. Hershman, MD: No financial relationships to disclose

Riha Vaidya, PhD: No financial relationships to disclose

Cathee Till, MS: No financial relationships to disclose

William E. Barlow, PhD: AstraZeneca: Contracted Research (Ongoing); Merck: Contracted Research (Ongoing)

Mike LeBlanc, PhD: No financial relationships to disclose

Joseph M. Unger, PhD: No financial relationships to disclose

12/7/2022

7:00 AM - 8:15 AM

PD6-05

PD6-05 Retrospective analysis of VES-13 questionnaires in the Senior Women's Breast Cancer Clinic at Sunnybrook Health Sciences, Toronto, Ontario, Canada

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Purpose: Vulnerable Elder Survey (VES-13) is a screening tool used in assessing older vulnerable patients at risk of functional decline. We sought to evaluate how VES-13 tool would impact oncologist referral pattern to geriatricians as our primary outcome. We also sought to better understand how VES-13 scores impacted referral to additional services (allied healthcare), and modification to oncological treatment. **Methods:** A retrospective review of VES-13 questionnaires completed by older women (age 70 or older) with breast cancer referred to the Senior Women's Breast Cancer Clinic (SWBCC) was undertaken. Patients with a VES-13 score of three or greater, who were at significantly higher risk of functional decline, had further retrospective chart review for risk factors that would contribute to functional decline such as Eastern Cooperative Oncology Group (ECOG) score, social supports, and current living situation. The primary and secondary endpoints described above were analyzed through bivariate comparisons and multivariable logistical regression to determine if there was any statistical significance ($p < 0.05$). **Results:** 701 patients completed VES-13 form, of which 235 (33.5%) had a VES-13 score of three or greater. Less than 5% of oncologists documented VES-13 scores in their notes, with less than 5% of patients being referred for geriatric services. Neither VES-13 ($p= 0.900$) nor ECOG ($p= 0.424$) were associated with referral for geriatrics assessment. Referral to allied healthcare services was significantly associated with (ECOG) score (OR 2.24 [1.49-3.37], $p < 0.0001$), while not significantly associated with VES-13 score (OR 0.89 [0.78-1.02], $p= 0.102$). VES-13 (OR 1.23 [1.04-1.45], $p=0.014$) and ECOG (OR 2.37 [1.29-4.37], $p=0.005$) were both associated with modification in oncology treatment (chemotherapy or radiation). **Conclusion:** Approximately one third of our population was at risk of functional decline. VES-13 scores were infrequently mentioned in oncologists notes from their clinical assessments, with very few patients being referred for geriatric assessment. By not collecting and analyzing VES-13 scores, and relying on performance status alone, there is a missed opportunity in assessing for functional decline and reducing potential complications from treatment for our patients. **Keywords:** Allied healthcare professionals; Breast cancer; Frailty; Geriatric oncology; Geriatrics; Multidisciplinary; VES-13.

Disclosure(s):

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7:00 AM - 8:15 AM

PD6-06

PD6-06 Racial and ethnic disparities with influenza vaccine use in long-term survivors of metastatic breast cancer

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Background: Due to therapeutic advancements, people diagnosed with metastatic breast cancer (MBC) are living longer. This is particularly true for elderly patients who are often diagnosed with more indolent disease. However, elderly patients have higher rates of comorbidity and are vulnerable to other adverse health outcomes, but the primary care management of patients with advanced cancer may be sub-optimal. Every year influenza results in hundreds of thousands of hospitalizations and tens of thousands of deaths. Guidelines recommend the influenza vaccine annually for those over the age of 65 as well as those with cancer based on studies showing a 40-60% reduction in hospitalizations and death. Patterns of use in patients with MBC is unknown. Methods: A retrospective analysis was conducted using the Surveillance, Epidemiology, and End Results (SEER)–Medicare linked data. Patients were included if they were diagnosed with stage IV MBC from 1/1/2008 – 12/31/2017, were ≥ 65 years of age, and had continuous Medicare enrollment for 12 months prior to diagnosis and at least three months after. Our primary outcome of interest was influenza vaccine use identified via CPT codes and defined as any use, use among patients surviving > 3-years, use among patients surviving >5-years, and repeated vaccine use. We then conducted bivariate analyses using demographic variables, including race, ethnicity, SES, age, and marital status, and clinical factors, including chemotherapy use, ER/PR positivity, and HER2 positivity. A multivariable logistic model was used to identify factors associated with influenza vaccine use in each cohort. Results: We identified 5182 patients with stage IV MBC during the study period that met our inclusion criteria. Overall, the median survival was 21 months and only 44% received at least one vaccination at any time after diagnosis. Within the cohort with the > 3-year survival (n=1864), only 1222 (66%) received an influenza vaccination at least one time and only 54% received the vaccine at least two times during 3 years of follow-up. Among patients with at least five-years of survival (n=763), 73% received at least one vaccination and only 65% received the vaccine at least two times during 5 years of follow-up. In a bivariate analysis in the 3-year survival cohort, we found that black race (47% vs 67%, $p <$

0.001) and Hispanic ethnicity (53% vs 66%, $p=0.026$), compared to white race and non-Hispanic ethnicity, respectively, were significantly associated with decreased vaccine use. The only factor associated with increased use was chemotherapy exposure. A multivariable model found lower odds of influenza vaccine receipt for black patients (OR=0.44, 95% CI 0.30-0.65, $p<0.001$) and Hispanic patients (OR=0.58, 95% CI 0.36-.94, $p=0.026$). Similar findings were found in the 5-year survival cohort. Ongoing landmark analyses will be presented evaluating the impact of vaccination on survival. Conclusions: Over 50% of survivors with MBC do not receive the influenza vaccine after diagnosis. Importantly black and Hispanic patients with MBC are about half as likely to receive the influenza vaccine as white patients. Given the known impact of influenza vaccination in the elderly, improving access to vaccination could be an important strategy to reduce disparities in health outcomes. Our findings demonstrate primary care access disparities amongst the MBC population and indicate a need for educational and policy-based interventions.

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7:00 AM - 8:15 AM

PD6-08

PD6-08 Mortality risks over 20 years in men with stage I-III hormone receptor-positive breast cancer.

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Background: In women with hormone receptor-positive (HR+) breast cancer, the risk of distant recurrence and death persists for at least 20 years (y) from diagnosis. The risk of late mortality

in men with HR+ breast cancer has not been reported. The aims of this study were to evaluate long-term risks of breast cancer-specific mortality (BCSM) and non-BCSM in men with stage I-III HR+ breast cancer. In addition, we aimed to identify factors associated with late deaths from breast cancer in men.

Methods: Using data from the Surveillance, Epidemiology, and End Results (SEER) program, we identified men diagnosed with stage I-III HR+ breast cancer between 1990-2008. We used cumulative incidence function to estimate the effect of baseline clinical and pathologic variables including age at diagnosis, stage, tumor size (T), nodal status (N), and tumor grade, on cumulative risks of BCSM and non-BCSM over time. We estimated annual rate of events per 100 person-years. We plotted smoothed hazard estimates over time for BCSM by stage and nodal status. Fine and Gray multivariable regression was used to evaluate the association of pre-selected variables with BCSM, conditional on having survived 5 y.

Results: We included 2,836 patients (pts) with a median follow-up of 15.41 y. Median age at diagnosis was 67 y (IQR 57-76 y). Stage distribution was: 34.5% stage I, 46% stage II, and 19.5% stage III. The table shows risks of BCSM and non-BCSM and annual event rates by stage, N status, and grade. The cumulative risk of BCSM in y 0-20 was 12.4% for stage I, 26.2% for stage II and 46.0% for stage III. In contrast, the cumulative risk of non-BCSM over the same period ranged from 42.8% in stage III to 52.4% in stage I. Of all BCSM events, the proportion that occurred 0-< 5y, 5-< 10y and ≥10y was: For stage I 22.55%, 50% and 27.45%; For stage II 37.58%, 38.93% and 23.49%, For stage III 49.15%, 31.62% and 19.23%; respectively ($p < 0.001$). Among pts with stage II breast cancer, we observed a peak in the risk of BCSM at 6 y with a hazard rate of 3%, followed by a minimal decline in risk thereafter. However, among pts with stage III ($n=554$), and those with N3 ($n=160$), we observed a risk of BCSM that peaked first at 4-5 y (hazard rates: 6.3% and 9.9% for stage III and N3, respectively) followed by a small decline and then peaked again at 11-12 y (hazard rates: 7.5% and 12.7% for stage III and N3, respectively). In adjusted Fine and Gray regression conditional on having survived 5 y, risks of BCSM were higher for pts aged < 50 y vs >64 y (Hazard ratio [HzR] 1.59; 95% CI, [1.17 – 2.16]), grade III/IV vs grade I (HzR 1.85; 95% CI, [1.22 – 2.79]), and stage III vs stage I (HzR 3.93; 95% CI, [2.93 – 5.26]).

Conclusions: In HR+ male breast cancer, risks of BCSM persist for at least 20 y after diagnosis and depend on traditional clinicopathologic factors such as age, tumor stage and tumor grade. Among the relatively small group of men with higher stages of disease, we observed a prolonged risk of BCSM with an early and late peak, which is different from the risk that is reported in women (Leone JP, BCRT 2021). Whether the observed trends in hazards over time reflect biologic differences in tumor characteristics, tumor dormancy, and/or host factors between male and female breast cancer cannot be elucidated from these data. Better adjuvant therapies are warranted to reduce early and late BCSM risks.

Risks of BCSM, non-BCSM and annual event rates in men with stage I-III hormone receptor-positive breast cancer

	N	BCSM							non-BCSM	
		% Event-Free		Annual rate (%)				Cumulative risk (%)	Cumulative risk (%)	
		at 5 y	at 10 y	y 0-<5	y 5-<10	y 10-<15	y 15-20	y 0-20	y 0-20	
Stage										
I	978	97.6	92.4	0.5	1.4	0.9	1.0	12.4	52.4	
II	1304	91.3	82.3	1.9	2.9	2.7	2.6	26.2	51.2	
III	554	79.1	65.6	5.1	5.8	7.3	4.8	46.0	42.8	
Nodal status										
N0	1538	95.8	90.4	0.9	1.6	1.4	1.1	15.2	55.5	
N1	868	89.5	78.1	2.4	3.7	3.1	3.5	33.3	44.5	
N2	270	82.5	69.9	4.2	5.1	5.3	4.5	40.6	46.3	
N3	160	69.8	52.6	7.6	8.5	14.3	5.2	59.8	32.9	
Tumor grade										
Grade I	325	97.2	92.6	0.6	1.2	1.5	1.1	12.6	54.1	
Grade II	1415	93.1	84.8	1.5	2.5	2.6	1.9	23.5	51.8	
Grade III/IV	948	86.5	76.0	3.1	3.8	2.7	2.4	32.4	47.3	

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12/7/2022

7:00 AM - 8:15 AM

PD6-10

PD6-10 The impact of post mastectomy radiation therapy on clinical outcomes of male breast cancer: A meta-analysis of comparative studies

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Background/Rationale: Male breast cancer accounts for less than 1 percent of all cancer diagnoses in men. Because it is rare, it does not lend itself to large, randomized trials. In general, the approach to the treatment of early, non-metastatic male breast cancer has largely been extrapolated from female breast cancer trials. Specifically, the data on early-stage post mastectomy radiation therapy (PMRT) is limited, and its benefits remain unclear. Objectives: We conducted this meta-analysis to determine the impact of PMRT on clinical outcomes of men with breast cancer. Methods: A review of the medical literature was conducted using online databases. Inclusion criteria consisted of English language, diagnosis of invasive non-metastatic male breast cancer (MBC), comparative studies of PMRT versus none, and studies that reported the incidence of local and distant recurrences as well as survival data in the compared arms. A meta-analysis using the Mantel-Haenszel method for calculating the weighted pooled relative risk (RR) under the fixed effects model. Subsequently, the heterogeneity statistic gets incorporated to calculate the summary RR under the random effects model. Results: Ten retrospective comparative studies with 3912 patients were included and analyzed. Eight studies reported survival data. Six and three studies reported local and distant recurrence incidence, respectively. PMRT did not have an impact on overall survival or distant recurrences. However, PMRT significantly lowered the RR of locoregional recurrences (RR=0.53, 95%CI 0.31-0.92). In addition, when survival was analyzed by TNM stage and N status, PMRT was found to have a significant reduction in RR of death in stage III (RR=0.85, 95%CI 0.75-0.97), N1 (RR=0.77, 95%CI 0.61-0.98), and N2 (RR=0.61, 95%CI 0.49-0.78) disease. Conclusions: This is the first meta-analysis to show that PMRT is associated with a lower relative risk of death in stage III MBC as well as N1 and N2 disease. It also demonstrates a significant reduction in RR of locoregional recurrences. In the absence of randomized clinical trials, it represents the most compelling data supporting the use of PMRT in this MBC patient population.

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Philip A. Haddad, MD, MPH, MHA: No financial relationships to disclose

Usman Zaheer, MD: No financial relationships to disclose

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7:00 AM - 8:15 AM

PD6-11

PD6-11 Evaluation of the Sensitivity to Endocrine Therapy Index (SET_{2,3}) in Early Male Breast Cancer: Results from an analysis in the EORTC 10085/TBCRC/BIG/NCTN International Male Breast Cancer Program

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Introduction Breast cancer is uncommon in men. Almost all male breast cancers are hormone receptor-positive, HER2-negative, although the pathogenesis is not always attributable to an endocrine condition. A few studies have compared biological characteristics or molecular signatures with breast cancers in women. We sought to evaluate whether hormone receptor-related gene expression is different in cancers from men compared to equivalent cancers from women. SET2,3 index measures non-proliferative hormone receptor-related transcriptional activity in the cancer (SET-ER/PR index) and adjusts this for a Baseline Prognosis Index (BPI) that combines the measurements of tumor and nodal stage with a 4-gene molecular subtype (ESR1, PGR, ERBB2, and AURKA). Methods We received aliquots of total RNA from male patients with breast cancer included in the retrospective cohort study of the EORTC 10085/BCG/TBCRC/BIG/NCTN International Male Breast Cancer Program (NCT01101425). SET2,3 assay was performed using the QuantiGene assay (Thermo Fisher) using bead-based hybridization and laser spectroscopy (Luminex). The statistical analyses were performed by the EORTC statistician. The primary objective of the study was the assessment of the prognostic value of the SET2,3 index score in patients with early-stage hormone receptor-positive, HER2-negative male breast cancer, treated with endocrine therapy. Clinical outcomes (recurrence-

free survival – RFS; overall survival – OS) were estimated by Kaplan-Meier curves and secondarily compared using multivariable Cox models adjusted for continuous SET2,3 index, tumor size, nodal status, age, and chemotherapy and radiotherapy use. An exploratory analysis to compare the SET2,3 index scores distribution in female and male breast cancer patients was also performed using results from the same assay performed on cancers from women selected on the same inclusion criteria. Due to the low numbers of male patients treated with neoadjuvant treatment (N=6), this analysis was restricted to patients treated with adjuvant treatment (n=315 male and 660 female). Results Of the 321 male patients with breast cancer analyzed, treated between 1990 and 2010, 211 (65.7%) were categorized as high SET2,3 index score, reflecting a high endocrine activity in the cancer and low risk of recurrence, and 110 patients (34.3%) categorized as being low score, reflecting low endocrine activity and high risk of recurrence. At 5 years, the RFS was 75.0% (95% CI, 67.4-81.1) in the high SET2,3 group versus 60.7% (95% CI, 49.1-70.5) in the low SET2,3 group (HR univariate, 0.49; 95% CI, 0.34-0.70; P< 0.0001). The 5-year OS rate among patients with a high SET2,3 index was 84.3% (95% CI, 45.5-73.8), in contrast of 67.8% (95% CI, 56.6-76.7) in the low SET2,3 group (HR univariate, 0.44; 95% CI, 0.30-0.65; P< 0.0001). SET2,3 was independently prognostic for OS, but not RFS in multivariable Cox models. In patients classified as low SET2,3, the addition of neo/adjuvant chemotherapy to adjuvant endocrine therapy was associated with 5-year OS of 76.0% (95% CI, 59.5-86.4) and in patients who received endocrine therapy alone the 5-year OS was 61.3% (95% CI, 45.5-73.8), an absolute difference of 14.7 percentage points. Overall, we did not observe a difference in the distributions (median, interquartile range) of SET2,3 index between men (2.4, 1.9–2.6) and women (2.3, 2.0–2.7). Conclusion SET2,3 index measurements of endocrine-related transcriptional activity in male patients with breast cancer were not different from measurements in female patients with breast cancer. SET2,3 was prognostic in male breast cancer and our exploratory analysis suggests that chemotherapy might improve the poor prognosis for men with breast cancer that has low SET2,3 index. This study was funded by the Breast Cancer Research Foundation (BCRF).

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12/7/2022

8:20 AM - 8:30 AM

Opening Ceremony/Welcome Message

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Virginia Kaklamani, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Daiichi Sankyo: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Genentech: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Genomic Health: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Gilead Sciences: Honoraria (Ongoing); Novartis: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Pfizer: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Puma Biotechnology: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing)

Carlos Arteaga, MD: Arvinas: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Research Funding (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Research Funding (Ongoing); MERCK: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); OrigiMed: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Research Funding (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing); TAIHO Oncology: Consulting Fees (e.g., advisory boards) (Ongoing); Takeda: Research Funding (Ongoing)

12/7/2022

8:30 AM - 9:00 AM

Leveraging Preclinical Models for Translational Breast Cancer Research

Presenting Author(s) and Co-Author(s):

Jeffrey Rosen, PhD - *Baylor College of Medicine*

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Leveraging Preclinical Models for Translational Breast Cancer Research

Jeffrey M Rosen, Department of Molecular & Cellular Biology, Dan L Duncan Comprehensive Cancer Center, Baylor College of Medicine, 1 Baylor Plaza, Houston, TX 77030

My laboratory originally begin utilizing mouse models several decades ago to better understand normal mammary gland development. Subsequently we developed genetically engineered mouse models for both prostate and breast cancer. As one of the inaugural members of the NCI Mouse Models of Human Cancer Consortium we were fortunate to collaborate with Daniel Medina at BCM and later with Chuck Perou at the University of North Carolina Chapel Hill on the characterization of spontaneous tumors derived from transplantation of Tp53 null mammary epithelial cells isolated from Balb/c mice into the cleared fat pad of wildtype hosts. This led to the development of a large bank of spontaneous tumors which are representative of several of the subtypes of triple negative breast cancer including the claudin-low subtype. These transplantable syngeneic models have been characterized genomically and with respect to their immune microenvironments. These models first were used in my laboratory to study cancer stem cells, intratumoral heterogeneity and the response to radiation and hyperthermia using gold nanoparticles. Subsequently, in collaboration with Shawn Zhang's laboratory we integrated the immunological characterization of murine syngeneic mammary tumor models with analyses of human breast cancer datasets, and demonstrated a relationship between EMT and myeloid cells, specifically tumor-associated macrophages. We also have leveraged our syngeneic GEM models to define the response to immune checkpoint blockade therapy with emphasis on the myeloid cell environment. In collaboration with colleagues at BCM and MD Anderson these models more recently have been employed to study the effects of diverse classes of therapeutics targeting the spliceosome, the unfolded protein response, and mRNA translation, and to elucidate the importance of replication stress for immune checkpoint blockade therapy. Some of these therapeutics are now in clinical trials. Finally, examples of how these models have been employed for combination treatment with chemotherapy and immunotherapy in both the primary and metastatic setting will be discussed, and how durable treatment responses require targeting both tumors and the tumor-immune microenvironment.

Disclosure(s):

Jeffrey Rosen, PhD: No financial relationships to disclose

12/7/2022

8:30 AM - 9:00 AM

William L. McGuire Memorial Award Lecture

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12/7/2022

9:00 AM - 9:15 AM

GS2-01

GS2-01 Trastuzumab deruxtecan vs physician's choice in patients with HER2+ unresectable and/or metastatic breast cancer previously treated with trastuzumab emtansine: primary results of the randomized, phase 3 study DESTINY-Breast02

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In DESTINY-Breast01 (NCT03248492) and DESTINY-Breast03 (NCT03529110), trastuzumab deruxtecan (T-DXd) demonstrated unprecedented activity in patients (pts) with HER2+ (immunohistochemistry 3+; immunohistochemistry 2+/in situ hybridization+) advanced metastatic breast cancer (mBC), leading to regulatory approvals in several countries for HER2+ unresectable/mBC after a prior anti-HER2-based regimen. DESTINY-Breast02 (NCT03523585) is a phase 3 trial of T-DXd vs treatment of physician's choice (TPC) in patients with centrally confirmed HER2+ mBC previously treated with trastuzumab emtansine (T-DM1). It acts as a confirmatory study for the pivotal phase 2 DESTINY-Breast01 trial. Here we report the primary results of DESTINY-Breast02.

Methods

Pts with HER2+ mBC were randomized 2:1 to receive T-DXd or TPC (trastuzumab + capecitabine or lapatinib + capecitabine) and stratified by hormone receptor (HR) status (HR+/HR-), prior pertuzumab treatment, and history of visceral disease. The primary endpoint of this time-driven primary analysis was progression-free survival (PFS) as determined by blinded independent central review (BICR). The powered secondary endpoint was overall survival (OS). Other secondary endpoints included confirmed objective response rate (ORR) by BICR, duration of response (DoR) by BICR, PFS by investigator assessment, safety, and others.

Results

608 pts were randomized to receive T-DXd (n = 406) or TPC (n = 202). Pts receiving T-DXd and TPC had a median age of 54.2 years (range, 22.4-88.5 years) and 54.7 years (range, 24.7-86.5 years), respectively, with a median of 2 (range, 0-10 and range, 1-8) prior lines of systemic therapy (excluding hormone therapy) in the metastatic setting. Median treatment duration was 11.3 mo in the T-DXd arm and ~4.5 mo in the TPC arm. Efficacy and safety results are shown in the table below. T-DXd significantly improved PFS (HR, 0.36; 95% CI, 0.28-0.45; P <0.000001) and OS (HR, 0.66; 95% CI, 0.50-0.86; P = 0.0021) compared with TPC. Confirmed ORR was 69.7% (14% complete response) with T-DXd and 29.2% (5.0% complete response) with TPC. Grade ≥3 treatment-emergent adverse events (TEAEs) occurred in 52.7% and 44.1% of pts receiving T-DXd and TPC, respectively. Adjudicated drug-related interstitial lung disease (ILD) occurred in 10.4% of pts with T-DXd vs 0.5% of pts with TPC. In pts receiving T-DXd, most ILD cases (88.1%) were grade 1/2 and grade 5 ILD was reported in 2 (0.5%) pts.

Conclusions

Results from DESTINY-Breast02 confirmed the clinical benefit and superiority of T-DXd over

conventional chemotherapy-based regimens in pts with HER2+ mBC previously treated with T-DM1, as evidenced by significant and clinically meaningful improvements in PFS and OS. These data, together with earlier reported results from the DESTINY-Breast03 study of T-DXd vs T-DM1 solidify T-DXd as an optimal treatment option in pts with progressive HER2+ mBC across broad settings.

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Table. Summary of Efficacy and Safety Results for T-DXd and TPC in Patients With HER2+ mBC Previously Treated With T-DM1

Table. Summary of Efficacy and Safety Results for T-DXd and TPC in Patients With HER2+ mBC Previously Treated With T-DM1 (Data cutoff: June 30, 2022)

	T-DXd	TPC
Efficacy	N = 406	N = 202
mPFS by BICR, months (95% CI)	17.8 (14.3-20.8)	6.9 (5.5-8.4)
HR (95% CI)	0.36 (0.28-0.45); <i>P</i> < 0.000001 ^a	
mPFS by investigator, months (95% CI)	16.7 (14.3-19.6)	5.5 (4.4-7.0)
HR (95% CI); <i>P</i> -value	0.28 (0.23-0.35); <i>P</i> < 0.000001 ^a	
mOS, months (95% CI)	39.2 (32.7-NE)	26.5 (21.0-NE)
HR (95% CI); <i>P</i> -value	0.66 (0.50-0.86); <i>P</i> = 0.0021 ^a	
Confirmed ORR, % (95% CI) ^b	69.7 (65.0-74.1)	29.2 (23.0-36.0)
	<i>P</i> < 0.0001 ^a	
mDoR, months (95% CI) ^b	19.6 (15.9-NE)	8.3 (5.8-9.5)
Median follow up, ^c months (range)	21.5 (0.1-45.6)	18.6 (0-45.7)
Safety, n (%)	N = 404^d	N = 195^d
Any grade TEAEs	403 (99.8)	185 (94.9)
Grade ≥3	213 (52.7)	86 (44.1)
Serious TEAEs	103 (25.5)	46 (23.6)
TEAEs associated with:		
Drug interruption	183 (45.3)	90 (46.2)
Dose reduction	102 (25.2)	89 (45.6)
Drug discontinuation	80 (19.8)	19 (9.7)
Death	11 (2.7)	7 (3.6)

^aTwo-sided.

^bBased on blinded independent central review.

^cMedian follow up for a patient is defined as the date last known alive minus date of randomization plus 1.

^dOf 608 randomized patients, 404 and 195 received ≥1 dose of T-DXd and TPC, respectively.

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12/7/2022

9:00 AM - 9:45 AM

General Session 2

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12/7/2022

9:15 AM - 9:30 AM

GS2-02

GS2-02 Trastuzumab deruxtecan versus trastuzumab emtansine in patients with HER2-positive metastatic breast cancer: Updated survival results of the randomized, phase 3 study DESTINY-Breast03

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Background

Trastuzumab deruxtecan (T-DXd) is approved in the United States and European Union for use in patients (pts) with HER2+ unresectable/metastatic breast cancer (mBC) after ≥ 1 prior anti-HER2 regimen(s). Approval was based on the randomized, multicenter, open-label, phase 3 DESTINY-Breast03 study (NCT03529110), in which T-DXd demonstrated statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared with trastuzumab emtansine (T-DM1). At the primary interim analysis (data cutoff May 21, 2021), the risk of disease progression or death was reduced by 72% with T-DXd ($P < 0.001$; Cortes et al. *N Engl J Med* 2022). Overall survival (OS) data were immature for both treatment groups; although the prespecified cutoff for significance was not reached (NR), a trend toward benefit with T-DXd was observed. With further follow-up, we report results from the prespecified OS analysis of DESTINY-Breast03 (data cutoff July 25, 2022), including updated efficacy and safety.

Methods

Pts with HER2+ mBC previously treated with trastuzumab and a taxane in either the metastatic setting or (neo)adjuvant setting with progression within 6 mo of therapy, who could have

received pertuzumab, were randomly assigned 1:1 to receive T-DXd 5.4 mg/kg every 3 weeks (Q3W) or T-DM1 3.6 mg/kg Q3W until disease progression. The primary endpoint was PFS by blinded independent central review (BICR). The key secondary endpoint was OS (80% powered at 2-sided significance level of 5%); other secondary endpoints included objective response rate (ORR), duration of response (DoR), PFS based on investigator assessment, and safety.

Results

524 pts received either T-DXd (n = 261) or T-DM1 (n = 263). As of the updated data cutoff, median duration of study follow-up was 28.4 mo (range, 0.0-46.9 mo) for T-DXd and 26.5 mo (range, 0.0-45.0 mo) for T-DM1. Median treatment duration was 18.2 mo (range, 0.7-44.0 mo) for T-DXd and 6.9 mo (range, 0.7-39.3 mo) for T-DM1. The risk of death was reduced by 36% (HR, 0.64; P = 0.0037) with T-DXd; median OS (mOS) was NR (95% CI, 40.5 mo-not evaluable [NE]), with 72 (27.6%) OS events, for T-DXd vs NR (95% CI, 34.0 mo-NE), with 97 (36.9%) OS events, for T-DM1. Landmark 12-mo OS rate was 94.1% (95% CI, 90.4-96.4) for T-DXd vs 86.0% (95% CI, 81.1-89.8) for T-DM1; 24-mo OS rate was 77.4% (95% CI, 71.7-82.1) for T-DXd vs 69.9% (95% CI, 63.7-75.2) for T-DM1. The P value for OS crossed the prespecified boundary (P = 0.013) and was statistically significant. mPFS by BICR was 28.8 mo (95% CI, 22.4-37.9 mo) with T-DXd, compared with 6.8 mo (95% CI, 5.6-8.2 mo) with T-DM1; HR, 0.33; nominal P < 0.000001. Key efficacy and safety results are shown in the table. Grade ≥ 3 treatment-emergent adverse events were experienced by 56.4% of T-DXd-treated pts and 51.7% of T-DM1-treated pts. Drug-related interstitial lung disease/pneumonitis, as evaluated by an independent adjudication committee, was experienced by 39 pts (15.2%) in the T-DXd arm and 8 pts (3.1%) in the T-DM1 arm; no adjudicated drug-related grade 4 or 5 events were observed in pts who received T-DXd.

Conclusions

Updated results confirm the superiority of T-DXd compared with T-DM1 for pts with HER2+ mBC previously treated with an anti-HER2 therapy, with highly clinically meaningful and statistically significant benefit in OS and PFS and a manageable safety profile with longer treatment duration.

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Table. Summary of Efficacy Results for T-DXd and T-DM1

Table. Summary of efficacy and safety results for T-DXd and T-DM1

	T-DXd N = 261	T-DM1 N = 263
Efficacy		
OS HR (95% CI); <i>P</i> value	0.64 (0.47-0.87); 0.0037 ^a	
mOS, mo (95% CI)	NR (40.5-NE)	NR (34.0-NE)
OS rate, % (95% CI)		
12 mo	94.1 (90.4-96.4)	86.0 (81.1-89.8)
24 mo	77.4 (71.7-82.1)	69.9 (63.7-75.2)
36 mo	69.3 (62.5-75.1)	55.4 (47.4-62.8)
mPFS by BICR, mo (95% CI)	28.8 (22.4-37.9)	6.8 (5.6-8.2)
HR (95% CI); <i>P</i> value	0.33 (0.26-0.43); <0.000001 ^{a,b}	
mPFS by investigator, mo (95% CI)	29.1 (23.7-NE)	7.2 (6.8-8.3)
HR (95% CI); <i>P</i> value	0.30 (0.24-0.38); <0.000001 ^{a,b}	
Confirmed ORR by BICR, % (95% CI)	78.5 (73.1-83.4)	35.0 (29.2-41.1)
<i>P</i> value	<0.0001 ^{a,b}	
Complete response	55 (21.1)	25 (9.5)
Partial response	150 (57.5)	67 (25.5)
mDoR by BICR, mo (95% CI)	36.6 (22.4-NE)	23.8 (12.6-34.7)
Safety, n (%)	N = 257	N = 261
Grade ≥3 TEAEs	145 (56.4)	135 (51.7)
Serious TEAEs	65 (25.3)	58 (22.2)
TEAEs associated with:		
Drug interruption	136 (52.9)	76 (29.1)
Dose reduction	66 (25.7)	38 (14.6)
Drug discontinuation	55 (21.4)	24 (9.2)
Death	6 (2.3)	6 (2.3)

^aTwo-sided.

^bNominal *P* value.

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12/7/2022

9:30 AM - 9:45 AM

GS2-03

GS2-03 TRIO-US B-12 TALENT: Neoadjuvant trastuzumab deruxtecan with or without anastrozole for HER2-low, HR+ early stage breast cancer

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Background

Although patients (pts) with hormone receptor-positive (HR+)/HER2-negative breast cancer (BC) frequently experience disease response to neoadjuvant therapy, fewer than 10% achieve a pathologic complete response (pCR) with standard chemotherapy or endocrine therapy, even in combination with CDK4/6 inhibitors. Thus, finding more effective therapies for this disease remains an unmet need. HER2 is expressed at a low level (IHC 1+ or 2+) in approximately 60-70% of HR+ BC. Trastuzumab deruxtecan (DS-8201a, T-DXd) is a novel HER2-targeting antibody drug conjugate (ADC) that is FDA approved in the US for HER2-positive and HER2-low metastatic BC (with boxed warnings for interstitial lung disease). However, the efficacy of T-DXd in the neoadjuvant setting is not known. The primary objective of TALENT (TRIO-US B-12, NCT04553770) is to evaluate the clinical activity and safety of neoadjuvant T-DXd alone or in combination with endocrine therapy in pts with HR+/HER2-low early BC.

Methods

Men and women with previously untreated, operable invasive early stage, non-recurrent, HR+, HER2-low (IHC 1+ or 2+/ISH- by local or central review) BC measuring > 2 cm were eligible. In stage 1 of clinical trial, participants were randomized 1:1 to receive T-DXd (5.4 mg/kg IV q21 days) alone, Arm A, or in combination with anastrozole AI (1 mg PO QD), Arm B. Originally 6 cycles (cy) were given but in 02/2022, an amendment increased the number of treatment cy

from 6 to 8 for newly enrolled pts, or those who had not yet had surgery. Men and pre/perimenopausal women randomized to Arm B also received a GnRH agonist. Stratification factors were HER2 expression (1+ vs. 2+) and menopausal status (men as postmenopausal). Tumor tissue collected at baseline, cy 1 day 17-21, and at surgery. Breast imaging performed at baseline, cy 2 and pre-surgery/EOT. Primary endpoint is pCR rate (ypT0/is ypN0) at surgery. In stage 1, intent was to randomize 58 pts (if at least 2 pCR occurred in an arm, arm progresses to Stage 2 and an additional 15 pts to be enrolled). Other endpoints include safety, objective response rate (ORR), changes in Ki67 expression, Residual Cancer Burden index, exploratory biomarker analysis, and health-related quality of life. Here we present results from stage 1 of the trial.

Results:

From 09/21/2020 to 10/13/2022, 58 pts were enrolled and treated (29 Arm A, 29 Arm B) in stage 1 of trial. Five pts came off study before completing study therapy (2 after cy 1, 2 after cy 2, 1 after cy 3). As of data cut-off (10/05/2022), 33 pts completed study treatment and have had surgery (17 Arm A, 16 Arm B), 13 are on treatment and 7 are pending surgery; 27 pts completed 6 cy and 13 completed 8 cy. Baseline characteristics were balanced between arms. 19/58 pts were Stage IIA, 26/58 Stage IIB, 12/58 Stage IIIA, and 1/58 Stage IIIB at baseline. 46/58 pts had baseline HER2 expression (from central review) of 1+, 4/58 were 0, 6/58 were 2+, 1/58 had multicentric lesion 1+ and 2+, and 1/58 had a single lesion with 1+ and 2+. In Arm A, 1/17 pt had pCR after 8 cy, 2/17 pts had RCB-I after 6 cy (17.6% RCB 0/1). In Arm B, 1/16 pt had RCB-I after 8 cy (6.3%). The ORR for response-evaluable pts in Arm A was 75% (12/16, 1 CR, 11 PR) and in Arm B was 63.2% (12/19, 2 CR, 10 PR); 1 patient (Arm B) had PD. ILD occurred in 1 pt (1.7%), Gr 2 and resolved 11 days after stopping therapy. Most common treatment-related Grade \geq 3 AEs in Arms A and B, respectively, include hypokalemia (1.7%, 5.2%), diarrhea (3.4%, 3.4%), neutropenia (3.4%, 1.7%), fatigue (1.7%, 3.4%), headache (3.4%, 1.7%), vomiting (3.4%, 1.7%), dehydration (1.7%, 1.7%) and nausea (3.4%, 0%).

Conclusions:

This is the first report of a trial evaluating neoadjuvant T-DXd in HER2 low breast cancer. T-DXd +/- endocrine therapy demonstrates promising clinical activity for pts with HR+ BC. Updated study results will be provided at the time of presentation.

Disclosure(s):

Sara Hurvitz, MD, FACP: Ambrx: Contracted Research (Ongoing); Amgen: Contracted Research (Ongoing); Arvinas: Contracted Research (Ongoing); Astra Zeneca: Contracted Research (Ongoing); Bayer: Contracted Research (Ongoing); Cytomx: Contracted Research (Ongoing); Daiichi-Sankyo: Contracted Research (Ongoing); Dignitana: Contracted Research (Ongoing); Eli Lilly: Contracted Research (Ongoing); Genentech/Roche: Contracted Research (Ongoing); Gilead: Contracted Research (Ongoing); GSK: Contracted Research (Ongoing); Ideal Implant: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Immunomedics: Contracted Research (Ongoing); MacroGenics: Contracted Research (Ongoing); Novartis: Contracted Research (Ongoing); OBI Pharma: Contracted Research (Ongoing); Orinove: Contracted Research (Ongoing); Pfizer: Contracted Research (Ongoing); Phoenix Molecular Designs, Ltd.: Contracted Research (Ongoing); Pieris: Contracted Research (Ongoing); PUMA: Contracted Research (Ongoing); Radius: Contracted Research (Ongoing); Sanofi: Contracted Research (Ongoing); Seattle Genetics/Seagen: Contracted Research (Ongoing); Zymeworks: Contracted Research (Ongoing)

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12/7/2022

9:45 AM - 11:00 AM

Debate: Is HER2 low a separate entity?

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9:45 AM - 11:00 AM

Discussion 1: Defining HER2 low: a pathologist's perspective

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9:45 AM - 11:00 AM

Special Session 3: HER2 Low: A Separate Entity?

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9:45 AM - 11:00 AM

HER2-01

HER2-01 Clinical and Molecular Characteristics of HER2-low/zero Early Stage Triple-Negative Breast Cancer

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Background: In the metastatic setting, low HER2 expression is associated with clinical benefit from trastuzumab deruxtecan, a HER2-targeting antibody drug conjugates. However, little is known about the biological significance of low HER2 expression in patients with early stage triple-negative breast cancer (TNBC) receiving neoadjuvant therapy (NAT). Methods: Out of 595 patients with stage I-III TNBC enrolled on the prospective ARTEMIS trial (NCT02276443) from 2015-2021, we identified 367 patients with available HER2 immunohistochemistry (IHC) results on pre-NAT tumor tissue (HER2-zero: n=218; HER2-low [IHC 1+, 2+]: n=149). All patients were treated with anthracycline-based NAT. In cases where sufficient pre-NAT tumor tissue were available, additional IHC and/or RNAseq were performed. Differential gene expression (DGE) and pathway analysis were performed using DEseq2. Gene set enrichment analysis (GSEA) was performed using the Hallmark gene sets. Deconvolution analyses were performed using CIBERSORT. We controlled for multiple hypothesis using a false discovery rate (FDR) threshold with the Benjamini-Hochberg method, accepting as significant genes with at least a 2-fold change and < 5% FDR. Results: Table 1 summarizes baseline clinicopathological features of the 367 patients. Compared to HER2-zero tumors, HER2-low

tumors were less likely of metaplastic histology ($p=0.001$), associated with lower Ki67 ($p=0.017$) and were more likely to be androgen receptor (AR)-positive ($p=0.01$). There were no significant differences in tumor-infiltrating lymphocytes (TILs) infiltration and PD-L1 expression between HER2-zero and HER2-low tumors. Among the 226 patients with sufficient pre-NAT tissue for RNAseq, DGE analyses demonstrated upregulation of genes involved in fatty acid metabolism (ACSM1) and steroid hormone metabolism (DHRS2, UGT2B28) in HER2-low tumors compared with HER2-zero tumors. Deconvolution analyses revealed no significant differences between predicted proportions of immune cell subpopulations between HER2-low and HER2-zero tumors. Although rates of pCR were not significantly different between patients with HER2-zero (46%) and HER2-low tumors (40%) ($p=0.34$), non-pCR in patients with HER2-low tumors was associated with increased expression of EREG, which encodes an EGFR ligand, while non-pCR in patients with HER2-zero tumors was associated with downregulation in genes involved in immune response pathways. GSEA further identified the Hallmark allograft rejection (FDR $q=0.001$), interferon gamma response (FDR $q=0.002$), and interferon alpha response pathways (FDR $q=0.007$) as the 3 most significantly downregulated pathways in HER2-zero tumors from patients experiencing a non-pCR relative to HER2-zero tumors from patients experiencing a pCR. Conclusion: In early stage TNBC, low HER2 expression is associated with increased AR expression and upregulation of genes associated with fatty acid and steroid hormone metabolism. Gene expression analyses suggest that drivers of resistance to NAT differ between HER2-low and HER2-zero tumors. Biological differences between HER2-zero and HER2-low tumors exist and may influence future personalized treatment for patients with early stage TNBC.

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9:45 AM - 11:00 AM

HER2-02

HER2-02 HER2-Low Status is Associated with Worse Clinical Outcomes in Hormone Receptor-Positive, HER2-Negative Advanced Breast Cancer Patients Treated With First-Line Cyclin-Dependent Kinase 4/6 Inhibitors Plus Endocrine Therapy

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Introduction: Cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) in combination with endocrine therapy (ET) are the standard first-line treatment for patients with hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer (HR+/HER2- aBC). HER2-low BC, which is defined by an IHC score for HER2 of 1+ or 2+ with negative ISH assay, accounts for more than half of all HR+/HER2- aBC cases, and it is associated with remarkable clinical benefit from the novel anti-HER2 antibody drug conjugate (ADC) trastuzumab-deruxtecan. Evidence on the prognostic impact of HER2-low status is controversial in both limited-stage and advanced BC. Here, we sought to investigate the possible prognostic relevance of HER2-low status in a population of aBC patients treated with CDK4/6i plus ET. Methods: We conducted a retrospective-prospective study in six Italian Cancer Centers to investigate the impact of HER2 status (low vs. 0) on the progression-free survival (PFS) and overall survival (OS) of consecutive HR+/HER2- aBC patients treated with

CDK4/6i plus ET (aromatase inhibitors or fulvestrant) as a first-line therapy. In the main study analysis, we considered HER2 status in the last tumor assessment (i.e., primary tumor, or, when available, a metastatic lesion). We also performed a subgroup analysis including only patients with HER2 status evaluation in a metastatic lesion collected before CDK4/6i plus ET therapy initiation. The association between HER2 status (low vs. 0) and PFS or OS was evaluated using log-rank test and Cox regression modeling. Results: We evaluated 767 consecutive HR+/HER2- aBC patients treated with CDK4/6i plus ET between January 2017 and January 2022. Of these, 436 patients (56.8%) received CDK4/6i plus ET as a first-line therapy, and they were included in this analysis. Median age was 63 years (range 27-87), and 362 patients (83.0%) were postmenopausal. The majority of patients were treated with palbociclib (68.3%), while 91 (20.9%) and 47 (10.8%) patients received ribociclib and abemaciclib, respectively. Regarding HER2 status, 269 (62.9%) patients had HER2-low tumors, while 159 (37.1%) patients had HER2-0 neoplasms. HER2-low status was associated with significantly lower PFS when compared to HER2-0 status [median PFS (mPFS) 23.6 vs. 32.3 months, respectively; $p=0.014$]. HER2-low status was also associated with significantly worse OS (mOS 48.7 vs 58.3 months, respectively; $p=0.025$). These results were confirmed in multivariable models adjusting the impact of HER2 status for clinically-relevant covariates, namely estrogen receptor status, Ki-67, age, number of metastatic sites, presence of liver metastases, disease free interval, ECOG Performance Status. In this analysis, HER2-low status, compared with HER2-0 status, was independently associated with worse PFS [adjusted Hazard Ratio (aHR): 1.62; 95% confidence interval (CI): 1.17-2.24; $p < 0.01$] and OS (aHR: 1.74; 95% CI: 1.09-2.76; $p=0.019$). Subgroup analysis conducted in the subset of 256 patients with available metastatic tumor samples collected before CDK4/6i plus ET initiation confirmed that HER2-low status ($n=157$), when compared to HER2-0 status ($n=99$), was independently associated with worse PFS (mPFS 24.5 vs 35.2 months, $p=0.01$; aHR 2.07; 95% CI: 1.28-3.34, $p < 0.01$) and worse OS (mPFS 48.7 vs 72.3 months, $p=0.027$; aHR 3.12; 95% CI 1.44-6.77, $p < 0.01$). Conclusions: This multicenter Italian study revealed that HER2-low status has independent, negative prognostic value in patients with HR+/HER2- aBC treated with CDK4/6i plus ET in the first-line setting. Our results suggest that HER2-low status might be associated with different clinical benefit from standard anticancer therapies in specific clinical settings. The definition of treatment algorithms also taking into account HER2 status is a clinical priority in patients with HR+/HER2- aBC.

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12/7/2022

9:45 AM - 11:00 AM

HER2-04

HER2-04 Prevalence of HER2-low among Metastatic Breast Cancer Patients and Their Outcomes Compared to HER2 IHC 0

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Prevalence of HER2-low among Metastatic Breast Cancer Patients and Their Outcomes Compared to HER2 IHC 0 Background: Amplification and/or overexpression of the HER2 gene is detected in approximately 15% to 20% of breast cancer (BC) patients. HER2-targeted therapies improve survival in HER2+ BC. Current HER2 diagnostic tests and thresholds were designed and optimized to predict benefit from HER2-directed therapies. The DESTINY-Breast04 trial demonstrated notable efficacy of HER2 antibody-drug conjugate trastuzumab deruxtecan, in patients whose tumors are not conventionally HER2+, but defined as HER2-low (IHC 1 or 2+ without HER2 amplification). A better understanding of the HER2-low phenotype is therefore of critical importance. Methods: Eligible pts were adults with metastatic HER2 IHC (0,1+,2+/FISH negative) BC seen at MD Anderson between 2006 and 2019. Primary biopsy of the breast was used to test biomarkers. HER2 low was defined as IHC 1+ or 2+ and FISH-negative. HER2-negative was defined as HER2 IHC 0. Multi-covariate logistic regression models were used to evaluate effect of clinical factors on HER2 low status and pCR. Overall survival (OS) was defined as time from diagnosis date until death. Disease free survival (DFS) was defined as time from definitive surgery date until the first local/distant recurrence or death from any cause. Patients alive without events (death for OS, recurrence/death for DFS) were censored at last follow-up date. OS and DFS times were estimated by Kaplan-Meier method. Multivariate Cox proportional hazards regression models were applied to assess effect of covariates of interest on OS and DFS. Results: A total of 3053 early stage and 1203 de novo female BC patients were included in the analysis. The prevalence of HER2 low for early stage patients was 59.3% (1811/3053) and for de novo metastatic disease 59.3% (713/1203). In early stage patients, white race, higher nuclear grade and positive ER status were significantly associated with HER2 low status in multivariate logistic regression. Univariately, pCR rate was significantly associated with negative ER (10.2% in negative vs 2.7% in positive), negative PR (8.6% vs 2%) and negative lymphatic vascular invasion (9.2% vs 2%). Multivariate logistic regression showed ER (p=0.0124), PR (p=0.0439) status and lymphatic vascular invasion (p< 0.0001) were significantly associated with pCR status. With median follow-up of

8.5 years, median OS time was 5.3 years (95% CI: [4.9, 5.4]), 5.4 years and 4.8 years in HER2 low and HER2 0 groups, respectively. In multivariate Cox regression, HER2 low was significantly associated with longer OS (HR=0.87, p=0.008), adjusted for age, race, stage, nuclear grade, lymphatic-vascular invasion and ER/PR status. In patients who received neoadjuvant chemotherapy, adjusted for stage, nuclear grade, ER and PR status and pCR, HER2 low was significantly associated with a longer OS time (HR=0.87, p=0.04). Median DFS time was 1.9 years (95% CI: (1.8, 2.0)). Age, stage, histology, nuclear grade, and ER and PR status were significantly associated with DFS by multivariate Cox regression. Among de novo cases, higher nuclear grade (HR [II vs I]=1.838, p =0.008; HR [III vs I]=1.856, p=0.007) and positive ER status (OR=1.933, p <.0001) were associated with high percentage of HER2 low by multivariate logistic regression. Median OS time was 3.2 years (95% CI: (3.0, 3.5)). By multivariate Cox regression, race, histology, nuclear grade, ER and PR status, and HER2 low status (HR=0.834, p=0.0260) were significantly associated with OS time. Conclusions: In metastatic BC pts, HER2 low status was significantly associated with a longer OS and DFS when compared to HER2 0. Nuclear grade and ER positivity was significantly associated with HER2 low status. Biomarkers on recurrence tumor will be presented. This real world data helps to establish the prevalence of HER2 low and their outcomes for this selective cohort.

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12/7/2022

9:45 AM - 11:00 AM

HER2-05

HER2-05 Comprehensive genomic characterization of HER2-low breast cancer

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Background: About half of all breast cancers exhibit low HER2 expression. Despite lack of ERBB2 amplification, HER2-low tumors respond to trastuzumab deruxtecan (T-DXd), leading to the NCCN recommendation of T-DXd both for patients with HER2+ and HER2-low metastatic breast cancer (MBC). It remains however unclear if HER2-low represents a distinct molecular entity, as compared to HER2-0 MBC. Here, we compare the genomic landscape of HER2-low versus HER2-0 breast cancers in a large, single institution cohort. Methods: We identified consecutive patients with MBC seen at Dana-Farber Cancer Institute between 07/2013 and 12/2020. Patients were included if they had HER2-negative MBC per ASCO/CAP Guidelines and had undergone next generation sequencing (NGS) testing with a targeted, tumor-only platform (OncoPanel). Based on the HER2 status of the specimen tested by NGS, patients were divided into 2 groups: (i) HER2-low if immunohistochemistry (IHC) 1+ or 2+ non-amplified, or (ii) HER2-0 if IHC 0. Mutations of interest detected on NGS were classified as oncogenic using the OncoKB tool and additional annotation. Genomic profiles of HER2-low and HER2-0 tumors were compared using Chi-Square and Kruskal-Wallis tests. To determine genomic event enrichment between the two HER2 groups, logistic regression models were used, accounting for background rate and estrogen receptor (ER) expression. ERBB2 copy counts were calculated for tumors with recorded histology-estimated purities and copy-number segmentation using a simple model of allelic gain/loss. Results: Among 1847 patients with HER2-negative MBC, 1043 underwent NGS testing on a HER2-low (n=489, 47%) or HER2-0 sample (n=554, 53%). Most samples were metastatic (71%, n=743) while 29% (n=300) were from primary tumors. 73% had ductal histology, 13% were lobular and 14% had mixed or other histology. ER expression was enriched among HER2-low vs. HER2-0 tumors (76% vs. 60%; $p < 0.001$). Focusing on the most commonly occurring genetic mutations, no major differences were observed in HER2-low vs. HER2-0 tumors, after correcting for ER status (Table 1). Among all mutational events, any mutation in MPL, CYLD, and MAP3K and oncogenic mutations in TP53 and NF1 were more common in HER2-0, while any mutation in MTOR, RAD21, DNMT3A, and PDGFRA were enriched in HER2-low patients, when controlling for ER status and background mutational rate ($p < 0.05$). However, no mutation reached significance after accounting for multiple hypothesis testing. Similarly, no deep deletion or high amplification CNV events reached significance for either group. Analysis of tumor mutational burden in HER2-low vs. HER2-0 tumors revealed no significant differences (median: 7.26 muts/Mb vs. 7.60 muts/Mb, $p=1.00$), including when accounting for ER status. Finally, among tumors with sufficient tumor purity for ERBB2 copy count analysis (n=374 and 419 for HER2-low and HER2-0, respectively), HER2-low tumors had a significantly higher number of ERBB2 alleles as compared to HER2-0 (< 2 copies, 15.0% vs. 30.9%, 2 copies 67.4% vs. 60.5%, and >2 copies, 17.6% vs. 8.6%; $p < 0.001$ by Kruskal-Wallis). Conclusions: To our knowledge, this is the largest comprehensive genomic analysis of HER2-low MBC to date. In our cohort of patients with HER2-negative MBC, the genomic landscape of HER2-low and HER2-0 tumors did not differ significantly, apart from a higher number of ERBB2 alleles. These data further support the notion that HER2-low, as currently defined, is not a distinct molecular subtype of breast cancer.

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9:45 AM - 11:00 AM

HER2-06

HER2-06 Outcome analysis of HER2-zero or HER2-low hormone receptor-positive (HR+) breast cancer patients - characterization of the molecular phenotype in combination with molecular subtyping

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Background: Breast cancer with low HER2 expression (HER2-low) is of high clinical relevance because of new therapeutic options with antibody-drug conjugates. We have recently shown in a large cohort from neoadjuvant clinical trials that HER2-low breast cancer has different molecular characteristics as well as different clinical outcomes compared to HER2-zero. Considering the positive correlation between HER2-low expression and hormone receptor positivity observed consistently in many investigations, we have extended our analysis to HR+ tumors from the post-neoadjuvant PenelopeB trial. In PenelopeB, patients with HR+ breast cancer and residual disease after neoadjuvant chemotherapy (NACT) were randomized to post-neoadjuvant palbociclib versus placebo in addition to endocrine therapy. We evaluated the molecular phenotype and clinical outcomes of HER2-low compared to HER2-zero patients. Methods: A total of 1250 patients were randomized, HER2 status was available for 1151 tumors from pretherapeutic core biopsy, determined mainly by local pathology, and from 1213 tumors from the post-NACT sample, determined as part of central pathology. For 1119 patients a paired HER2-status was both available. HER2-zero was defined as IHC0 and HER2-low-positive was defined as IHC1+ or IHC2+/ISH-. Gene expression analysis of 2549 genes using the HTG oncology biomarker panel was performed in 620 pretherapeutic biopsies and 780 post-NACT residual tumor samples, with 539 paired gene expression samples. Breast cancer subtypes were determined using the AIMS approach. Results: In pretherapeutic biopsies, 695 tumors (60%) were HER2-low and 457 (40%) were HER2-zero. A HER2-low status in the biopsy was significantly linked to improved iDFS (HR 0.76 (0.60-0.96; p=0.02). In residual tumors, 632 tumors (60%) were HER2-low and 581 (40%) were HER2-zero, without any prognostic impact of HER2 low status. In addition, a shift of HER2-low-status comparing core biopsy and residual tumor was observed in 415 (37%) of 1119 tumors. 161 (14%) had a shift from HER2-zero to HER2-low and 254 (23%) shifted from HER2-low to HER2-zero. A shift from HER2-zero to HER2-low in the post-NACT samples was significantly linked to reduced iDFS

(HR 1.43 [95%CI 1.01-2.01]), $p=0.04$), compared to HER2-low group, while a shift from HER2-low to HER2-zero was associated with better iDFS compared to HER2-zero group, although not statistically significant ($p=0.17$). We did not observe a significant correlation of HER2-low status and AIMS molecular subtypes. In particular, the HER2-enriched (HER2E) subtype was assigned to only 4.3% of HER2-zero and 3.1% of HER2-low tumors. Significant iDFS differences were observed for HER2-low-status in combination with AIMS subtypes (lumB/basal/HER2E vs. lumA/normL; overall p -value < 0.0001) for both pretherapeutic biopsies and residual tumor. Patients with post-NACT HER2-low tumors had an improved survival in the subgroups of aggressive AIMS subtypes (lumB/basal/HER2E), but not in the less aggressive AIMS subtypes (lumA/normL), with a positive test for interaction ($p=0.02$). For the pre-NACT samples a similar, but non-significant trend was observed. We evaluated a total of 620 core biopsies for differences in gene expression comparing HER2-low and HER2-zero tumors. A total of 417 genes were statistically significantly different, but in a hierarchical clustering there was no clear separation of HER2-low and HER2-zero tumors. Conclusions: In the PenelopeB cohort of HR+ tumors, a HER2-low status in pretherapeutic core biopsies is related to improved disease-free survival, especially for those tumors that have a more aggressive intrinsic subtype. A shift of HER2-low status was observed before and after chemotherapy, indicating an adaptation of the pathway activity to therapy-induced stress, which might become relevant for future diagnostic and therapeutic approaches.

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12/7/2022

9:45 AM - 11:00 AM

HER2-07

HER2-07 Genomic Characterization of Primary and Metastatic HER2-low Breast Cancers

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Background: Varying levels of HER2 expression without ERBB2 gene amplification can be detected by immunohistochemistry (IHC) in approximately 60% of all invasive breast cancers (BCs). HER2-low-expressing BCs have recently been shown to respond to novel anti-HER2 antibody drug conjugates. Several studies have demonstrated that HER2-low BCs do not seem

to constitute a distinct clinical and transcriptomic subtype as compared to HER2-0 BCs. Here we sought to define the clinicopathologic features and repertoire of somatic genetic alterations in HER2-low BCs. Methods: We retrieved clinical, pathological, and genomic data of BCs that were subjected to targeted sequencing using the FDA-cleared MSK-IMPACT assay from April 2014 to December 2021. After removing cases where any available biopsy had HER2 3+ and/or positive ERBB2 fluorescence in situ hybridization (FISH), 3608 samples (primary=1347; post-treatment/metastatic=2261) were included. Tumors were classified as HER2-low if they had an HER2 IHC score of 1+ or 2+ with a non-amplified FISH assay and HER2-0 if they had an HER2 IHC score of 0. Somatic mutations and DNA copy number alterations from MSK-IMPACT were analyzed. Multiple testing correction using the Benjamini-Hochberg method was applied to control for the false discovery rate (q). Q values < 0.1 were considered significant. Results: Among 3608 HER2- BCs, 1460 (40%) and 2148 (60%) were HER2-0 and HER2-low, respectively. Hormone receptor (HR) expression was significantly higher in HER2-low than HER2-0 tumors in both primary (781 [68.3%] vs 362 [31.7%]; $p < 0.001$) and metastatic (1031 [60.5%] vs 673 [39.5%]; $p < 0.001$) samples. A higher proportion of HER2-low tumors was found in metastatic than primary samples (59% vs 41%; $p < 0.001$) in this cohort. No difference in histology subtype, tumor grade, disease stage (among primary tumors), mutational signatures, and tumor mutational burden was found overall and when cases were stratified by HR expression. In HR-positive BCs, HER2-0 BCs harbored higher frequency of TP53 (33% vs 25%; odds ratio [OR] 1.49, 95% confidence interval [CI] 1.25-1.78, $q < 0.001$) and CDKN1A (1% vs 0%; OR 17.47, 95% CI 2.48-756.37, $q = 0.02$) alterations than HER2-low BCs. Similar findings were observed in metastatic but not in primary HR-positive BCs. No differences were detected in HR-negative BCs stratified into HER2-low and HER2-0. Given the potential misclassification that exists between IHC HER2-0 and HER2-1+, we then conducted an exploratory analysis splitting the HER2-low group into HER2 1+ and 2+. TP53 alterations remained significantly enriched in HER2-0 compared to HER2-1+ HR-positive tumors (33% vs 24%; OR 1.55, 95% CI 1.28-1.87, $q < 0.001$). In HR-positive BCs, HER2-2+ displayed a higher frequency of genetic alterations in genes encoding for transcription factors, such as MYC (14.2% vs 7.3%; OR 2.09, 95% CI 1.44-3.04, $q = 0.02$) and YAP1 (2% vs 0.3%; OR 6.86, 95% CI 1.7-39.57, $q = 0.1$), and DNA damage response, such as FAM175A (1.6% vs 0%; OR 18.23, 95% CI 2.43-807.73, $q = 0.03$) and BRCA2 (4% vs 1%; OR 3.09, 95% CI 1.49-6.55, $q = 0.1$), than HER2-0 tumors. In HR-negative HER2-2+ tumors, a higher frequency of PIK3CA mutations was observed in comparison to HER2-0 (36.9% vs 19.5%; OR 2.41, 1.4-4.1, $q = 0.1$), overall and in the metastatic setting. Conclusions: HER2-low BCs seem not to represent a distinct pathologic subtype. At the genomic level, however, some differences were identified and these became more conspicuous upon subclassification of HER2 IHC expression into 1+ and 2+. Further investigation into methods that more accurately detect and quantify low levels of HER2 expression in BC samples as well as better characterize the biology behind the HER2-low/ultralow expression is warranted.

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12/7/2022

9:45 AM - 11:00 AM

HER2-08

HER2-08 Molecular characterization of HER-2 low patients identifies basal-enriched subset with poor clinical outcomes in real-world data

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Background: Recent groundbreaking work has shown that patients with lower levels of HER2-expression (HER2-low) may benefit from treatment with trastuzumab deruxtecan—an HER2 antibody-drug conjugate FDA-approved for treatment for HER2-positive (HER2+) patients and thus can represent a new molecular subtype. In fact, this HER2-low patient population is enriched with luminal disease but is clinically heterogeneous and outcomes have therefore not been extensively characterized due to the lack of annotated multimodal real-world data (RWD). We used Tempus RWD to identify unique HER2-low subtypes using RNA sequencing and compare outcomes across subtypes. Methods: We retrospectively analyzed 1,545 breast cancer samples from the Tempus database tested with the Tempus xT assay that includes whole-exome capture RNA-seq. Only tumors with known HER2 status determined via immunohistochemistry [IHC] and/or FISH were included. A HER2 RNA gene signature was developed by comparing HER2- (n=464, IHC 0+) and HER2+ (n=161, IHC 3+ or IHC 2+ and FISH+) patients—controlling for HR status—to identify genes associated with HER2 over-expression. This HER2 signature was used to stratify independent HER2-low samples (n=920, determined by IHC 1+ or IHC2+ and FISH-) via hierarchical clustering. Treatment use in this cohort was not assessed. Clusters were subsequently assessed according to clinical, demographic, and molecular factors including PAM50 molecular subtype classification of the RNA signatures. Real-world progression-free survival (rwPFS) was evaluated based on

progression and death captured through manual expert abstraction for a subset of stage 4 patients (n=336) and estimated via Kaplan-Meier analysis. Results: HER2-low patients were clustered according to our HER2 expression signature identifying three distinct molecular clusters (Table 1). Stage and demographic distributions (race, ethnicity, age) were similar across clusters. Of note, cluster 3 (n=186, 20% of the HER2-low population) was significantly enriched in hormone receptor negative (HR-) patients ($p < 1e-5$) and had lower ERBB2 RNA expression ($p < 1e-5$). Interestingly, molecular characterization using PAM50 demonstrated that cluster 3 was predominantly a basal-like subtype, whereas luminal-like samples dominated cluster 1 and 2, and cluster 2 had the largest composition of HER2-like samples (Table 1). Strikingly, cluster 3 stage 4 patients (n=57) had a median rwPFS that was significantly shorter (>12 months) than cluster 1 and 2 stage 4 patients (n=279, HR>1.66, $p < 2e-2$, Table 1). Conclusions: Tempus multimodal RWD reveals that HER2-low breast cancers are comprised of distinct molecular subtypes. In a preliminary analysis, a cluster of HER2-low, predominantly basal-like patients demonstrated dramatically worse outcomes than other clusters. These data further emphasize the importance of using RNA expression to fully characterize clinically relevant subpopulations. Further prospective studies are urgently needed to assess treatment response in this heterogenous emerging HER2-low distinct population.

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12/7/2022

9:45 AM - 11:00 AM

HER2-09

HER2-09 Multiomics Profiling Characterizes Distinct HER2-low Breast Cancer Subgroups in the East Asian Population

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Background: The emergence of anti-HER2 antibody–drug conjugates (ADCs) gave rise to the concept of HER2-low breast cancer (BC). HER2-low BC, which refers to a subgroup of HER2-negative BC with relatively higher HER2 expression (defined as 1+ or 2+ by immunohistochemistry (IHC) staining, without ERBB2 amplification), represents a rather large part of all BCs. However, the molecular nature and internal heterogeneity of HER2-low breast cancer remain obscure, and little is known about the ethnic differences of HER2-low BC. These limitations prevent us from a more precise patient selection and better drug combination strategies in the era of ADCs. To provide a comprehensive and intensive landscape of HER2-low BCs, we characterized HER2-low BCs both clinically and molecularly, which may help clinicians to achieve a more precise clinical management of these patients. Patients and methods: We established a HER2-low BC cohort (N=441) in early-stage Chinese patients and included HER2-0 (N=114) and HER2-positive (N=181) tumors as auxiliary cohorts to characterize HER2-low breast cancers both clinically and molecularly. Whole-exome sequencing, copy number variation assays, RNA sequencing and isobaric quantitative proteomics were conducted to obtain multiomics data. We compared the clinicopathological and molecular features between HER2-low tumors and other HER2 status subgroups stratified

and not stratified hormone receptor (HR) status to clarify the distinctness of HER2-low BCs. And we analyzed the internal heterogeneity and ethnic difference of HER2-low BCs by characterizing a distinct subgroup of patients with unique driving mechanisms. Results: HER2-low BCs showed different molecular manifestations from HER2-0 BCs in different HR subgroups. In the HR-negative subgroup, HER2-low BCs consisted of more non-basal-like subtypes than HER2-0 tumors (40.0% vs. 9.1%, $P = 0.002$), which was an East Asian-specific phenomenon absent in Western cohorts. Also, HR-negative HER2-low BCs showed significant internal molecular heterogeneity, of which basal-like tumors closely mimicked HER2-0 BCs, whereas non-basal-like tumors were similar to HER2-positive BCs. These non-basal-like tumors were mostly categorized as HER2-enriched and luminal androgen receptor (LAR) subtypes. These molecularly distinct tumors might be driven by frequent mutation in PIK3CA and overexpression of FGFR4 and PTK6, which may also serve as therapeutic targets. These results have also been proved in a triple negative breast cancer cohort we reported previously. In contrast, in the HR-positive subgroup, HER2-low BCs showed no large-scale molecular difference from HER2-0 BCs or internal heterogeneity. However, HER2-low patients showed significantly better distant metastasis-free survival than HER2-0 patients ($P = 0.029$), which might be attributed to the lower loss/deletion levels of 17q11.12 and 17q21.31 in HER2-low breast cancers, in which genes including NF1 and BRCA1 are located. Conclusions: We reported the largest single-center multiomics HER2-low BC cohort in East Asian hitherto, and revealed its molecular nature, internal heterogeneity and ethnic difference. Compared with HR-positive diseases, HER2-low BCs in the HR-negative subgroup were more likely to be a molecularly distinct entity from HER2-0 tumors. Furthermore, HR-negative HER2-low BC also accommodates higher internal heterogeneity, which was ethnicity-specific in our East Asian cohort and may infer a different treatment response. Our work emphasized the need of a more precise stratification within HER2-low BCs and across ethnic groups, which has also been inferred by the results in the subgroup analysis of DESTINY-Breast04 trial.

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Zhi-Ming Shao, M.D. Ph.D.: No financial relationships to disclose

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9:45 AM - 11:00 AM

HER2-10

HER2-10 Dynamics of HER2-low expression in triple-negative breast cancer

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Background: With the development of novel antibody drug conjugates (ADC), it is increasingly important to understand the changes that occur in cell-surface targets over time from early-stage to metastatic breast cancer. Discordance in HER2 expression per immunohistochemistry (IHC) has been reported between primary and metastatic tumors in patients (pts) with HER2-negative breast cancer defined per ASCO/CAP guidelines, with both gain and loss of expression described. Representation of HR-negative (TNBC) tumors has been limited in these studies, and HER2 status at multiple time points in TNBC has not been described. Here we report changes in HER2 IHC in patients diagnosed with TNBC, using a collection of matched tumor samples over time. Methods: Pts were identified from two sources: 1) an institutional database including all consecutive pts who underwent surgery for stage I-III breast cancer at Dana-Farber/Brigham Cancer Center between 2015-2018, and 2) a prospective research biopsy protocol for pts with known or suspected metastatic breast cancer. Pts were included in the present analysis if they received neoadjuvant chemotherapy (NAC) for stage I-III TNBC (eTNBC), or if they were diagnosed with any stage TNBC and ultimately developed metastatic TNBC (mTNBC). Clinical pathology records were reviewed for HER2 IHC results of samples collected at: initial diagnosis (DX); residual disease (RD) post-NAC, if applicable; and at recurrence (M). HER2 IHC was classified as HER2-0 if HER2 IHC 0, and HER2-low if 1+ or 2+ (and ISH non-amplified). For matched comparisons, if IHC was performed in more than one DX sample (e.g., breast, node), only the breast was considered; if more than one M sample, only the first M biopsy with available IHC was considered. Results: Among 110 pts in this cohort, 101 were initially diagnosed with eTNBC (79 received NAC; 22 underwent surgery as first intervention) and 9 with de novo mTNBC. Median age was 48.7 years (range 19.8-71.6). Among all pts, a total of 292 samples (136 DX, 53 RD, 103 M) had available HER2 IHC scores. When restricting to one sample per time point, HER2-low prevalence was 49/102 (48.0%) in DX breast tumors, 21/53 (39.6%) in RD, and 13/58 (22.4%) in first M samples (with all remaining samples HER2-0, except one HER2 3+ sample). In eTNBC pts, HER2 IHC scores were available for 50 paired DX and RD, and 48 paired DX and M samples. Among 50 pts with paired DX and RD, HER2 IHC was discordant in 56% (28/50) (Table 1). Of the 21 HER2-0 DX tumors, 23.8% (5/21) became HER2-low at RD. Of the 29 HER2-low DX tumors, 51.7% (15/29) became HER2-0 at RD. Among 48 eTNBC pts who recurred and had paired DX and M samples, HER2 IHC was discordant in 50% (24/48) (Table 1). Change from HER2-0 to low was 12.5% (3/24), and from HER2-low to HER2-0 was 66.7% (16/24). Among 9 de novo mTNBC pts, 5 had HER2 IHC available in paired DX breast and M prior to starting therapy; 3 were concordant (IHC 0, n=2; IHC 1+, n=1), one had IHC 0 in DX breast and IHC 2+ in M (liver), one had IHC 1+ in DX breast and IHC 0 in M (node). Conclusions: HER2 IHC classification was discordant in about half of the TNBC cases we examined, with more frequent rates of conversion from HER2-low to HER2-0 in both paired DX/RD post-NAC, and paired DX/M samples. Additional analyses will be presented exploring HER2 IHC changes among multiple metastases per patient. Genomic and molecular analysis, including whole exome sequencing,

RNA sequencing, and methylation profiling, are underway in these samples to further elucidate HER2 evolutionary dynamics.

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12/7/2022

9:45 AM - 11:00 AM

HER2-11

HER2-11 Epidemiology and Prognosis of HER2-Low Breast Cancer (BC) in the National Cancer Data Base (NCDB)

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Title: Epidemiology and Prognosis of HER2-Low Breast Cancer (BC) in the National Cancer Data Base (NCDB) Background: Characterization of HER2 status has focused on HER2 overexpressing BC, which are uniquely sensitive to HER2-directed therapy. However,

approximately 60% of BC traditionally characterized as HER2-negative express low levels of HER2 on immunohistochemistry (IHC). Although these 'HER2-low' cancers are insensitive to traditional HER2 blockade, a recent randomized clinical trial showed that antibody drug conjugates such as trastuzumab deruxtecan (T-DXd) are effective in this population. Given the heterogeneity of low level HER2 expression and the impact of T-DXd on outcomes in this population, further data on the epidemiology and prognosis of HER2-low BC is needed.

Methods: We conducted a retrospective cohort study of patients (pts) in the NCDB diagnosed from 2010 to 2019 with invasive BC classified as HER2-negative, and with HER2 IHC results available. We compared demographics and other clinical characteristics of HER2 0 vs HER2-low (defined as IHC score of 1+ or 2+) cases in this cohort. A logistic regression was used to quantify the independent association of demographic and clinical factors with HER2-low status, and odds ratios (OR) and 95% confidence intervals (CI) were reported. Overall survival (OS) was compared for HER2 0 vs HER2-low by receptor subtype and stage, and a multivariable Cox model was fit to also control for age, race / ethnicity, comorbidity score, treatment facility type, grade, and histologic type. In pts who received neoadjuvant chemotherapy (NAC), a logistic regression was used to determine if pathological complete response (pCR) rate was different between HER2-low and HER2 0 pts. Results: We identified 1,191,389 pts, including 394,937 HER2 0 and 796,452 HER2-low; median follow-up was 54 months with 84.1% of pts surviving. Hispanic and Black pts and pts with higher grade, non-ductal, triple-negative breast cancer (TNBC) and affect minority Hispanic and Black women (table 1). On multivariable analysis, TNBC (odds ratio [OR] 0.48, 95% confidence interval [CI] 0.47 – 0.49), lobular (OR 0.74, 95% CI 0.73 – 0.75) and other non-ductal histology (OR 0.66, 95% CI 0.64 – 0.67) had lower likelihood of HER2-low status. Hispanic ethnicity remained associated with lower likelihood of HER2-low (OR 0.89, 95% CI 0.87 – 0.91), whereas Black race was associated with a slight increased likelihood of HER2-low status (OR 1.06, 95% CI 1.04 – 1.08). In multivariable survival analysis of TNBC patients, HER2-low BC was associated with improved OS for stage 2 (hazard ratio [HR] 0.93, 95% CI 0.90 – 0.96), stage 3 (HR 0.92, 95% CI 0.88 – 0.96) and stage 4 (HR 0.92, 95% CI 0.87 – 0.97) cancer. By contrast, survival analysis of hormone receptor positive cancer showed that HER2-low BC was associated with improved OS only for stage 4 disease (HR 0.96, 95% CI 0.92 – 0.99). In 62,667 pts receiving NAC, HER2-low status was associated with a lower likelihood of pCR (OR 0.88, 95% CI 0.84 – 0.92). Conclusions: HER2-low BC is most frequently HR+ with a ductal histology, and is associated with a lower likelihood of response to chemotherapy but an improved OS, especially for metastatic cases. This lower pCR in the HER2-low population could be explained by a higher proportion of these tumors being HR+. There are racial / ethnic differences in the incidence of HER2-low BC, largely mediated by differences in rates of TNBC, and fewer Black and Hispanic pts will be candidates for therapies targeting low level HER2 expression.

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12/7/2022

9:45 AM - 11:00 AM

HER2-12

HER2-12 Genomic and Transcriptomic Landscape of HER2-Low Breast Cancer

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Introduction: Breast cancer has pioneered precision medicine with prognostic and predictive subtypes, defined by immunohistochemistry (IHC). Novel therapeutic strategies have led to the emergence of HER2-Low (H2L) as a new entity, defined as tumors with HER2 IHC score of 1+ (>10% cell stained), as well as those with 2+ (>10% cell stained) with paired negative in-situ hybridization (ISH) assay. H2L has been reported to represent up to half of all breast cancer. Further investigation into the mutational landscape of H2L compared to historical subtypes is needed to understand the clinical and biologic factors driving mechanisms of resistance and to consider post-progression treatment options within H2L populations. Methods: The Caris Life Sciences database was used to identify H2L breast tumors by IHC and CISH and evaluated for mutations detected by DNA next-generation sequencing (NextSeq 592-gene panel or NovaSeq whole exome panel). PD-L1 expression was tested by IHC (SP142 IC \geq 1%). Tumor mutational burden (TMB) was measured by totaling somatic mutations per tumor (high \geq 10 mutations per Mb). Statistical significance was determined using Fisher's-Exact/Mann Whitney/X2 test with Benjamini-Hochberg-correction-adjusted p value (q value) of <0.05 . Results: A total of 19789 breast tumors were included in this study. Using standard definitions, 12480 were defined as hormone receptor positive (HR+), 7309 hormone receptors negative (HRneg), 5564 were TNBC, and 1784 HER2 positive (HER2pos). 4349 cases were also identified as H2L, which included 3403 HR+H2L and 946 HRneg H2L. H2L was 22% (4349/19789) of total population; 27% (3403/12480) of the HR+ population and 12.9% (946/7309) of the HRneg population. Within the H2L tumors, when stratified by HR status, we observed in the HR+H2L tumors an increased frequency of amplifications in CCND1 (15.6% vs 5.0%), FGF3 (13.3% vs 4.7%), FGF4 (13.3% vs 4.2%), FGF19 (14.4% vs 4.7%), ZNF703 (15.6% vs 4.4%), NSD3 (12.9% vs 5.2%), ADGRA2 (13.1% vs 5.3%), FGFR1 (11.7% vs 3.6%) and EMSY (5.2% vs 1.4%) compared to the HRnegH2L tumors. TP53 mutations were strikingly higher in the HRnegH2L group (74.4% vs 25.0%) compared to HR+H2L tumors. Markers of IO response also showed elevated positivity in PD-L1 (39.6% vs 19.5%) however, no difference was detected in TMB-H status in HRnegH2L tumors compared to HR+H2L tumors, all $q < 0.05$. The genomic landscape differed when comparing HR+HER2pos tumors to HR+H2L tumors. Significantly more prevalent alterations in HR+HER2pos included amplifications in RNF43 (4.4% vs 1.4%), RARA (13.6% vs 0.1%), MLLT6 (19% vs 0.0%), MYC (6.1% vs 2.7%), DDX5 (10.1% vs 2.0%), CLTC (10.4% vs 3.3%) as well as TP53 (64.0% vs 25.0%) mutations and PD-L1 expression (26.6% vs 19.5%). Furthermore, mutations in PTEN (2.5% vs 7.8%), MAP3K1 (2.8% vs 7.1%), ESR1 (4.4% vs 14.3%), CDH1 (5.2% vs 16.4%), AKT1 (0.0% vs 4.3%) were elevated in the HR+H2L tumors compared to the HR+HER2pos tumors, all $q < 0.05$. Interestingly, when the HRnegH2L tumors were compared to TNBC subtype differences were seen in the mutation rate of PIK3CA (33.5% vs 16.7%; $q < 0.0001$), a master regulator of cell growth, and tumor suppressor gene TP53 (74% vs 86%). Conclusions: With some exceptions, H2L breast cancer shared genomic features with

its more classically defined subset of either HR+ or HRneg disease. Notable differences in PIK3CA (an actionable mutation) and TP53 (a prognostic alteration) warrant additional assessment, as do amplifications variable between HR+H2L and HR+Her2pos groups. Our findings add tremendously to the current understanding of the molecular profile of the H2L subgroup and comparison to the classically defined breast cancer subgroups. Genomic risk assessments after progression on novel therapeutics will be needed to better define implications for mechanisms of resistance.

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12/7/2022

9:45 AM - 11:00 AM

HER2-13

HER2-13 Proficiency assessment of HER2-low breast cancer scoring with the Ventana PATHWAY 4B5 and Dako HercepTest HER2 assays and the impact of pathologist training

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Background

Based on the results of the DESTINY-Breast04 study, the HER2-targeted antibody-drug conjugate trastuzumab deruxtecan (T-DXd) and the Ventana PATHWAY 4B5 companion diagnostic were recently approved by the US Food and Drug Administration for the treatment and identification of patients with HER2-low (IHC2+/ISH- or IHC1+) (Modi et al. *N Engl J Med* 2022). The efficacy of T-DXd in HER2-low mBC highlights the need to distinguish lower ranges of HER2 IHC expression, which has been reported to be more challenging than scoring high HER2 expression (Fernandez et al. *JAMA Oncol* 2022). Here we report on current real-world HER2-low interpretation proficiency and the impact of training for participating pathologists in HER2-low scoring.

Methods

Pathologists from laboratories across the US, EU, Japan, Australia, and Brazil were invited to use a digital pathology platform (Pathotrainer) to interpret HER2 digital images using ASCO/CAP 2018 scoring criteria. Two whole-slide imaging sample sets of representative study cases were compiled for Ventana PATHWAY 4B5 or Dako HercepTest (HcT) stained tumors. Another sample set (n = 25) was developed for a 4 hour virtual training session based on the ASCO/CAP 2018 guideline with some practical considerations. A steering committee (SC) of 8 pathology experts was formed to guide the study. Pathologists' score was compared with a reference score as determined by independent review of 3 experts in HER2 pathology. Paired study cases (n = 14) considered challenging due to difficult-to-interpret staining patterns were reevaluated by the SC members. Concordance and efficacy of training were measured by Cohen's weighted kappa (κ) coefficient, overall rater agreement (ORA), and receiver operating characteristic curve statistics. The primary endpoint was real-world concordance and ORA. The secondary endpoints were post-training concordance and ORA and correct identification of HER2 IHC 0 and HER2-low.

Results

Pre-training baseline or real-world scores were taken by 77 pathologists in 14 countries (n = 49 for 4B5, n = 28 for HcT) and 74 pathologists completed post-training scores (n = 48 for 4B5, n = 26 for HcT). HER2 scoring proficiency of pathologists was high for both assays when assessed on ASCO/CAP binary HER2-negative and -positive status, irrespective of training (4B5: κ = 0.96, ORA = 98.9%; HcT: κ = 0.84, ORA = 94.3%) Concordance per ORA for the new 3-tier classification (HER2 IHC 0 vs HER2-low [IHC 2+/ISH- or IHC 1+] vs HER2-positive [IHC 3+ or IHC 2+/ISH+]) was greater than 80% for both assays at baseline and after training (see Table). In a subgroup analysis assessing training effect for 4B5 assay, concordance rates for HER2 IHC 0 were 74.6% at baseline and 89.2% after training (P < 0.001), and for HER2-low, NPA was 80.6% before and 91.1% after training (P < 0.001); there were no statistically significant changes after training for HcT (data not shown).

Conclusions

Results from this real-world global study demonstrate that overall score concordance with a new category of HER2-low was above the 80% ORA benchmark for both 4B5 and HcT and is higher than previously reported (Fernandez et al. *JAMA Oncol* 2022). These data demonstrate pathologists' ability to achieve an acceptable level of accuracy for identifying HER2 IHC 0 and HER2-low patients even after short-term training; however, additional training techniques and

experience are needed to further improve accuracy.

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Table. Summary of Pathologist Concordance and Interobserver Variability

Test: Scoring Criteria	Concordance κ analysis and ORA (%)	
	Baseline	After training
Ventana 4B5:		
ASCO/CAP ^a	0.96 (98.9)	0.97 (99.4)
Historical FDA ^b	0.82 (92.4)	0.81 (92.2)
New Class ^c	0.75 (82.8)	0.79 (84.9)
HercepTest:		
ASCO/CAP ^a	0.84 (94.3)	0.85 (94.7)
Historical FDA ^b	0.72 (88.3)	0.75 (89.8)
New Class ^c	0.81 (84.1)	0.82 (85.3)

^aCurrent ASCO/CAP 2018 guideline classification; HER2-positive (IHC 3+ or IHC 2+/ISH+) vs HER2-negative (IHC 2+/ISH-, IHC 1+, IHC 0).

^bHistorical US Food and Drug Administration classification; HER2-positive (IHC 3+ or 2+) vs HER2-negative (IHC 1+ or 0).

^cNew classification with a category for HER2-low; HER2-positive (IHC 3+ or IHC 2+/ISH+) vs HER2-low (IHC 2+/ISH- or IHC 1+) vs HER2 IHC 0.

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12/7/2022

9:45 AM - 11:00 AM

HER2-14

HER2-14 HER-2 low status in early stage invasive lobular carcinoma of the breast: associated factors and outcomes in an institutional series

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Objectives: The concept of human epidermal growth factor receptor 2 (HER2)-low status has been proposed as a potential treatment target for breast cancers previously considered to be HER2-negative. Defined by an immunohistochemistry (IHC) score of 1+ or 2+ and negative fluorescent in situ hybridization (FISH) for HER2, HER2-low status predicts significant clinical benefit from novel therapeutic compounds in recent clinical trials. The prevalence and clinical implications of HER2-low status in patients with early stage invasive lobular carcinoma (ILC) has not been described. We aimed to describe the clinicopathologic features and prevalence of HER2-low status in ILC, and identify any potential differences in clinical outcome. **Methods:** We evaluated stage I-III ILC tumors from a prospectively maintained institutional database of patients where both IHC and FISH testing for HER2 status was performed as standard clinical care. Tumors were classified as HER2 negative (IHC=0), HER2-low (IHC=1+ or 2+ and negative FISH), or HER2 positive (IHC=3+ or FISH ratio =>2). Data were analyzed in Stata 16.1 using chi-squared tests, t-tests, and Cox proportional hazards models for disease free survival (DFS). **Results:** 666 ILC tumors with available HER2 status were available for analysis. The mean age at diagnosis was 59.8 years (range 21-91). The majority of patients had stage I disease (63.1%) with an average follow up time of 6.7 years (standard deviation [5.4]). Overall, 184 (27.6%) tumors were HER2 negative, 434 (65.1%) were HER2-low, and 48 (7.2%) were HER2 positive. There were no associations between HER2 status and age, menopausal status,

body mass index, tumor stage, grade, presence of lymphovascular invasion, or molecular assay results. Hormone receptor status was significantly associated with HER2 status, with HER2 positive tumors significantly less likely to be estrogen receptor (ER) positive than both HER2 negative and HER2-low tumors (89.6% versus 97.3% and 96.8% respectively, $p=0.03$). HER2-low tumors were also significantly more likely to have progesterone receptor (PR) positivity (86.6% compared to 79.9% of HER2 negative and 72.9% of HER2 positive tumors, $p=0.01$). This difference remained significant when comparing just HER2-low to HER2 negative cases ($p=0.034$). While there were no differences in use of neoadjuvant or adjuvant chemotherapy by HER2 status, HER2-low patients were significantly more likely to undergo mastectomy versus lumpectomy when compared to HER2 negative and HER2 positive patients (53.7% versus 38.0% and 43.8% respectively, $p=0.001$). In a multivariable Cox proportional hazards model adjusting for tumor size, number of positive nodes, ER/PR status, and local therapy received, patients with HER2-low status had worse DFS than those with HER2 negative tumors (hazard ratio 2.0, 95% confidence interval 1.0 - 4.1, $p=0.05$). Conclusions: In this analysis of 666 early stage ILC cases, we found that most tumors were HER2-low, and that those with HER2-low disease were significantly more likely to have PR positive tumors and to undergo mastectomy. When adjusting for these variables, we identified a difference in DFS between HER2 negative and HER2-low early stage ILC. These findings support the contention that HER2-low and HER2 negative disease represent two different clinical entities. Further investigation of the potential benefit of HER2 targeted therapy in ILC, which predominately lacks HER2-amplified disease, is needed to ensure optimal outcomes in this understudied tumor type.

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Rita Mukhtar, M.D.: No financial relationships to disclose

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9:45 AM - 11:00 AM

HER2-15

HER2-15 Retrospective Study to Estimate the Prevalence and Describe the Clinicopathological Characteristics, Treatment Patterns, and Outcomes of HER2-Low Breast Cancer

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Background: About 60% of breast cancers (BCs) traditionally categorized as HER2 negative (HER2-neg; immunohistochemistry [IHC] 0, IHC 1+ or IHC 2+/in situ hybridization [ISH]-) express low levels of HER2 (HER2-low; IHC 1+ or IHC 2+/ISH-; Schettini, NPJ Breast Cancer 2021). In the phase 3 DESTINY-Breast04 trial (NCT03734029), trastuzumab deruxtecan (T-DXd) showed significantly longer progression-free survival and overall survival (OS) vs physician's choice of chemotherapy in patients (pts) with HER2-low metastatic BC (mBC) who previously received chemotherapy (Modi, NEJM 2022). As HER2-low becomes a clinically relevant HER2 status among pts with BC, greater understanding of pts with HER2-low disease is needed, including identification of these pts using conventional IHC assays. Our objectives were to assess the prevalence of HER2-low among HER2-neg mBC based on rescored HER2 IHC slides, to describe characteristics of pts with HER2-low mBC, and to characterize concordance between historical HER2 scores and rescoring. Methods: This global, multicenter, retrospective study (NCT04807595) included pts with confirmed HER2-neg (HER2 IHC 0, 1+, or 2+/ISH-) unresectable/mBC diagnosed from 2014 through 2017. HER2 IHC-stained slides were rescored after training on low-end expression scoring using Ventana 4B5 and other assays by local laboratories at 13 sites in 10 countries blinded to historical HER2 scores. BCs were categorized as HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2 IHC 0 (IHC 0 or >0< 1+). Prevalence of HER2-low and concordance between historical HER2 scores and rescoring were assessed. Demographics, clinicopathological characteristics, treatment patterns, and outcomes were examined via data from medical charts/health records. Results: HER2 rescoring was obtained for 781 pts with HER2-neg mBC. HER2-low prevalence was 67.1% overall; 71.1% in hormone receptor (HR)-positive (HR+) and 52.5% in HR-negative (HR-) subgroups. There were no notable differences in characteristics (Table) or treatment patterns between pts with HER2-low and HER2 IHC 0. The most frequent therapies used in the first treatment in the metastatic setting were endocrine therapy (64.1%) for pts with HR+ mBC and chemotherapy (94.4%) for pts with HR- mBC. Among pts with HR+ mBC, 10.2% received cyclin-dependent kinase 4/6 inhibitors as part of their first treatment. There were no statistically significant differences in clinical outcomes between the HER2-low and HER2 IHC 0 groups within each HR subgroup. For pts with HR+ mBC, median time to first subsequent treatment was 10 and 8 months for the HER2-low and HER2 IHC 0 groups, respectively. Overall, concordance was 81.2% (kappa=0.582). Concordance between historical HER2 scores and rescoring was 87.3%

for HER2-low and 70.1% for HER2 IHC 0 samples. Conclusions: The prevalence of HER2-low (67.1%) among pts previously categorized as HER2-neg mBC in this study was similar to that of an earlier study (\approx 60%). No obvious differences in patient characteristics or clinical presentation were seen between pts with HER2-low and HER2 IHC 0 mBC. Overall percentage agreement between rescored and historical HER2 scores was 81.2%; agreement was numerically greater for HER2-low than HER2 IHC 0. As HER2-targeted therapies such as T-DXd for the treatment of pts with HER2-low BC are emerging, a greater understanding of pts with HER2-low expression who may benefit from these therapies is important.

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12/7/2022

9:45 AM - 11:00 AM

HER2-16

HER2-16 Inter-lesion heterogeneity of HER2-status in metastatic breast cancer: possible implications for treatment with anti-HER2 antibody-drug conjugates.

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Background. Trastuzumab deruxtecan (T-DXd) has shown promising activity in patients with HER2-low metastatic breast cancer. As the HER2-status can vary between the primary and its corresponding metastases, treatment decisions should ideally be based on HER2 assessment of a recent biopsy. However, limited data is available on intra-patient inter-metastatic heterogeneity in HER2-status, affecting representability of a single biopsy and potential therapeutic options and outcome. We therefore assessed HER2 status on multiple metastases from patients with primary ER-positive/HER2-non-amplified breast cancer in our prospective post-mortem tissue donation program UPTIDER (NCT04531696). Methods. Ninety-one metastatic samples retrieved during the autopsies of 6 patients (range: 13–16/patient) and their respective primary tumours were immunohistochemically (IHC) stained for HER2 (HercepTest™, RTU, ISO-15189 accredited) in our institution. Consensus scoring was performed between two pathologists according to ASCO/CAP 2018 guidelines. The observers were blinded for patient ID. Reflex fluorescence in situ hybridization (FISH) testing was

performed for samples with IHC score of 2+. HER2 status was categorized as HER2-zero (IHC 0), HER2-low (IHC 1+ or IHC 2+ with negative FISH), or HER2-positive (IHC 3+ or IHC 2+ with positive FISH). To assess stability of the performance of IHC scoring in the post-mortem setting, an additional 13 samples taken from 3 metastases at regular (every 1.5h) time intervals during the autopsy underwent HER2 IHC scoring. Results. Evaluation of HER2-status in the primary tumour showed 2 patients with HER2-zero disease and 4 with HER2-low disease. A discordance between HER2 status of the metastases and their respective primary was seen in all patients. Not a single lesion was found to be HER2-positive. For every patient, at least one HER2-low metastasis was observed, with the percentage being highly variable between patients and ranging between 7 and 100%. No association was observed between HER2 status and organ site: HER2-low as well as HER2-zero lesions were found in all organs evaluated in at least 4 patients (liver, bone, pleura, lymph nodes). For 5 patients, multiple lesions within the liver were evaluated: while HER2-zero versus HER2-low status was concordant in those lesions in 4 patients, a mix of HER2 IHC scores was seen in 3 of them. IHC scores were stable over time for tumour lesions assessed repeatedly. Discussion. Important inter-lesion heterogeneity in terms of HER2-low status was observed in patients with primary ER-positive/HER2-non-amplified breast cancer participating to our post-mortem tissue donation program. This observed heterogeneity is unlikely to be due to post-mortem changes in HER2 expression. HER2-low status was found in at least one distant lesion in all patients, complicating therapeutic decision-making based on a single biopsy. Of note, IHC 1+ and 2+ scores varied between metastases of each patient too, making assessment on a single biopsy less reliable for stratification in clinical trials. Further assessment on samples from UPTIDER-patients with ER-negative disease is currently ongoing and results will be available to be presented.

Disclosure(s):

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12/7/2022

9:45 AM - 11:00 AM

HER2-17

HER2-17 Novel Quantitative HER2 Assay for Determining Dynamic HER2 Expression in the HER2 IHC 0 “Ultra-Low” Setting: Implications for Precision Therapy in HER2- Breast Cancer

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Background: The HER2 antibody drug conjugate (ADC) fam-trastuzumab deruxtecan-nxki (T-DXd) significantly improves outcomes over standard chemotherapy in pts with HER2-LOW (IHC 1+ and IHC 2+ FISH-) metastatic breast cancer (MBC). Data from the DAISY (NCT04132960) trial in pts with HER2 IHC 0 or “ultra low” MBC revealed median progression-free survival (PFS) of 4.2 mos vs 6.7 mos in HER2-LOW and 11.1 mos in HER2 3+ pts (Diéras V, et al. Cancer Res. 2022;82(4_Suppl):PD8-02). There is an urgent need to develop methods to accurately discern HER2 LOW expression versus HER2 IHC 0/ultra-low expression so appropriate pts may receive T-DXd. We have developed a quantitative HER2 assay using reverse phase protein array (RPPA) technology with laser capture microdissection (LCM) enrichment of tumor epithelium that measures HER2 expression over a 65-fold dynamic range in HER2 IHC 0 to 3+ breast cancers. In I-SPY 1 and 2 trials we found that RPPA-assessed quantitative HER2 and activated/phosphorylated HER2 expression predicted for pathologic complete response in pts with HER2 IHC 0, HER2-LOW and HER2 3+ disease with various HER2 and other targeted agents. We then developed and validated the first CLIA/CAP-accredited quantitative HER2 protein expression and activation assay, and now explore quantitative HER2 expression in

HER2 IHC 0/ultra low disease. Given the recent approval of sacituzumab govitecan-hziy in TNBC and the results of the TROPiCS-02 (NCT03901339), we also evaluated quantitative RPPA-based TROP-2 expression levels in HER2 IHC 0 breast cancer. Methods: LCM-enriched tumor epithelium was obtained from freshly cut FFPE core needle and resected breast cancer samples from 175 pts with pathology-determined HER2 IHC 0 status (N=68 ER+ and N=107 ER-). Quantitative HER2 output is generated as a relative intensity unit (RU) that is interpolated to an internal calibrator curve and a population referent comprised of known HER2+ (IHC 3+ and 2+/FISH+), HER2-LOW and HER2 IHC 0/ultra-low tumors to generate population-based cut-points as a referent. RPPA-based quantitative HER2 expression are reported as one of four levels of expression across the HER2 dynamic range observed: “non/extremely low”, “modest”, “moderate”, and “high”. Quantitative TROP2 protein expression levels were also measured for each case by the RPPA assay on the same lysate using the same adjectival determinants of relative expression as HER2. Results: For the HER2 IHC 0 ER+ cohort, we observed HER2 protein expression over a 25-fold dynamic range and that 57% (N=39) had HER2 non/extremely low, 37% (N=25) modest, and 4 (6%) moderate/high HER2 expression by RPPA. For the HER2 IHC 0 ER- cohort, we observed HER2 protein expression over a 15-fold dynamic range and that 71% (N=76) had non/extremely low, and 31% (N=29%) modest HER2 expression. We observed TROP-2 protein expression over a 35-fold dynamic range across all tumors measured, and it was found to be at least modestly expressed in 95% (37/39) ER+ and 95% (72/76) ER- of the IHC 0/ultra-low tumors that were also found to be HER2 non/extremely low by RPPA. Conclusions: LCM-RPPA quantitative assessment of HER2 expression showed that nearly 40% of ER+ IHC 0 and 30% of ER- IHC 0 “ultra-low” breast cancers actually had modest to moderate HER2 expression. Interestingly, this frequency approximates the response rate of 30% seen with T-DXd in HER2 IHC 0 pts in the DAISY trial. Quantitatively measured TROP2 is at least modestly expressed in the vast majority of RPPA-assessed HER2 IHC 0 cancers regardless of ER status, making a TROP2-directed ADC an attractive therapeutic option for these pts. If validated in larger studies, LCM-RPPA-based HER2 expression could provide a better understanding of the potential for therapeutic efficacy with T-DXd in patients with HER2 IHC “ultra-low” disease, and may better define true ultra-low HER2 expression in HER2 IHC 0 tumor biopsies at baseline and refine the lower limit of the HER2-LOW designation.

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12/7/2022

9:45 AM - 11:00 AM

HER2-18

HER2-18 Determination of HER2-low status in tumors of patients with unresectable and/or metastatic breast cancer in DESTINY-Breast04

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Background In DESTINY-Breast04, the HER2-targeted antibody drug conjugate trastuzumab deruxtecan (T-DXd) demonstrated significant survival benefit vs treatment of physician's choice (TPC) in patients (pts) with HER2-low unresectable or metastatic breast cancer (mBC) (Modi et al. N Engl J Med 2022). These results emphasize the importance of accurately identifying HER2 expression in breast tumor tissue. Here, we describe concordance between previously determined (historical) HER2 scores and central HER2 scores, and tumor sample characteristics for pts with mBC screened and enrolled in DESTINY-Breast04. Methods DESTINY-Breast04 was a randomized, open-label, phase 3 study in pts with centrally determined HER2-low (immunohistochemistry [IHC] 1+ or IHC 2+ with negative in situ hybridization [ISH]) mBC who had previously received 1-2 lines of chemotherapy. Pts were randomized 2:1 to T-DXd or TPC. HER2 scores were determined via central testing of tumor specimens by the investigational Ventana PATHWAY 4B5 IHC assay, using the 2018 American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) testing guidelines HER2 scoring algorithm, and Ventana INFORM HER2 dual ISH assay (as applicable). Results 1340 pts identified as having HER2-low mBC per historical data submitted tumor samples for central HER2-low testing. Of those, 557 pts met all eligibility criteria and were enrolled in

DESTINY-Breast04. The proportion of samples from metastatic vs primary tumors was 59% vs 41% for all submitted tumor samples and 65% vs 35% for enrolled patients. Of those with available data, most were biopsy specimens (995 [74%] vs 344 [26%] resection/excisions) and were submitted as archived formalin-fixed, paraffin-embedded tissue (1183 [88%] vs 157 [12%] freshly collected samples); historical testing dates ranged from 2000-2020. Of samples with data on the historical HER2 IHC test used (31%), most were scored using local Ventana 4B5 (63%) or Agilent HercepTest (32%) assays. Tumor distribution characteristics were similar between screened and enrolled pts. For samples with historical and central HER2 results (N = 1108), 849/1108 (77%) were centrally scored as HER2-low. Of the samples that were not centrally scored as HER2-low, 88% were scored as HER2 IHC 0. Historical and central HER2 score concordance was assessed by sample region of origin (North America, Europe, China, or Asia without China) and collection date (2013 or earlier, 2104-2018, or 2019 or after) and scoring agreement was associated with these factors. Efficacy of T-DXd vs TPC for pts in DESTINY-Breast04 was consistent across all tumor sample characteristics (primary vs metastatic, specimen type, archival vs fresh, and tissue collection date). Conclusions Despite the lack of prior clinical utility and training in distinguishing HER2 IHC 0 from HER2-low (IHC 1+, 2+/ISH-), evolving guidelines since historical HER2 status provision, differences in local testing methods, and differences in key sample characteristics (primary vs metastatic; archived vs fresh; widely variable sample biopsy and testing dates), there was a 77% agreement between historical and central HER2-low status using the Ventana PATHWAY 4B5 IHC assay and Ventana INFORM HER2 Dual ISH assay. This rate is comparable to the reported initial concordance rates for HER2 overexpression IHC testing (range 74-82%; Roche J. Natl Cancer Inst 2002, Perez. J Clin Oncol 2006). Moreover, consistent benefit of T-DXd vs TPC was generally seen across patient groups with various tumor sample characteristics in DESTINY-Breast04. Determination of HER2-low status using the Ventana PATHWAY 4B5 IHC assay (and ISH when applicable) demonstrated the ability of the test, analyzed by pathologists using current ASCO/CAP guidelines, to identify pts who benefit from T-DXd. Funding This study was funded by Daiichi Sankyo and AstraZeneca.

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Junji Tsurutani, MD, PhD: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Chugai: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); FSJD: Contracted Research (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Oncotherapy: Contracted Research (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Taiho: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); West Japan Oncology Group: Contracted Research (Ongoing)

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Charo Garrido, PhD: Daiichi-Sankyo Inc.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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Naoto T. Ueno, PhD, MD: Angle plc: Contracted Research (Terminated, April 1, 2021); AnHeart Therapeutics Inc.: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca Pharmaceutical: Consulting Fees (e.g., advisory boards) (Ongoing); Carisma Therapeutics, Inc.: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); CARNA Biosciences, Inc.: Consulting Fees (e.g., advisory boards) (Ongoing); ChemDiv, Inc.: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Chugai Pharmaceutical: Consulting Fees (e.g., advisory boards) (Terminated, February 21, 2022); Dalichi Sankyo, Inc.: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); DualityBio: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); DynaMed: Consulting Fees (e.g., advisory boards) (Terminated, June 22, 2022); Eisal Medical Research Inc: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Epic Science: Contracted Research (Ongoing); Gilead Sciences, Inc.: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Kechow Pharma: Consulting Fees (e.g., advisory boards) (Ongoing); Kirilys Therapeutics, Inc.: Consulting Fees (e.g., advisory boards) (Ongoing); Kyowa Hakko Kirin Co., Ltd.: Speaker (Ongoing); LARVOL: Consulting Fees (e.g., advisory boards) (Terminated, April 16, 2021); Merck Co.: Contracted Research (Ongoing); OBI Pharma Inc.: Contracted Research (Ongoing); OncoCyte Co.: Consulting Fees (e.g., advisory boards) (Ongoing); Oncolys BioPharma Inc.: Contracted Research (Ongoing); Ourotech, Inc., DBA Pear Bio: Royalty (Ongoing); Peptilogics, Inc.: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer Inc.: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Phoenix Molecular Designs: Consulting Fees (e.g., advisory boards) (Ongoing); Preferred Medicine, Inc.: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Rakuten Medical, Inc.: Consulting Fees (e.g., advisory boards) (Ongoing); Sumitomo Dainippon Pharma, Inc.: Contracted Research (Ongoing); Sysmex Co. Ltd.: Consulting Fees (e.g., advisory boards) (Ongoing); Takeda Pharmaceuticals, Ltd.: Consulting Fees (e.g., advisory boards) (Ongoing); Unitech Medical, Inc.: Consulting Fees (e.g., advisory boards) (Terminated, March 31, 2022)

12/7/2022

9:45 AM - 11:00 AM

HER2-19

HER2-19 Impact of HER2 low status on clinical outcomes in participants with 1-3 positive lymph nodes, HR+/HER2- breast cancer with recurrence score < / 25 randomized to endocrine therapy +/- chemotherapy: results from SWOG S1007 (RxPONDER)

Presenting Author(s) and Co-Author(s):

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Country: United States

Background:

HER2 low breast cancer, defined as tumors with HER2 IHC expression 1+ or 2+ without HER2 gene amplification, represents a potential new therapeutic subgroup of metastatic breast cancer (BC). However, the clinical significance of HER2 low status in early BC remains unclear. Previously, the RxPONDER trial (NCT01272037), a prospective, randomized trial of endocrine therapy (ET) vs. chemoendocrine therapy (CET) in women with lymph node positive (LN+) BC, demonstrated invasive disease-free survival (IDFS) with ET vs CET varies by menopausal status. We evaluated the impact of HER2 low vs zero status in the RxPONDER trial (SWOG S1007), stratified by menopausal status and treatment groups.

Methods:

Eligibility criteria included women > / 18 years of age with hormone receptor-positive (HR+), HER2-negative (HER2-) BC, Recurrence Score (RS) < / 25, 1-3+ LN and no contraindications to taxane and/or anthracycline based CT. The impact of HER2 low status and other baseline

clinicopathological features on clinical outcomes were evaluated using covariates in Cox regression analysis. HER2 IHC status was per local testing. HER2 low was defined as IHC 1+ or IHC 2+ without HER2 gene amplification, and HER2 zero was defined as IHC 0. The primary endpoint was IDFS, defined as the time from the date of randomization to the date of a first invasive recurrence (local, regional, or distant), a new invasive primary cancer (breast cancer or another type of cancer), or death from any cause. Secondary objectives included distant-relapse free survival (DRFS).

Results:

Among the 4,983 eligible participants, 4,588 had IHC HER2 status available. 52% of 2,052 premenopausal women had HER2 low BC and 57% of 3,042 post-menopausal women had HER2 low BC. There was a small, but statistically significant ($p=0.03$) difference, in RS between HER2 low (mean 14.5) and HER2 zero (mean 14.1) status. The proportion of participants with HER2 low and zero were balanced between treatment group assignment (CET vs ET). Among premenopausal women adjusting for RS, CET led to an observed improvement in IDFS among both HER2 low (HR=0.67; 95% CI 0.43-1.04) and HER2 zero subgroups (HR=0.57; 95% CI 0.36-0.89) (interaction $p=0.55$). Similarly, among post-menopausal women, there was no difference in IDFS between CET vs ET among both HER2 low (HR=0.98; 95% CI 0.75-1.29) and HER2 zero (HR=1.12; 95% CI 0.80-1.56) subgroups (interaction $p=0.57$). In multivariable analysis, adjusting for treatment arm, RS, and menopausal status, HER2 low status was not associated with worse IDFS compared to HER2 zero status (HR=0.93; 95% CI 0.78-1.11). Additionally, no differences were noted in DRFS.

Conclusion:

HER2 low or zero status had no impact on clinical outcomes with CET vs ET among premenopausal or post-menopausal women with HR+/HER- BC with 1-3+ LNs and RS $< / 25$. HER2 low evaluation should not be currently used for CET vs ET clinical decision making among patients with HR+/HER2- breast cancer with 1-3+ LN and RS $< / 25$. Further research on the role of HER2 low status in other settings may be warranted.

Disclosure(s):

Laura M. Spring, MD: Gilead: Contracted Research (Ongoing); Lilly: Contracted Research (Ongoing); Merck: Contracted Research (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Phillips: Contracted Research (Ongoing); Puma: Consulting Fees (e.g., advisory boards) (Terminated, December 31, 2021)

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Merck: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing)

Lajos Pusztai, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria; Research Funding (Institution) (Ongoing); Bristol Myers Squibb: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria; Research Funding (Institution) (Ongoing); Clovis: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Daiichi: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Genentech: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); H3Bio: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Immunomedics: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria; Research Funding (Institution) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Personalis: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria; Research Funding (Institution) (Ongoing); Pieris: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Radius Health: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Seagen Inc: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria; Research Funding (Institution) (Ongoing); Syndax: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing)

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12/7/2022

10:00 AM - 5:00 PM

Exhibits

12/7/2022

11:00 AM - 11:15 AM

Special Guest: C. Kent Osborne, MD

Presenting Author(s) and Co-Author(s):

C. Kent Osborne, MD - *Baylor College of Medicine*

City: Houston

State: TX

Country: United States

Disclosure(s):

C. Kent Osborne, MD: Gene Tex: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

12/7/2022

11:00 AM - 12:00 PM

Mini-Symposium 1: C. Kent Osborne

HER2 and ER Crosstalk: Signaling Mechanisms and Clinical Implications Symposium

Presenting Author(s) and Co-Author(s):

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Virginia Kaklamani, MD - *UT Health San Antonio*

City: San Antonio

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Country: United States

Disclosure(s):

Carlos Arteaga, MD: Arvinas: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Research Funding (Ongoing); MERCK: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); OrigiMed: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Research Funding (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing); TAIHO Oncology: Consulting Fees (e.g., advisory boards) (Ongoing); Takeda: Research Funding (Ongoing)

Virginia Kaklamani, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Daiichi Sankyo: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Genentech: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Genomic Health: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Gilead Sciences: Honoraria (Ongoing); Novartis: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Pfizer: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Puma Biotechnology: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing)

12/7/2022

11:15 AM - 11:30 AM

Oncogene signal transduction and antiestrogen resistance

Presenting Author(s) and Co-Author(s):

Rachel Schiff, PhD - *Baylor College of Medicine*

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State: TX

Country: United States

Background: Recent studies suggest that enhancer reprogramming underlies heterogeneity and disease progression in estrogen receptor-positive (ER+) BC. Cell-type/state specific transcription is governed by high-order assemblies of master transcription factors (TFs) and epigenetically defined regulatory regions including super-enhancers (SEs). We previously showed that aberrant activation of the pioneer TF FOXA1 promotes enhancer and transcriptional reprogramming in endocrine-resistant BC, involving the ER and the AP-1 FRA1 and c-JUN TFs. As SEs maintain a robust cell-type/state specific core transcriptional regulatory circuitry (CRC) in developmental and tumorigenic processes, we sought to identify key additional TFs in SE/FOXA1-driven CRCs in endocrine resistance, which could serve as attractive therapeutic targets.

Methods: TF binding motif at the shared SEs (mapped by H3K27ac ChIP-seq) between MCF7-parental (P) cells with ectopic FOXA1 overexpression (OE) and the endogenous FOXA1-amplified tamoxifen-resistant (TamR) cells was analyzed by HOMER. ER-bound SEs distinguishing TamR vs. P cells were defined by integrating the SEs with our prior ER ChIP-seq data (PMID 28507152). KLF4 motif within these ER-bound SEs was scanned using FIMO and linked to nearby genes by intersection with the previously defined promoter-tethered regions (PTRs) (PMID 24141950). Differential gene expression in MCF7-TamR cells upon KLF4 knockdown (KD) by 3 unique siRNAs was analyzed using limma from edgeR. The biological and clinical significance of the KLF4-dependent genes was analyzed using Gene Ontology and survival modeling with METABRIC and the ER+ metastatic BC cohort ([SABCS19-GS2-02](#)). Cell migration was assessed by the wound-healing assay.

Disclosure(s):

Rachel Schiff, PhD: MacroGenics: Advisory Committee (Ongoing); Patent (filed and owned by Baylor College of Medicine): Pending patent application # PCT/US21/70543 (Ongoing); Puma Biotechnology: Contracted Research (Ongoing); Wolters Kluwer/UpToDate: Royalty (Ongoing)

12/7/2022

11:30 AM - 11:45 AM

HER2 signaling the ER cistrome

Presenting Author(s) and Co-Author(s):

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Country: United States

Disclosure(s):

Rinath Jeselsohn, MD: Carrick Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Contracted Research (Ongoing); Luminex: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Contracted Research (Ongoing)

12/7/2022

11:45 AM - 12:00 PM

Treatment of ER+/HER2+ breast cancer

Presenting Author(s) and Co-Author(s):

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Co-expression of hormone receptors (HR) and human epidermal growth factor receptor 2 (HER2) occurs in 10% of all breast cancers, and due to cross-talk mechanisms that influence cell signalling the co-expression of these receptors modulates response of these cancers to both HER2-directed and endocrine therapies. Prior to the advent of HER2 targeted therapies, patients with HR+/HER2+ breast cancer had a significantly worse prognosis compared with HR+/HER2- breast tumours, primarily related to HER2 signalling driving endocrine resistance. Likewise, prior clinical studies in the neoadjuvant setting showed that patients with HR+/HER2+ primary breast cancer had a lower pathological complete response rate to HER2-targeted therapy plus chemotherapy that those with HR-/HER2+ tumours, suggesting a different biology. As such, strategies that combine receptor blockade against HER2 and HR have been developed in metastatic breast cancer (MBC), confirming that combined blockade is better than endocrine therapy (ET) alone, and then that dual HER2 blockade + ET was superior to single HER2 therapy + ET. More recently combinations of a CDK 4/6 inhibitor with ET and HER2 therapy has shown significant clinical efficacy and survival benefit in heavily pre-treated patients, confirming the efficacy for non-chemotherapy targeted combinations in HR+/HER2+ MBC. In the early breast cancer (EBC) setting, most HER2 directed therapy is given in combination with chemotherapy in the neoadjuvant setting, while studies of combined ET and HER2 targeted strategies without chemotherapy work slower with lower pCR rates. As such, the real benefit for combined targeted therapy may be in the adjuvant setting where ET and HER2 therapy are routinely given together following completion of chemotherapy. Furthermore, extended adjuvant ET/HER2 therapy beyond completion of antibody based treatment may also provide extra benefit, and in higher risk patients longer treatment may prove an important consideration.

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Stephen Johnston, MBBS: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Sanofi Genzyme: Consulting Fees (e.g., advisory boards) (Ongoing)

12/7/2022

12:00 PM - 12:30 PM

Plenary Lecture 1: Lineage-Defined Metabolism of Normal Mammary Cells and Origins of Cancer Metabolic Heterogeneity

Presenting Author(s) and Co-Author(s):

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Sex-hormone driven fundamental programs govern breast physiology and mammary stem and progenitor cell biology. Mammary epithelium is composed of two lineages, basal and luminal. Understanding breast cell heterogeneity in the context of these mammary lineages is essential for designing new classes of drugs aimed at early breast cancer interception and/or treatment. Distinct cell subsets constitute the highly organized epithelial ductal tree and we have been systematically building new knowledge on breast cell composition through multi-modal global profiling, which has pinpointed new mammary cell vulnerabilities. One core pathway is that of lineage-rooted differences in the metabolic programs which can be exploited to suppress unwarranted breast progenitor activity. This lecture will describe our work laying the foundation for breast-progenitor guided new therapeutic opportunities.

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12/7/2022

12:30 PM - 1:00 PM

AACR Distinguished Lectureship in Breast Cancer Research, supported by Aflac Inc.

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Charles M. Perou, PhD: Bioclassifier LLC: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Royalty (Ongoing)

12/7/2022

12:30 PM - 1:00 PM

Quantitative Medicine for Breast Cancer Patients

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12/7/2022

12:30 PM - 1:30 PM

Career Development Forum

12/7/2022

1:00 PM - 2:00 PM

Clinical Case Discussion

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1:00 PM - 2:00 PM

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Michael Gnant, MD, FACS, FEBShon: Amgen: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); DaiichiSankyo: Consulting Fees (e.g., advisory boards) (Terminated, July 1, 2022); EliLilly: Consulting Fees (e.g., advisory boards) (Ongoing); LifeBrain: Consulting Fees (e.g., advisory boards) (Ongoing);

MSD: Consulting Fees (e.g., advisory boards) (Terminated, July 1, 2022); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); PierreFabre: Consulting Fees (e.g., advisory boards) (Terminated, July 1, 2022); Sandoz: Salary (Ongoing); Veracyte: Consulting Fees (e.g., advisory boards) (Terminated, July 1, 2022)

Celina Kleer, MD: No financial relationships to disclose

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Julia Maues: No financial relationships to disclose

George Sledge, MD: No financial relationships to disclose

12/7/2022

1:00 PM - 1:20 PM

Tumor stroma in DCIS progression

Presenting Author(s) and Co-Author(s):

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The interaction between cancer cells and the surrounding stroma plays a significant role in tumor growth and progression. The rapidly growing field of study involving the tumor microenvironment is discovering stromal-specific genes and cells that participate in this process. In invasive breast cancer, transcriptional analysis of stroma derived samples has identified stromal gene expression features that are correlated with clinical outcome with features characteristic of angiogenesis, hypoxia, and inflammation. The role of the microenvironment in DCIS is less well studied and has significant variation across and within DCIS. The basement membrane and myoepithelial cell layers provide a barrier for the interaction between neoplastic cells and the tumor microenvironment. DCIS tumor cells may be variably exposed to the immune environment. An immune infiltration is common in some DCIS, including high grade DCIS with necrosis. How this influences the transition from DCIS to IBC is complex.

Disclosure(s):

Robert West, MD, PhD: NCI Precancer Atlas: Contracted Research (Ongoing)

12/7/2022

1:00 PM - 2:00 PM

Forum 1: Molecular Aspects of DCIS Progression

Presenting Author(s) and Co-Author(s):

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Disclosure(s):

E Shelley Hwang, MD, MPH: NCI Precancer Atlas: Contracted Research (Ongoing); Patient-Centered Outcomes Research Institute (AFT-25 COMET): Contracted Research (Ongoing)

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1:20 PM - 1:40 PM

Clonal evolution of DCIS to invasion

Presenting Author(s) and Co-Author(s):

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Clonal evolution of DCIS to invasion

Ductal carcinoma in situ (DCIS) is the most common form of preinvasive breast cancer and, despite treatment, a small fraction (5-10%) of DCIS patients develop subsequent invasive breast cancer (IBC). If not treated, at least 3 out of 4 women with DCIS will not develop IBC¹⁻³. This implies many women with non-progressive, low-risk DCIS are likely to carry the burden of overtreatment. To solve this DCIS dilemma, two fundamental questions need to be answered. The first question is, how the subsequent IBC is related to the initial DCIS lesion. The second question is how to distinguish high- from low-risk DCIS at the time of diagnosis. This is essential to take well-informed DCIS management decisions, i.e., surgery, followed by radiotherapy in case of breast conserving treatment with or without subsequent endocrine treatment, or test whether active surveillance for low-risk DCIS is safe.

How is the subsequent IBC related to the initial DCIS?

The high genomic concordance in DNA aberrations between DCIS and IBC suggest that most driver mutations and CNA events are acquired at the earliest stages of DCIS initiation. It has therefore been assumed that most solid tumours arise from a single cell and that the probability of two independent tumours arising from the same tissue is low⁴⁻⁶. However, lineage tracing and genomic studies strongly suggest both direct and independent clonal lineages during the initiation of DCIS and evolution to IBC. In these processes, mammary stem cells have been implicated in DCIS initiation.

Role of mammary stem cells in DCIS initiation

Lineage tracing mouse model experiments have shown the fate of individual cells and lineages that acquire mutations before a tumour is established⁷⁻⁹. This is also relevant for DCIS initiation^{10,11}, as different pools of MaSCs drive the growth and development of the ductal network and are considered the cell of origin for breast cancers^{9,10}. The ductal trees remain quiescent until puberty, during which extension, branching and termination of terminal end buds (TEBs) leads to its expansion throughout the fat pad^{7,12,13}. Any oncogenic mutation that occurs in a fetal MaSC will spread throughout the ductal network to a large part of the ductal tree, leading to sick lobes⁹. By contrast, oncogenic mutations acquired by a single MaSC during puberty spread to a smaller number of offspring located in small clusters in a part of the ductal network^{8,14}.

Direct lineage models for DCIS progression

Direct lineage models postulate that DCIS has a single cell of origin that acquires mutations and progresses to IBC¹⁵⁻¹⁸. This is also supported by the high genomic concordance of CNAs

and mutations in synchronous DCIS–IBC regions^{6,15,17,19-21} and the results of a recent large longitudinal study that profiled pure DCIS and recurrent IBC using multiple sequencing techniques, which estimated direct clonal lineages in approximately ~80% of patients¹⁸.

Two distinct direct lineage models have been proposed: the evolutionary bottleneck model and the multiclonal invasion model. In the evolutionary bottleneck model, a single clone (or a limited number of clones) with an invasive genotype is selected and breaks through the basement membrane to migrate into surrounding tissues^{15,16,22}, while other clones are unable to escape the ducts²¹⁻²⁸. The multiclonal invasion model posits that most or all subclones can escape the basement membrane, establishing invasive disease^{6,16,17,20}. The multiclonal model has not been studied widely in pure DCIS and recurrent IBC samples.

Independent lineage model for DCIS progression

DCIS lesions and IBCs can arise from different initiating cells in the same breast independently^{5,20,29-32}. An analysis of sequential DCIS–IBC pairs in a unique, large-scale, in-depth study of 95 matched pure DCIS and recurrent IBC showed that ~20% of the IBC recurrences were indeed clonally unrelated to the primary DCIS¹⁸, as is also supported by some mathematical model studies³³.

The potential role of a field effect

IBC can develop in the same breast as an initial DCIS even after treatment, which could be explained by the presence of a field effect³⁴⁻³⁷. Alternatively, the sick lobe hypothesis proposes that a single lobe harbours first-hit mutations, acquired in utero or during early mammary development³⁷⁻⁴². This could also explain the restriction of IBC to the ipsilateral side of the breast^{39,43,44}. Germline mutations may also explain the emergence of independent lineages in DCIS and IBC patients, lowering the threshold for cancer development^{32,43-46}.

Convergent evolution model of DCIS progression

A third model for the emergence of IBC from DCIS is convergent evolution, in which the same mutations and CNA are selected and expanded during tumour growth such that environmental factors fuel competition between distinct clones and push them towards a similar genotype. Ultimately, two independent clonal lineages from different ancestral cells then happen to share multiple genomic aberrations or driver mutations across regions⁴⁷⁻⁴⁹. Although independent lineages are considered uncommon (~20%) in ipsilateral recurrences, they occur at much higher frequencies in contralateral recurrences (>80%), in which single-nucleotide polymorphism and comparative genomic hybridization microarrays show few (or no) genomic alterations shared in tumours from the contralateral breast cancer^{18,50,51}.

How to distinguish high- from low-risk DCIS at the time of diagnosis?

The genomic and transcriptomic profile present at the time of DCIS diagnosis may contain crucial information on the risk of progression of DCIS to IBC. Thus far, it has been unclear whether prognostic gene expression markers can be used to separate indolent DCIS from potentially progressive DCIS. To this end, microarrays and RNA-seq have been applied for the comparison of bulk RNA from microdissected DCIS and IBC tissue. In synchronous DCIS–IBC, a limited number of transcriptional differences have been found and the few events discovered

often varied extensively across different tumours⁵²⁻⁵⁶. Although these differences were strong, the added value of these studies is uncertain as they are often confounded by small sample size, lack of matched receptor status data, and low sample purity. Despite these limitations, these studies have implicated the epithelial-mesenchymal transition (EMT) and extracellular matrix (ECM) remodelling pathways as potentially relevant for the progression of DCIS to IBC⁵⁵⁻⁶².

We studied two large DCIS cohorts: the Sloane cohort, a prospective breast screening cohort from the UK (median follow-up of 12.5 years), and a Dutch population-based cohort (NKI, median follow-up of 13 years). FFPE tissue specimens from patients with pure primary DCIS after breast-conserving surgery (BCS) +/- RT that did develop a subsequent ipsilateral event (DCIS or invasive) were considered as cases, whereas patients that did not develop any form of recurrence up to the last follow-up or death were considered as controls. We performed copy number analysis (CNA) and RNAseq analysis on 229 cases (149 IBC recurrences and 80 DCIS recurrences) and 344 controls.

We classified DCIS into the PAM50 subtypes using RNAseq data which revealed an enrichment of luminal A phenotype in DCIS that did not recur ($P = 0.01$, Fisher Exact test). No single copy number aberration was more common in cases compared to controls. RNAseq data did not reveal any genes significantly over/under expressed in cases versus controls after false discovery rate (FDR) correction. However, by limiting the analysis to samples that had not had RT and excluding pure DCIS recurrences we developed a penalized Cox model from RNAseq data. The model was trained on weighted samples (to correct for the biased sampling of the case control dataset) from the NKI series with double loop cross validation. Using this predicted hazard ratio, the samples were split into high, medium and low risk quantiles, with a recurrence risk of 20%, 9% and 2.5%, respectively at 5 years ($p < 0.001$, Wald test). The NKI-trained predictor was independently validated in the Sloane No RT cohort ($p = 0.02$, Wald test). GSEA analysis revealed proliferation hallmarks enriched in the recurrence predictor (FDR = 0.058). The NKI-RNAseq predictor was more predictive of invasive recurrence than PAM50, clinical features (Grade, Her2 and ER) and the 12-gene Oncotype DCIS score ($p < 0.001$, permutation test using the Wald statistic) in both the NKI and Sloane series.

In the methylation analysis, 50 controls were compared with 35 cases. We could identify Variably Methylation Regions (VMRs) and Differentially Methylated Regions (DMRs) between cases and controls. Interestingly, VMRs were enriched in cell adhesion pathways

Conclusion

The recently acquired knowledge described above on how often the subsequent IBC is directly related to the initial DCIS and on molecular markers predicting the risk of DCIS progression is essential for accurate DCIS risk assessment. This is essential to aid accurate clinical decision making to personalize DCIS management in the near future.

References

1. Falk, R. S., Hofvind, S., Skaane, P. & Haldorsen, T. Second events following ductal carcinoma in situ of the breast: a register-based cohort study. *Breast Cancer Res Treat* **129**, 929-938, doi:10.1007/s10549-011-1531-1 (2011).
2. Ryser, M. D. *et al.* Cancer Outcomes in DCIS Patients Without Locoregional Treatment. *Jnci J National Cancer Inst* **111**, 952-960, doi:10.1093/jnci/djy220 (2019).

3. Maxwell, A. J. *et al.* Unresected screen detected Ductal Carcinoma in Situ: outcomes of 311 women in the Forget-me-not 2 study. *Breast* **61**, 145-155, doi:10.1016/j.breast.2022.01.001 (2022).
4. Hanahan, D. & Weinberg, R. A. Hallmarks of cancer: the next generation. *Cell* **144**, 646-674, doi:10.1016/j.cell.2011.02.013 (2011).
5. Kim, H., Kim, C. Y., Park, K. H. & Kim, A. Clonality analysis of multifocal ipsilateral breast carcinomas using X-chromosome inactivation patterns. *Hum Pathol* **78**, 106-114, doi:10.1016/j.humpath.2018.04.016 (2018).
6. Bergholtz, H. *et al.* Comparable cancer-relevant mutation profiles in synchronous ductal carcinoma in situ and invasive breast cancer. *Cancer Rep (Hoboken)* **3**, e1248, doi:10.1002/cnr2.1248 (2020).
7. Girardi, R. R. *et al.* Stem and progenitor cell division kinetics during postnatal mouse mammary gland development. *Nat Commun* **6**, 8487, doi:10.1038/ncomms9487 (2015).
8. Scheele, C. L. *et al.* Identity and dynamics of mammary stem cells during branching morphogenesis. *Nature* **542**, 313-317, doi:10.1038/nature21046 (2017).
9. Ying, Z. & Beronja, S. Embryonic Barcoding of Equipotent Mammary Progenitors Functionally Identifies Breast Cancer Drivers. *Cell Stem Cell* **26**, 403-419.e404, doi:10.1016/j.stem.2020.01.009 (2020).
10. Zhou, J. *et al.* Stem Cells and Cellular Origins of Breast Cancer: Updates in the Rationale, Controversies, and Therapeutic Implications. *Front Oncol* **9**, 820, doi:10.3389/fonc.2019.00820 (2019).
11. Watson, C. J. & Khaled, W. T. Mammary development in the embryo and adult: new insights into the journey of morphogenesis and commitment. *Development* **147**, doi:10.1242/dev.169862 (2020).
12. Williams, J. M. & Daniel, C. W. Mammary ductal elongation: differentiation of myoepithelium and basal lamina during branching morphogenesis. *Dev Biol* **97**, 274-290, doi:10.1016/0012-1606(83)90086-6 (1983).
13. Silberstein, G. B. & Daniel, C. W. Glycosaminoglycans in the basal lamina and extracellular matrix of serially aged mouse mammary ducts. *Mech Ageing Dev* **24**, 151-162, doi:10.1016/0047-6374(84)90067-8 (1984).
14. Davis, F. M. *et al.* Single-cell lineage tracing in the mammary gland reveals stochastic clonal dispersion of stem/progenitor cell progeny. *Nat Commun* **7**, 13053, doi:10.1038/ncomms13053 (2016).
15. Hernandez, L. *et al.* Genomic and mutational profiling of ductal carcinomas in situ and matched adjacent invasive breast cancers reveals intra-tumour genetic heterogeneity and clonal selection. *J Pathol* **227**, 42-52, doi:10.1002/path.3990 (2012).
16. Casasent, A. K., Edgerton, M. & Navin, N. E. Genome evolution in ductal carcinoma in situ: invasion of the clones. *J Pathol* **241**, 208-218, doi:10.1002/path.4840 (2017).
17. Casasent, A. K. *et al.* Multiclonal Invasion in Breast Tumors Identified by Topographic Single Cell Sequencing. *Cell* **172**, 205-217 e212, doi:10.1016/j.cell.2017.12.007 (2018).
18. Lips, E. H. *et al.* Genomic analysis defines clonal relationships of ductal carcinoma in situ and recurrent invasive breast cancer. *Nat Genet* **54**, 850-860, doi:10.1038/s41588-022-01082-3 (2022).
19. Miron, A. *et al.* PIK3CA mutations in in situ and invasive breast carcinomas. *Cancer Res* **70**, 5674-5678, doi:10.1158/0008-5472.CAN-08-2660 (2010).
20. Yates, L. R. *et al.* Subclonal diversification of primary breast cancer revealed by multiregion sequencing. *Nat Med* **21**, 751-759, doi:10.1038/nm.3886 (2015).
21. Pareja, F. *et al.* Whole-Exome Sequencing Analysis of the Progression from Non-Low-Grade Ductal Carcinoma In Situ to Invasive Ductal Carcinoma. *Clin Cancer Res* **26**, 3682-3693, doi:10.1158/1078-0432.CCR-19-2563 (2020).

22. Trinh, A. *et al.* Genomic Alterations during the In Situ to Invasive Ductal Breast Carcinoma Transition Shaped by the Immune System. *Mol Cancer Res* **19**, 623-635, doi:10.1158/1541-7786.MCR-20-0949 (2021).
23. Poste, G. & Fidler, I. J. The pathogenesis of cancer metastasis. *Nature* **283**, 139-146, doi:10.1038/283139a0 (1980).
24. Greaves, M. & Maley, C. C. Clonal evolution in cancer. *Nature* **481**, 306-313, doi:10.1038/nature10762 (2012).
25. Kroigard, A. B. *et al.* Clonal expansion and linear genome evolution through breast cancer progression from pre-invasive stages to asynchronous metastasis. *Oncotarget* **6**, 5634-5649, doi:10.18632/oncotarget.3111 (2015).
26. Martelotto, L. G. *et al.* Whole-genome single-cell copy number profiling from formalin-fixed paraffin-embedded samples. *Nat Med* **23**, 376-385, doi:10.1038/nm.4279 (2017).
27. Walens, A. *et al.* Adaptation and selection shape clonal evolution of tumors during residual disease and recurrence. *Nat Commun* **11**, 5017, doi:10.1038/s41467-020-18730-z (2020).
28. Welter, L. *et al.* Treatment response and tumor evolution: lessons from an extended series of multianalyte liquid biopsies in a metastatic breast cancer patient. *Cold Spring Harb Mol Case Stud* **6**, doi:10.1101/mcs.a005819 (2020).
29. Maggiah, A. *et al.* Paired ductal carcinoma in situ and invasive breast cancer lesions in the D-loop of the mitochondrial genome indicate a cancerization field effect. *Biomed Res Int* **2013**, 379438, doi:10.1155/2013/379438 (2013).
30. Desmedt, C. *et al.* Uncovering the genomic heterogeneity of multifocal breast cancer. *J Pathol* **236**, 457-466, doi:10.1002/path.4540 (2015).
31. Visser, L. L. *et al.* Discordant Marker Expression Between Invasive Breast Carcinoma and Corresponding Synchronous and Preceding DCIS. *Am J Surg Pathol* **43**, 1574-1582, doi:10.1097/PAS.0000000000001306 (2019).
32. McCrorie, A. D. *et al.* Multifocal breast cancers are more prevalent in BRCA2 versus BRCA1 mutation carriers. *J Pathol Clin Res* **6**, 146-153, doi:10.1002/cjp2.155 (2020).
33. Sontag, L. & Axelrod, D. E. Evaluation of pathways for progression of heterogeneous breast tumors. *J Theor Biol* **232**, 179-189, doi:10.1016/j.jtbi.2004.08.002 (2005).
34. Mai, K. T. Morphological evidence for field effect as a mechanism for tumour spread in mammary Paget's disease. *Histopathology* **35**, 567-576, doi:10.1046/j.1365-2559.1999.00788.x (1999).
35. Foschini, M. P. *et al.* Genetic clonal mapping of in situ and invasive ductal carcinoma indicates the field cancerization phenomenon in the breast. *Hum Pathol* **44**, 1310-1319, doi:10.1016/j.humpath.2012.09.022 (2013).
36. Asioli, S., Morandi, L., Cavatorta, C., Cucchi, M. C. & Foschini, M. P. The impact of field cancerization on the extent of duct carcinoma in situ (DCIS) in breast tissue after conservative excision. *Eur J Surg Oncol* **42**, 1806-1813, doi:10.1016/j.ejso.2016.07.005 (2016).
37. Tan, M. P. Integration of 'sick lobe hypothesis' with concept of field cancerisation for a personalised surgical margin for breast conserving surgery. *J Surg Oncol* **116**, 954-955, doi:10.1002/jso.24728 (2017).
38. Going, J. J. & Mohun, T. J. Human breast duct anatomy, the 'sick lobe' hypothesis and intraductal approaches to breast cancer. *Breast Cancer Res Treat* **97**, 285-291, doi:10.1007/s10549-005-9122-7 (2006).
39. Tot, T. The theory of the sick breast lobe and the possible consequences. *Int J Surg Pathol* **15**, 369-375, doi:10.1177/1066896907302225 (2007).
40. Dooley, W., Bong, J. & Parker, J. Redefining lumpectomy using a modification of the "sick lobe" hypothesis and ductal anatomy. *Int J Breast Cancer* **2011**, 726384, doi:10.4061/2011/726384 (2011).

41. Tan, M. P. & Tot, T. The sick lobe hypothesis, field cancerisation and the new era of precision breast surgery. *Gland Surg* **7**, 611-618, doi:10.21037/gs.2018.09.08 (2018).
42. Petrova, S. C. *et al.* Regulation of breast cancer oncogenesis by the cell of origin's differentiation state. *Oncotarget* **11**, 3832-3848, doi:10.18632/oncotarget.27783 (2020).
43. Knudson, A. G., Jr. Heredity and human cancer. *Am J Pathol* **77**, 77-84 (1974).
44. Park, S., Supek, F. & Lehner, B. Systematic discovery of germline cancer predisposition genes through the identification of somatic second hits. *Nat Commun* **9**, 2601, doi:10.1038/s41467-018-04900-7 (2018).
45. Konishi, H. *et al.* Mutation of a single allele of the cancer susceptibility gene BRCA1 leads to genomic instability in human breast epithelial cells. *Proc Natl Acad Sci U S A* **108**, 17773-17778, doi:10.1073/pnas.1110969108 (2011).
46. Mazzola, E., Cheng, S. C. & Parmigiani, G. The penetrance of ductal carcinoma in situ among BRCA1 and BRCA2 mutation carriers. *Breast Cancer Res Treat* **137**, 315-318, doi:10.1007/s10549-012-2345-5 (2013).
47. Tegze, B. *et al.* Parallel evolution under chemotherapy pressure in 29 breast cancer cell lines results in dissimilar mechanisms of resistance. *PLoS One* **7**, e30804, doi:10.1371/journal.pone.0030804 (2012).
48. Gao, Y. *et al.* Single-cell sequencing deciphers a convergent evolution of copy number alterations from primary to circulating tumor cells. *Genome Res* **27**, 1312-1322, doi:10.1101/gr.216788.116 (2017).
49. Wang, F. *et al.* MEDALT: single-cell copy number lineage tracing enabling gene discovery. *Genome Biol* **22**, 70, doi:10.1186/s13059-021-02291-5 (2021).
50. Brommesson, S. *et al.* Tiling array-CGH for the assessment of genomic similarities among synchronous unilateral and bilateral invasive breast cancer tumor pairs. *BMC Clin Pathol* **8**, 6, doi:10.1186/1472-6890-8-6 (2008).
51. Regitnig, P., Ploner, F., Maderbacher, M. & Lax, S. F. Bilateral carcinomas of the breast with local recurrence: analysis of genetic relationship of the tumors. *Mod Pathol* **17**, 597-602, doi:10.1038/modpathol.3800089 (2004).
52. Ma, X. J. *et al.* Gene expression profiles of human breast cancer progression. *Proc Natl Acad Sci U S A* **100**, 5974-5979, doi:10.1073/pnas.0931261100 (2003).
53. Porter, D. *et al.* Molecular markers in ductal carcinoma in situ of the breast. *Mol Cancer Res* **1**, 362-375 (2003).
54. Castro, N. P. *et al.* Evidence that molecular changes in cells occur before morphological alterations during the progression of breast ductal carcinoma. *Breast Cancer Research* **10**, doi:ARTN R87 10.1186/bcr2157 (2008).
55. Dettogni, R. S. *et al.* Potential biomarkers of ductal carcinoma in situ progression. *BMC Cancer* **20**, 119, doi:10.1186/s12885-020-6608-y (2020).
56. Song, G. *et al.* Identification of aberrant gene expression during breast ductal carcinoma in situ progression to invasive ductal carcinoma. *J Int Med Res* **48**, 300060518815364, doi:10.1177/0300060518815364 (2020).
57. Abba, M. C. *et al.* Transcriptomic changes in human breast cancer progression as determined by serial analysis of gene expression. *Breast Cancer Res* **6**, R499-513, doi:10.1186/bcr899 (2004).
58. Schuetz, C. S. *et al.* Progression-specific genes identified by expression profiling of matched ductal carcinomas in situ and invasive breast tumors, combining laser capture microdissection and oligonucleotide microarray analysis. *Cancer Res* **66**, 5278-5286, doi:10.1158/0008-5472.CAN-05-4610 (2006).
59. Lee, S. *et al.* Differentially expressed genes regulating the progression of ductal carcinoma in situ to invasive breast cancer. *Cancer Res* **72**, 4574-4586, doi:10.1158/0008-5472.CAN-12-0636 (2012).

60. Coradini, D., Boracchi, P., Ambrogi, F., Biganzoli, E. & Oriana, S. Cell polarity, epithelial-mesenchymal transition, and cell-fate decision gene expression in ductal carcinoma in situ. *Int J Surg Oncol* **2012**, 984346, doi:10.1155/2012/984346 (2012).
61. Knudsen, E. S. *et al.* Progression of ductal carcinoma in situ to invasive breast cancer is associated with gene expression programs of EMT and myoepithelia. *Breast Cancer Res Treat* **133**, 1009-1024, doi:10.1007/s10549-011-1894-3 (2012).
62. Krstic, M. *et al.* TBX3 promotes progression of pre-invasive breast cancer cells by inducing EMT and directly up-regulating SLUG. *Journal of Pathology* **248**, 191-203, doi:10.1002/path.5245 (2019).

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12/7/2022

1:40 PM - 2:00 PM

Defining recurrence risk for DCIS: How do we tailor therapy

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In tailoring treatment for DCIS, the goal is to avoid overtreatment while minimizing risk of recurrence. This necessitates estimation of recurrence risk and assessment of efficacy of each intervention in reducing risk. There are several clinicopathologic and treatment factors that have been proven in prospective trials to affect risk. These have been combined into a multivariable nomogram that estimates 10-year risk of recurrence (DCIS Nomogram). It is available online and free-of-charge, and has been validated in at least 5 independent populations with assessments of calibration and discrimination to assess its utility.

There have also been attempts to develop genomic predictors of risk. The Oncotype DCIS score originally was based on a purely genomic analysis, but was "refined" to include clinicopathologic factors. DCISionRT was initially created with the inclusion of clinicopathologic factors. Neither has been prospectively validated and neither has published any assessments of calibration and discrimination. It is unclear what proportion of either risk estimate is due to the inclusion of clinicopathologic factors vs the actual genomic analysis. Both cost thousands of dollars.

Furthermore, neither the refined Oncotype DCIS score nor the DCISionRT score incorporates the use of endocrine therapy. Tamoxifen and aromatase inhibitors have been proven to reduce the risk of recurrence by about 30-50%, and their use should be expected to decrease risk of recurrence. Yet, neither score accounts for this fact, and therefore the risk predictions are too high for those that take endocrine therapy, and too low for those that do not.

In a sample of 59 women age ≥ 50 years old, with DCIS ≤ 2.5 cm in size and clear margins, 10-year recurrence risk estimates from the DCIS Nomogram and refined Oncotype DCIS score (RDS) were compared. Overall, RDS risk estimates were in agreement (within 1-2% of the nomogram risk estimate range, calculated with and without the use of endocrine therapy) in 92% of cases. Among the 5 patients for which the Nomogram and RDS estimates disagreed, all had close margins (≤ 2 mm). Close margins are associated with a statistically significant doubling of risk of recurrence. Nevertheless, the Oncotype DCIS score 10-year recurrence estimate was only 5-8% for these patients with close margins, while the Nomogram estimates were 11-14% (assuming use of endocrine therapy) or 21-27% (without endocrine therapy). From all published data, it seems clear that the refined Oncotype DCIS score markedly underestimates risk for those with close margins. And for those with clear margins, there was excellent (100%) agreement between the Nomogram and the refined Oncotype DCIS score.

Given the need for cost-based value in health care, and given the cost-free availability of a validated predictive online DCIS nomogram, rigorous evaluation of predictive accuracy and proof of significant *added* clinical benefit should be performed and made available before any new expensive commercially available test is adopted for clinical use.

Disclosure(s):

Kimberly Van Zee, MS, MD, FACS: No financial relationships to disclose

12/7/2022

2:00 PM - 2:20 PM

To clip or not to clip (Part 1)

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Clinically node positive breast cancer patients often receive neoadjuvant chemotherapy which can eradicate nodal disease. While sentinel node dissection alone has been shown to predict treatment response with a false negative rate of 12-14%, it is possible to increase the accuracy by performing targeted axillary dissection (TAD). To perform TAD, a clip is placed in a node if biopsy confirms disease. The procedure then involves selectively localizing and removing the clipped node in addition to the sentinel nodes. Multiple studies have shown that this approach has a false negative rate of <5%. These studies also show that the clipped node is not retrieved as a sentinel node in > 20% of cases. This means that evaluating the sentinel nodes alone would miss evaluating the node with confirmed disease in a significant proportion of patients. This session will focus on the question of whether there is benefit to placing clips in nodes and ensuring removal after neoadjuvant chemotherapy.

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2:00 PM - 2:20 PM

To clip or not to clip (Part 2)

Presenting Author(s) and Co-Author(s):

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Neoadjuvant chemotherapy (NAC) changed the breast surgery approach and increased indications in recent years. NAC allows to downstage the primary tumor and also may clear the axilla of lymph node metastases in some patients. In fact, NAC allows de-escalation of surgery: not only resulted in an increase in conservative surgery in 40%, which was the initial goal of chemotherapy, but in particular it allows for a reduction in axillary surgery. Furthermore, in relation to the molecular characteristics of the tumors we can have a pathological complete response (pCR) ranging from 20 to 80%. In node-positive patients who converted to cN0 different prospective studies ACOSOG Z1071, SENTINA, SN FNAC and GANEA 2, have demonstrated that the FNR of the SNB was high, more than the acceptable 10%. Therefore, strategies to reduce the FNR treatment in cN+ patients are being investigated: is to remove more than three negative axillary lymph nodes or marking of positive axillary nodes with a tattoo or clip, the so-called target axillary dissection (TAD), to document their removal. But all the effort to reduce the FNR rate do not have clinical prognostic significance. This has already been demonstrated in the literature in different randomized trials with long term follow up. The 10-year follow-up of our study confirmed our preliminary data that the use of standard sentinel node biopsy (SNB) without the use of clip is acceptable in cN1/2 patients who become cN0 after NAT and will not translate into a worse outcome. In fact, the axillary recurrences found were less than 2% in particular in the group that started from a positive axilla were 1.8 %, if we considered that 2 of them had a micrometastatic SN and refused the AD, but if we considered only those with a negative SN the percentage drops to 0.9% Similar positive data with different follow up were also confirmed by other studies that used SNB alone without TAD. All these studies data, with now comforting results on the follow up, confirm that SN surgery alone for selected patients who have an excellent response to NAC is not oncologically inferior to AD during a short- and long-term follow-up.

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Clinical Controversies

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Disclosure(s):

Lisa Carey, MD, ScM, FASCO: AstraZeneca/Daiichi Sankyo: Uncompensated Relationships (Ongoing); Eisai: Uncompensated Relationships (Ongoing); Exact Sciences: Uncompensated Relationships (Ongoing); Falcon Therapeutics: Receipt of Intellectual Property Rights / Patent Holder (Ongoing); G1 Therapeutics: Uncompensated Relationships (Ongoing); Genentech/Roche: Uncompensated Relationships (Ongoing); GSK: Uncompensated Relationships (Ongoing); Lilly: Uncompensated Relationships (Ongoing); NanoStringTechnologies: Contracted Research (Ongoing); Novartis: Contracted Research (Ongoing), Uncompensated Relationships (Ongoing); Sanofi: Uncompensated Relationships (Ongoing); Seagen: Uncompensated Relationships (Ongoing); Seattle Genetics: Contracted Research (Ongoing); Syndax: Contracted Research (Ongoing); Veracyte: Contracted Research (Ongoing)

12/7/2022

2:20 PM - 2:40 PM

Duration of endocrine therapy

Presenting Author(s) and Co-Author(s):

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Patients with hormone-receptor positive, early-stage breast cancer are at considerable risk for late recurrence.

Previous randomized clinical trials have shown that extending adjuvant tamoxifen to ten vs. five years improves disease-free survival (and overall survival in one trial). Adding five years of an aromatase inhibitor (AI) after five years of tamoxifen has also been shown to significantly improve disease-free survival in postmenopausal patients. Benefit from extending adjuvant AI therapy beyond five years in patients who have received five years of an AI or tamoxifen+AI has also been recently demonstrated in several clinical trials but the absolute benefit appears small and the ideal duration of the extended therapy is still a topic of debate.

Over the past decade, efforts have focused on identifying predictors of risk of late recurrence and predictors of benefit from extended endocrine therapy. Clinicopathologic factors and circulating tumor cells can predict risk of late recurrence but not benefit from extended ET. Several commercially available genomic classifiers can further stratify risk of late recurrence, and some have also been found to predict benefit from extended ET. Their clinical utility for tailoring the use of extended endocrine therapy continues to evolve.

Disclosure(s):

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Kathryn Ruddy, MD, MPH: UpToDate: Royalty (Ongoing)

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2:40 PM - 3:00 PM

Post neoadjuvant therapy in TNBC

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Heather McArthur, MD, MPH: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Bristol-Myers Squibb: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Crown Bioscience: Consulting Fees (e.g., advisory boards) (Terminated, April 24, 2021); Daiichi-Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Terminated, October 7, 2021); Immunomedics: Consulting Fees (e.g., advisory boards) (Terminated, December 10, 2020); Lilly: Consulting Fees (e.g., advisory boards) (Terminated, October 14, 2020); Merck: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Puma: Consulting Fees (e.g., advisory boards) (Terminated, May 1, 2021); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Terminated, October 7, 2021)

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2:00 PM - 2:20 PM

Activating a collaborative innate-adaptive immune response to control metastasis

Presenting Author(s) and Co-Author(s):

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Tumor-associated macrophages (TAMs) promote metastasis and inhibit T cells, but we have shown that macrophages isolated from pleural effusions can be polarized to kill breast cancer cells using monophosphoryl lipid A (MPLA) and interferon (IFN) γ . MPLA + IFN γ injected intratumorally or intraperitoneally reduces primary tumor growth and metastasis in breast cancer mouse models. Mechanistically, MPLA + IFN γ stimulates type I IFN signaling, reprograms CD206⁺ TAMs to inducible NO synthase (iNOS)⁺ macrophages, and activates cytotoxic T cells through macrophage-secreted interleukin-12 (IL-12) and tumor necrosis factor alpha (TNF α). MPLA and IFN γ are used individually in clinical practice and together represent a previously unexplored approach for engaging a systemic anti-tumor immune response.

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2:00 PM - 3:00 PM

Forum 2: New Targets and Strategies for Immunotherapy

Presenting Author(s) and Co-Author(s):

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12/7/2022

2:20 PM - 2:40 PM

Neutrophil elastase and anti-tumor effects

Presenting Author(s) and Co-Author(s):

Lev Becker, PhD - *The University of Chicago*

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Cancer cell genetic variability and similarity to host cells have stymied development of broad anti-cancer therapeutics. Our innate immune system evolved to clear genetically diverse pathogens and limit host toxicity; however, whether/how innate immunity can produce similar effects in cancer is unknown. Here, we show that human, but not murine, neutrophils release catalytically active neutrophil elastase (ELANE) to kill many cancer cell types while sparing non-cancer cells. On a molecular level, ELANE proteolytically liberates the CD95 death domain, which interacts with histone H1 isoforms to selectively eradicate cancer cells. In pre-clinical models, ELANE attenuates primary tumor growth and produces a CD8+ T cell-mediated abscopal effect to attack distant metastases, therapeutic effects that are improved on by porcine pancreatic elastase, an ELANE homolog that better resists protease inhibitors in the tumor microenvironment. Altogether, our studies suggest that ELANE kills genetically diverse cancer cells with minimal toxicity to non-cancer cells, raising the possibility of developing it as a broad anti-cancer therapy.

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2:40 PM - 3:00 PM

Immunosuppressive macrophages and PARP inhibitor resistance

Presenting Author(s) and Co-Author(s):

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Despite objective responses to poly(ADP-ribose) polymerase (PARP) inhibition and improvements in progression-free survival (PFS) compared to standard chemotherapy in patients with BRCA-associated triple-negative breast cancer (TNBC), benefits are transitory. Using high-dimensional single-cell profiling of human TNBC, here we demonstrate that macrophages are the predominant infiltrating immune cell type in breast cancer susceptibility (BRCA)-associated TNBC. Macrophages are an innate immune cell that play a critical role in host defense and maintaining tissue homeostasis, however their infiltration into tumors has been associated with disease progression and resistance to therapy. Tumor associated macrophages (TAMs) represent a significant proportion of solid tumors, including breast cancer. TAMs play a major role in tumorigenesis as they can enhance tumor cell growth, angiogenesis and metastasis. In addition, TAMs can inhibit anti-tumor responses of T cells. Our recent work has shown that removal or conversion of TAMs to an anti-tumor phenotype enhances chemo- and immuno-therapy establishing TAMs as targets for anti-cancer therapy. Through multi-omics profiling, we show that PARP inhibitors enhance both anti- and pro-tumor features of macrophages through glucose and lipid metabolic reprogramming, driven by the sterol regulatory element-binding protein 1 (SREBF1, SREBP1) pathway. Combining PARP inhibitor therapy with colony-stimulating factor 1 receptor (CSF1R)-blocking antibodies significantly enhanced innate and adaptive antitumor immunity and extended survival in mice with BRCA-deficient tumors *in vivo*, and this was mediated by CD8+ T cells. Collectively, our results uncover macrophage-mediated immune suppression as a liability of PARP inhibitor treatment and demonstrate that combined PARP inhibition and macrophage-targeting therapy induces a durable reprogramming of the tumor microenvironment (TME), thus constituting a promising therapeutic strategy for TNBC. Therefore, targeting TAMs offers great potential to enhance both chemo- and immuno-therapy. Deep analysis of TAMs in solid tumors has revealed the complexity of TAMs and revealed major gaps in our knowledge of the functional and phenotypic characterization of TAM subsets associated with cancer, before and after treatment. Here we will discuss the complexity of TAMs in solid tumors including characterizing TAM subsets, location, and crosstalk with neighboring cells, as well as novel TAM-modulating strategies and combinations that are likely to enhance current therapies and overcome chemo- and immuno-therapy resistance.

12/7/2022

2:00 PM - 2:20 PM

NK cell induced dormancy

Presenting Author(s) and Co-Author(s):

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12/7/2022

2:00 PM - 3:00 PM

Mini Symposium 2: Late Recurrence and Tumor Dormancy

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Alana Welm, PhD - *University of Utah*

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12/7/2022

2:20 PM - 2:40 PM

Extra cellular matrix and dormancy

Presenting Author(s) and Co-Author(s):

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Breast cancer metastasis develops from disseminated cancer cells (DCCs) that leave the primary tumor and seed in distant organs. In those organs, DCCs undergo a period of dormancy during which cancer cells remain occult, in a non-proliferative state, before metastases become detectable. In this seminar I will discuss how disseminated cancer cells enter in dormancy at metastatic sites and the importance of the ECM in this process. We have found that dormant cancer cells express a specific set of ECM genes, "*the matrisome*", that is lost upon break from dormancy. ECM proteomics identify tumor-derived COL3A1 as a key ECM component required for tumor cell dormancy at metastatic organs. Intravital imaging and SHG microscopy reveals that the dormancy-to-reactivation transition is accompanied by changes in collagen three-dimensional architecture. Our data reveal a novel barrier to metastasis through a mechanism by which DCCs depend on the assembly of a pro-quiescence ECM to establish a niche that sustains dormancy.

12/7/2022

2:40 PM - 3:00 PM

Implications for clinical care

Presenting Author(s) and Co-Author(s):

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Late recurrence, commonly considered to be distant recurrence five or more years after initial diagnosis remains a formidable challenge in breast oncology. Current management focuses on slowing the growth of macroscopic recurrent disease which is generally considered incurable. Emerging tools to identify minimal residual disease or tumor dormancy hold great promise to transform the treatment landscape in this space. This mini-symposium discussion will review the scope of the clinical challenge, highlighting the numbers at risk and the timeframe for recurrence risk. Current and emerging tools to assess the risk in individual patients beyond 5 years from diagnosis will be discussed. Evidence and guidelines on the use of clinically available anatomic-based and genomic assay-based late risk assessment tools including Clinical Treatment Score post-5 years (CTS5) and the Breast Cancer Index (BCI) will be highlighted. Current data on the role of circulating biomarkers including ctDNA, to identify at risk patients will be discussed as will open questions on how this might impact treatment approach. Finally, possible therapeutic approaches following the identification minimal residual or dormant disease will be reviewed, as will trial design options in this rapidly evolving space in breast oncology.

Disclosure(s):

Alexandra Thomas, MD, FACP: BeyondSpring Pharmaceuticals: Consulting Fees (e.g., advisory boards) (Ongoing); Bristol-Myers Squibb: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Doximity: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Genentech: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead Sciences: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Merck: Contracted Research (Ongoing); Pfizer: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Sanofi: Contracted Research (Ongoing)

12/7/2022

3:00 PM - 3:40 PM

Bioengineering and mechanism of action of ADCs

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12/7/2022

3:00 PM - 5:00 PM

Educational Session: Antibody Drug Conjugates: Future Directions and Opportunities

Presenting Author(s) and Co-Author(s):

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12/7/2022

3:40 PM - 4:20 PM

ADCs in breast oncology: Present and future

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12/7/2022

4:20 PM - 5:00 PM

Mechanisms of resistance

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Mechanisms of resistance to Antibody Drug Conjugates

Leif W. Ellisen, M.D., Ph.D.

Program Director, Breast Oncology, Mass General Hospital Cancer Center

Professor of Medicine, Harvard Medical School.

Antibody Drug Conjugates (ADCs) are emerging as promising therapeutics for all subtypes of breast cancer. ADCs are composed of a monoclonal antibody directed against a tumor-expressed antibody, conjugated via a variety of linker chemistries to a cytotoxic or other tumor-active payload. Tumor-selective drug delivery via ADCs has the potential to substantially improve the therapeutic window and efficacy for a variety of therapeutic agents. Indeed, recent clinical data have demonstrated significant improvements in overall survival with the use of single-agent ADCs across the spectrum of advanced breast cancer. However, both de novo and acquired resistance to ADCs is common, and may involve a diverse array of potential mechanisms that reflect the complexity of ADC action. These include alteration or downregulation of the ADC target, deregulation of intracellular trafficking or endolysosomal processing of the internalized ADC, and a variety of payload-specific mechanisms of resistance such as induction of drug efflux or activation of cell survival pathways. Which mechanism(s) dominates in a given setting may depend on both ADC-specific and tumor-specific factors. For example, linker design is likely to have a major influence on potential ADC resistance: ADCs with a non-cleavable linker (e.g. trastuzumab emtansine) are dependent upon fusion with acidified lysosomes for degradation and payload release, and attenuated acidification has been demonstrated pre-clinically as a resistance mechanism. In contrast, ADCs with a cleavable peptide linker (e.g. trastuzumab deruxtecan) may not require lysosomal processing for payload release. Furthermore, highly genetically unstable tumors may simultaneously generate multiple types of resistance mechanisms. We recently demonstrated the emergence of distinct acquired resistance mutations to sacituzumab govitecan, involving the ADC antibody target (TROP2) and the payload target (topoisomerase 1), within different metastatic lesions of an individual patient. General strategies to overcome ADC resistance include the sequential use of multiple ADCs, and/or the up-front use of select combination therapies incorporating ADCs. Clearly, the success of these approaches will require a more thorough evaluation and understanding of resistance mechanisms as they occur in patients. Fortunately, the relative success of ADCs for breast cancer treatment to date is spurring the identification of new targets, approaches for linker design, and a wide diversity of payloads that will be instrumental for efforts to overcome resistance.

Disclosure(s):

Leif Ellisen, MD, PhD: Kisoji Biotechnology: Consulting Fees (e.g., advisory boards) (Ongoing); Mersana Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing)

12/7/2022

3:00 PM - 3:30 PM

What are PROs and evidence for benefit?

Presenting Author(s) and Co-Author(s):

Shoshana Rosenberg, ScD, MPH - *Weill Cornell Medicine*

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Patient-reported outcomes (PROs) are self-reported assessments provided directly by patients. PROs can be used for research, to tailor and improve clinical and supportive care, and for quality assessment purposes. It is well-established that PROs, rather than clinician evaluations, better capture the patient experience. Additionally, there is growing evidence supporting the routine incorporation of PROs into clinical practice. In particular, the use of PRO-based interventions is associated with improved symptom management, enhanced patient-provider communication, and better outcomes, including quality of life and survival, in patients with advanced cancer. Among patients in the post-active treatment and survivorship phase of care, PROs are critical in identifying and understanding late and long-term effects of treatment, identifying unmet needs, and determining if survivors are receiving appropriate follow-up care. There are also data in the survivorship setting demonstrating how PROs can predict other outcomes, such as adherence to aromatase inhibitors in breast cancer survivors. Careful consideration of age (e.g., pediatric vs. adult measures), race and ethnicity (e.g., was the measure validated in a diverse and representative population), language (e.g., was the measure validated in other languages), literacy level (e.g., was the measure written for individuals with low literacy levels), mode of delivery (e.g., paper vs. tablet), and participant burden (e.g., does the assessment take a reasonable amount of time) when selecting PROs is critical to ensure that the information learned is generalizable and that the benefit patients can gain through the incorporation of PROs into cancer care is equitable.

Disclosure(s):

Shoshana Rosenberg, ScD, MPH: Pfizer: Contracted Research (Ongoing)

12/7/2022

3:00 PM - 5:00 PM

Educational Session: Digital Health and PROs in Breast Cancer Research and Care

Presenting Author(s) and Co-Author(s):

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Disclosure(s):

Ann Partridge, MD, MPH: Patient-Centered Outcomes Research Institute (AFT-25 COMET):

Contracted Research (Ongoing); UpToDate: Royalty (Ongoing)

12/7/2022

3:30 PM - 4:00 PM

How to incorporate PROs into clinical care

Presenting Author(s) and Co-Author(s):

Oluwadamilola (Lola) Fayanju, MD, MA, MPHS, FACS - *Perelman School of Medicine at the University of Pennsylvania*

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State: PA

Country: United States

Patient-reported outcomes (PROs) are self-reported assessments of health status that come from the patient's perspective. Communicated without interpretation by a physician, PROs can enhance shared-decision making. When administered in multi-lingual, level-appropriate, and culturally aware formats, PROs can be used to address the individual and collective health status of potentially vulnerable groups including children, older adults, those with disabilities, and those from racial/ethnic minority backgrounds thereby providing an opportunity not only to address the needs of individuals but also identify potential disparities across groups. In her talk, Dr. Fayanju will provide strategies to facilitate incorporation of PROs into routine patient care and describe the benefits and potential challenges associated with doing so.

Disclosure(s):

Oluwadamilola (Lola) Fayanju, MD, MA, MPHS, FACS: No financial relationships to disclose

12/7/2022

4:00 PM - 4:30 PM

Where are we going with digital interventions and PROs

Presenting Author(s) and Co-Author(s):

Ines Vaz Luis, PhD - *Gustave Roussy*

City: Villejuif

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Rational: Lately, digital health has shown potential to facilitate cancer care delivery. We now have data that demonstrated that systems integrating self-reporting of common symptoms during treatment for both adjuvant and metastatic breast cancer treatment and allowing for patient remote monitoring result not only result in better quality of life and less emergency room visits, but, in some settings, also lead to significant survival benefit. In addition, some studies incorporating self-management strategies that do not need heavy clinician involvement have shown promising results to manage acute and long and late term physical, social, and psychological effects of cancer and its treatment.

Objectives: In this talk, we will 1) review data on the existing digital health solutions that can be used in clinical care. In addition, 2) we will reflect on what is next in digital health innovation, particularly a) how the integration of technology, including digital companions facilitating remote monitoring, education and self-management, may serve as a vehicle to promote continuous care b) innovative emerging digital health tools (including, although not limited to wearables and digital therapeutics). Finally, 3) we will examine how digital health can address the needs of every patient, avoid pitfalls such as contributing to health disparities.

12/7/2022

4:30 PM - 5:00 PM

Patient Advocate Perspective

Presenting Author(s) and Co-Author(s):

Patty Spears, BS - *University of North Carolina*

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Patient reported outcome (PRO) measures can be collected in clinical trials or clinical care through questionnaires. PROs allow a direct measure of how a patient is feeling and functioning, directly from the patient without interpretation by another person or clinician. PROs give patients a voice. Although there are challenges to collecting PROs, these challenges can be overcome. When deciding which measures to collect there are some things to keep in mind. For example, if the questions are relevant and meaningful to what the patient is experiencing they will be more likely to fill them out, providing useful information. The questionnaires can also be given in multiple formats (electronic, paper, telephone) to accommodate the preferences of different patients. However, collecting PROs is not enough, the information collected needs to be used to inform future patients or inform patient care. Additional challenges and benefits of collecting PROs in breast cancer research and clinical care from the patient perspective will be discussed.

Disclosure(s):

Patty Spears, BS: Pfizer, Inc: Consulting Fees (e.g., advisory boards) (Ongoing)

12/7/2022

3:00 PM - 3:30 PM

Single cell profiling

Presenting Author(s) and Co-Author(s):

Alex Swarbrick, PhD - *Garvan Institute of Medical Research*

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Disclosure(s):

Alex Swarbrick, PhD: No financial relationships to disclose

12/7/2022

3:00 PM - 5:00 PM

Educational Session: Spatial and Single Cell Characterization of Breast Cancer Progression

Presenting Author(s) and Co-Author(s):

Christina Curtis, PhD, MSc - *Stanford University School of Medicine*

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Country: United States

Recent years have seen an explosion of single cell and spatial methods to interrogate cellular and tissue biology in native context. This session will highlight recent advances in single cell and spatial profiling of breast cancer. An expert faculty panel will share their experience with different platforms ranging from single cell sequencing (RNA, ATAC, DNA), to multiplexed proteomic profiling and imaging mass cytometry. Speakers will review study design considerations, measurement types and interpretation as well as practical considerations for the implementation of these methods. Focus will be placed on the application of these methods to breast cancer patient cohorts and the types of questions that can be addressed. Lastly, we will close with the future clinical outlook for these approaches.

12/7/2022

3:30 PM - 4:00 PM

Multiplex spatial proteomic profiling

Presenting Author(s) and Co-Author(s):

David Rimm, MD, PhD - *Yale University*

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Multiplex spatial analysis is touted as a potential solution for tissue biomarkers for prognostic and companion diagnostic applications. Spatial analysis infers maintaining the location of a biomolecule so that both its amount and context can contribute to the information obtained. Immunohistochemistry (IHC) is the archetypal method of spatial profiling and the only application that has made it to the clinic. In this session, we will discuss technologies based on IHC, but that allow assessment of at least two, and as many as 100 or more proteins within the cell or molecular compartment that maintains spatial context. The simplest and most common approach is multiplex immunofluorescence, followed by a number of next generation techniques that use alternative labeling of the antibodies or cycling strategies or both to generate spatially informed data. Excluding Mass spectrometry-based methods, still in early stages, the highest “plex” method for protein is digital spatial profiling. Digital spatial profiling (DSP) uses a molecular method to define spatial compartments which is different from other high-plex methods that use cell segmentation, an image analysis method that largely depends on the presence of a cell nucleus in the image. As a result, the DSP method allows assessment of both cellular and non-cellular stromal compartments. DSP and other high-plex methods that will be discussed are thought to be best used as biomarker discovery tools, that might find biomarkers that can be measured with a more traditional approach for assessment in the clinic.

12/7/2022

4:00 PM - 4:30 PM

Imaging mass cytometry of breast cancer

Presenting Author(s) and Co-Author(s):

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12/7/2022

4:30 PM - 5:00 PM

Beyond the lab: Clinical implications

Presenting Author(s) and Co-Author(s):

Christina Curtis, PhD, MSc - *Stanford University School of Medicine*

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During this talk, I will review the ever expanding repertoire of single cell and spatially resolved profiling techniques which enable the interrogation breast cancer pathology, immuno-biology and treatment response at unprecedented resolution. I will outline considerations for throughput, plex and resolution across different methods before providing several case studies in their application. As one example, I will outline the use of multi-omic single cell profiling and spatial proteomic profiling to characterize changes throughout the course of neoadjuvant Her2-targeted therapy and leading to the identification of candidate predictive biomarkers. I will go on to discuss translational and potential clinical applications of these techniques.

12/7/2022

3:00 PM - 3:30 PM

Beyond anthracyclines and trastuzumab: Cardiotoxicity of novel agents

Presenting Author(s) and Co-Author(s):

Susan Dent, MD - *Duke University*

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Breast cancer treatment can have a diverse array of delayed and long-term effects, including cardiovascular events such as heart failure, valvular damage, coronary artery disease, arrhythmias, and cardiac dysfunction. The adverse cardiovascular effects of anthracyclines and trastuzumab in the treatment of early and advanced breast cancer have been well elucidated with the literature; however, there is less understanding of the potential cardiovascular impact of more recent novel breast cancer therapies. Dual HER2 targeted therapy (pertuzumab/trastuzumab) is now standard of care for neoadjuvant and adjuvant treatment, particularly in the setting of lymph node involvement, but is there a higher risk of cardiotoxicity? There is a limited understanding of the potential short- and long-term cardiovascular toxicity associated with antibody-drug conjugates, such as T-DM1 and fam-trastuzumab deruxtecan, and well as oral anti-HER2 tyrosine kinase inhibitors such as lapatinib, neratinib, and more recently tucatinib. CDK4/6 inhibitors (eg ribociclib) combined with endocrine therapy have significantly improved clinical outcomes for individuals with hormone receptor positive, HER-2 advanced breast cancer but are associated with an increased risk of QTc prolongation, which can be compounded by electrolyte abnormalities and drug-drug interactions. Immune checkpoint inhibitors (pembrolizumab) are approved in the neoadjuvant (high risk) and advanced setting (PDL-1 positive) for triple negative breast cancer but are associated with several toxicities including endocrinopathies and rarely fatal myocarditis. The goal of this session is to improve the awareness and understanding of the potential cardiovascular toxicities associated with modern anti-cancer therapies used in the treatment of breast cancer.

12/7/2022

3:00 PM - 5:30 PM

Educational Session: Breast Cancer and Cardiovascular Toxicity: What an Oncologist Needs to Know

Presenting Author(s) and Co-Author(s):

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Susan Dent, MD - *Duke University*

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12/7/2022

3:30 PM - 4:00 PM

Radiation therapy and cardiovascular disease in breast cancer

Presenting Author(s) and Co-Author(s):

Carmen Bergom, MD, PhD - *Washington University in St. Louis*

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This presentation will review the topic of radiation-induced cardiac dysfunction in patients with breast cancer. Specific areas of discussion include the a review of the cardiac-sparing techniques available for radiation therapy in breast cancer treatment; guidelines for the prevention, diagnosis, and treatment of cardiac dysfunction after radiation exposure in patients with breast cancer; and new areas of research in the field of radiation-induced cardiac disease in breast cancer. Emerging knowledge of how concurrent systemic therapies may interact with radiation to affect heart function will also be discussed. In addition, future directions in the field of radiation-induced heart dysfunction will be reviewed.

12/7/2022

4:00 PM - 4:30 PM

Cardiovascular toxicity and breast cancer: Detection and prevention strategies

Presenting Author(s) and Co-Author(s):

Dinesh Thavendiranathan, MD, MSc - *Peter Munk Cardiac Center, Toronto General Hospital, University of Toronto*

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The presentation will discuss the potential cardiovascular toxicities (e.g., heart failure, coronary artery disease, arrhythmias) that are seen in women with breast cancer with a particular focus on those receiving cancer therapy. It will discuss the associated drugs, timing, the severity, and treatment options. The presentation will also include strategies that could be considered for risk stratification of patients prior to initiation of cancer therapy, methods to identify early cardiovascular injury, and primary prevention options. Recent guidelines including the ESC cardio-oncology guidelines and the prior ASCO guidelines will be highlighted. Practical approaches to assessment and management of cardiovascular toxicities will also be discussed. The presentation will wrap up providing potential future directions in the field.

12/7/2022

4:30 PM - 5:00 PM

Cardiac Problems Secondary to Chemotherapy Perspective 1

Presenting Author(s) and Co-Author(s):

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12/7/2022

5:00 PM - 5:30 PM

Cardiac Problems Secondary to Chemotherapy Perspective 2

Presenting Author(s) and Co-Author(s):

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12/7/2022

5:00 PM - 6:15 PM

Ongoing Trials 2

12/7/2022

5:00 PM - 6:15 PM

OT2-01-01

Trial in Progress: Clinical Utility of Fluoroestradiol F18 PET/CT in Metastatic Breast Cancer Patients with ER-Positive and HER2-Negative Primary Lesions after Progression on First Line Hormonal Therapy

Presenting Author(s) and Co-Author(s):

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BACKGROUND: Cyclin-dependent kinase 4/6 (CDK4/6) inhibitors combined with endocrine therapy are the recommended first-line standard-of-care (SOC) treatment for estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer (MBC) patients. After progression on first-line treatment, current clinical practice guidelines (NCCN, ESMO) recommend to sequence endocrine therapy (in absence of visceral crisis) until there is no clinical benefit after up to 3 regimens, and subsequently initiate chemotherapy regimens. However, clinical benefit for endocrine monotherapy after progression on first-line standard-of-care is limited, with median progression-free survival (PFS) of 2-5 months. Multiple factors can contribute to endocrine therapy resistance, including changes in ER expression, (epi)genetic mutations, and/or clonal selection under therapeutic pressure. ER heterogeneity can occur over time (temporal) as well as between lesions in a patient (spatial). As confirmed by tissue biopsy, greater than 20% of MBC patients have discordance in ER expression between their primary tumor and a metastatic lesion. Measuring total ER heterogeneity in a patient – the variation in ER expression at whole body level across all MBC lesions – is not clinically feasible by tissue biopsy alone. Fluoroestradiol F18 (Cerianna), also called 18F-FES, is a radioactive diagnostic agent that can be used with PET/CT for in vivo detection of ER-positive lesions in MBC with high accuracy. Results from 18F-FES PET/CT studies have shown that ER expression across MBC lesions at whole body level is heterogeneous in approximately half of ER-positive, HER2-negative MBC patients. In this study, we aim to evaluate the clinical utility of 18F-FES PET/CT to guide second-line treatment decision in ER-positive, HER2-negative MBC patients with progressive disease on first-line SOC hormonal therapy. **METHODS:** Fluoroestradiol F18 (Cerianna) is being evaluated in a phase 4, open-label, prospective cohort study enrolling 206 patients at 20-30 centers in the United States. Patients diagnosed with ER-positive, HER2-negative MBC who have progressive disease on first-line aromatase inhibitor therapy with or without CDK4/6 inhibitor

will be included in the study; patients with isolated hepatic metastases will be excluded. All patients will undergo an 18F-FES PET/CT scan. The treating physician will complete a standardized questionnaire to indicate the second-line therapeutic management plan before the scheduled 18F-FES PET/CT. After interpretation of 18F-FES PET/CT by local radiologist or nuclear medicine physician, imaging results will be provided to the treating physician who will then fill out a similar questionnaire to specify the final therapeutic decision. The proportion of patients with a change in therapeutic management plan based on incorporation of 18F-FES PET/CT results will be the primary endpoint. During the study follow-up period of 18 months, data on SOC imaging, treatments/procedures received, and clinical outcomes will be collected. Secondary endpoints include visual and quantitative heterogeneity assessment of tumor 18F-FES uptake, and PFS rates at 6 months and 18 months after 18F-FES PET/CT, which will be assessed between patients with and without a change in therapeutic management plan. The trial is planned to begin enrollment in Q3 2022. Clinical trial information: NCT05068726

Disclosure(s):

Stephanie van de Ven, MD, PhD: GE Healthcare: Salary (Ongoing)

Feng Luo, MD, PhD: GE Healthcare: Salary (Ongoing)

Nicholas DiGregorio, DO, MBA: GE Healthcare: Salary (Ongoing)

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12/7/2022

5:00 PM - 6:15 PM

OT2-01-02

The SMILE Study: A phase II trial of onapristone in combination with fulvestrant for patients with ER-positive and HER2-negative metastatic breast cancer after progression on endocrine therapy and CDK 4/6 inhibitors

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Background Antiprogestins, including selective progesterone receptor (PgR) modulators (SPRMs) that act as PgR antagonists, are a promising class of therapeutics for overcoming endocrine resistance including in patients who develop activating estrogen receptor alpha (ESR1) mutations after prior endocrine therapy (ET). The SMILE study is a multi-institutional phase II clinical trial to determine the efficacy and safety of an antiprogestin, onapristone in combination with fulvestrant as second-line therapy for patients with ER+,PgR+/-, HER2 - metastatic breast cancer (MBC). Methods Patients with locally advanced or MBC who progress on ≥ 2 lines of prior therapy with ET as a single agent or in combination with CDK4/6 inhibitors, mTOR inhibitors and one line of chemotherapy in the metastatic setting are eligible. Other criteria include ECOG performance status ≤ 2 , measurable disease per RECIST 1.1 criteria, adequate organ function, availability of an archived tumor biopsy block confirming the diagnosis of MBC, optional biopsy at disease progression on trial, and optional 18F-fluorofuranylnorprogesterone (18F-FFNP) PET/CT imaging. Ovarian suppression is allowed. Prior ET with tamoxifen or aromatase inhibitor therapy in the adjuvant or metastatic setting is allowed. Patients with prior exposure to fulvestrant, antiprogestins, or CDK inhibitors in the adjuvant setting are ineligible. Following consent, all subjects will receive fulvestrant at the recommended dosing schedule plus onapristone 50 mg orally, twice daily, until disease progression, unacceptable toxicity, or discontinuation for any other reason. Using the Simon Two-Stage design, a total of 39 patients will be enrolled over two years from 6-8 sites within Wisconsin Oncology Network (WON); study enrollment began in November 2021. In the first stage of the trial, thus far, nine patients were accrued who are tolerating the trial regimen well with no reported toxicities or serious events. The safety monitoring is planned when the cohort size reaches eleven patients, and interim analysis at 21 patients; if ≥ 2 responses are observed, then 18 additional subjects will be enrolled in the second stage. This design yields a one-sided type I error rate of 5% if the ORR is 7% and power of 80% when the combination's true response rate is 20%. The primary objective is to evaluate the objective response rate; secondary objectives include safety and tolerability, progression-free survival, disease control

rate, and duration of response. Other correlates include optional functional imaging of PgR binding with 18F-FFNP PET/CT and biomarker analysis (ER, total PgR, HER2, Ki67, CD24, CD44, LDH1, KLF4, CK 5/6, PhosphoSer294-PgR on tissue samples, ESR1 mutations, and circulating tumor DNA analysis).

Disclosure(s):

Sailaja Kamaraju, MD, MS: No financial relationships to disclose

Amy Amy Fowler, MD, PhD, FSBI: GE Healthcare: Consulting Fees (e.g., advisory boards) (Ongoing)

Lubna N. Chaudhary, MD, MS: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Pfizer assisted with data collection for this abstract. (Ongoing); Regeneron Pharmaceuticals: Contracted Research (Ongoing)

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12/7/2022

5:00 PM - 6:15 PM

OT2-01-03

ELEVATE: A phase 1b/2, open-label, umbrella study evaluating elacestrant in various combinations in women and men with metastatic breast cancer (mBC).

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Background: Elacestrant demonstrated significantly prolonged progression-free survival (PFS) and a manageable safety profile compared with standard of care endocrine therapy in the phase 3 EMERALD trial that enrolled patients with estrogen-receptor positive (ER+)/HER2– mBC following disease progression on prior endocrine and cyclin-dependent kinase 4/6 inhibitor (CDK4/6i) therapy. Benefit was observed in the overall population and in patients with ESR1 mutations. Combining elacestrant with targeted agents utilized in combination with endocrine therapy in mBC is of therapeutic interest. Methods: ELEVATE is a phase 1b/2 trial designed to evaluate the combination of elacestrant with alpelisib, everolimus, palbociclib, abemaciclib, or ribociclib. Eligible patients (pts) are women or men with ER+/HER2– locally advanced or mBC, measurable disease per RECIST v1.1 or ≥ 1 lytic or mainly lytic bone lesion, ECOG PS ≤ 1 , no inflammatory breast cancer or uncontrolled central nervous system metastases, in addition to treatment-arm specific eligibility criteria as detailed below. In the phase 1b portion, pts who have received prior aromatase inhibitor (AI) and CDK4/6i will be enrolled in three 6-patient cohorts for each combination except abemaciclib (under study in a separate trial). Patients will receive elacestrant with the targeted agent at reduced or full doses. The primary endpoint of phase 1b is to determine the recommended phase 2 dose for each combination. Secondary endpoints are safety, pharmacokinetics, pharmacodynamics, and efficacy (objective response rate [ORR], duration of response [DoR], clinical benefit rate [CBR], PFS, and overall survival [OS]). The phase 2 portion will enroll 5 separate arms: A) pts with PIK3CA mutation(s) and prior AI + CDK4/6i: alpelisib + elacestrant, n=50; B) pts with prior AI + CDK4/6i: everolimus + elacestrant, n=50; C) pts with prior AI + CDK4/6i: abemaciclib or ribociclib (investigator's [inv] choice) + elacestrant, n=60 (30 per combination); D) pts with prior AI only (no CDK4/6i): palbociclib, abemaciclib or ribociclib (inv choice) + elacestrant, n=90 (n=30 per combination); E) pts with no prior systemic therapy: palbociclib or ribociclib (inv choice) + elacestrant, n=90 (n=45 per combination). No prior fulvestrant or chemotherapy is allowed in any arm and no more than 2 prior hormonal therapies are permitted in arms A-D. Prior therapy restrictions apply to the mBC setting or within 12 months of adjuvant therapy. The primary endpoint for the phase 2 portion is the estimation of PFS at 6 months in arms A, B, and C and at 12 months in arms D and E. Secondary endpoints will include ORR, DoR, CBR, PFS, OS, and safety. The Kaplan-Meier method will be used to estimate PFS. Descriptive statistics will be used to evaluate response and safety.

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ELONA: An open-label, phase 1b-2 study of elacestrant, in combination with onapristone in patients with estrogen receptor-positive, progesterone receptor-positive, HER2-negative advanced or metastatic breast cancer

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Objectives: The addition of a CDK 4/6 inhibitors to endocrine therapy, in the first or second line setting, provides a significant improvement in progression free survival (PFS), and in some cases in overall survival (OS), with a tolerable toxicity profile. Regardless, most patients experience disease progression on these agents and ultimately develop endocrine resistance, thus, emphasizing the critical need for novel treatments. Elacestrant showed a statistically significant improvement in PFS when compared to standard of care endocrine therapy after progression on CDK4/6 inhibitors in combination with endocrine therapy (Bidard et al, 2022). Onapristone is a type I antiprogestin which prevents the progesterone receptor (PgR) from

dimerizing and blocks ligand-induced protein kinase-mediated phosphorylation of the PgR. The clinical anticancer activity of onapristone, in immediate release formulation, has been previously documented in patients with hormone therapy-naïve (Robertson et al, 1999) or tamoxifen-resistant (Jonat et al, 2002) breast cancer (BC). More recently, onapristone, in extended release formulation, was evaluated in doses up to 50 mg BID in a phase 1 trial that enrolled 52 heavily pretreated patients with metastatic solid tumors, with no dose limiting toxicity observed. Among the 20 breast cancer patients enrolled, 7 (35%) had stable disease (Cottou et al, 2018). Methods: ELONA is a phase 1b/2, open-label, multicenter study. The phase 1b portion of the study will assess the safety, pharmacokinetics (PK), pharmacodynamics, and preliminary efficacy of elacestrant plus onapristone to determine the combinations' recommended phase 2 dose. The primary endpoint of the phase 2 part of the trial is objective response rate and secondary endpoints will include safety, duration of response, clinical benefit rate, PFS, and OS, in addition to pharmacodynamics markers using ctDNA. Eligible patients are pre-, peri- and post-menopausal women and men aged ≥ 18 years with ER+/PgR+,HER2- tumors and an Eastern Cooperative Oncology Group performance status ≤ 2 with at least one measurable lesion at baseline, as per RECIST version 1.1. Prior therapy in the metastatic setting includes at least one anti-hormonal therapy in combination with a CDK4/6i. No prior chemotherapy regimen in the metastatic setting is allowed. The phase 1b dose-escalation portion of the study will evaluate dose-limiting toxicities (DLTs) of the combination in up to 4 cohorts of 6 patients each.

Disclosure(s):

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12/7/2022

5:00 PM - 6:15 PM

OT2-01-05

The CROWN Study (CaRdiac Outcomes With Near complete estrogen deprivation): A multicenter, prospective cohort study of cardiovascular outcomes in premenopausal women treated with ovarian suppression and an aromatase inhibitor

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Background: Treatment for premenopausal women with high or intermediate risk hormone receptor (HR)+ breast cancer (BC) now includes the concurrent use of ovarian function suppression (OFS) and an aromatase inhibitor (AI) therapy to induce near complete estrogen

deprivation (NCED). The long-term cardiovascular (CV) sequela for women treated with NCED is unknown. Premature menopause in the non-cancer population is associated with CV disease, including atherosclerosis and coronary artery disease, which can be detected pre-clinically by myocardial perfusion imaging and coronary artery plaques. This, together with the CV morbidity associated with other aspects of BC treatment and future life-years of these women, warrants further investigation with the goal of identifying pre-clinical markers of myocardial compromise. We seek to do this with the following specific aims:

1. Characterize and quantify the extent of coronary microvascular injury and perfusion changes experienced during early NCED therapy.
2. Characterize and quantify the extent of structural and functional alterations to the aorta and left ventricle while on NCED therapy.
3. Identify potential biomarkers and additional risk factors for CV morbidity in patients receiving NCED

Trial Design:

This is a federally funded (NHLBI) prospective cohort study conducted at 3 regional NCI-supported Cancer Centers (Atrium Health Wake Forest Baptist, Virginia Commonwealth and Duke) that will include premenopausal women, age ≤ 55 , with Stage I-III BC following completion of planned chemotherapy, surgery and radiation with an ECOG 0-1. HR+ BC patients will receive an AI and OFS. Women with HR- BC are included as comparators. CV imaging and biomarkers will be obtained at baseline, 1 year and 2 years (Table 1). These assessments will include serial cardiac magnetic resonance (CMR) and coronary computed tomography angiography (CCTA) imaging as well as laboratory measurements, including exploratory biomarkers. The primary outcome is myocardial perfusion reserve (MPR) as measured by CMR imaging stress studies. We will correlate CMR imaging with CCTA to provide complementary detail of coronary plaque changes. The study will also assess the relevance of pre-existing risk factors, including an emphasis on racial disparities, on study outcomes, and dynamic change in modifiable and treatment related risk factors.

Statistical Methods: We plan to enroll 90 women, 67 in the NCED group and 23 in the HR- group, allowing for a 10% drop out rate. There are two primary types of statistical analyses. The first includes testing hypotheses between group (NCED vs HR-) and within group (longitudinal changes within the NCED group) for Aims 1 and 2. Comparisons will be made using longitudinal mixed models to examine effects on outcomes measured. The second analyses, for Aim 3, involve developing predictive equations utilizing a stepwise linear regression approach to determine if patient demographics, clinical parameters and serum biomarkers are associated with MPR. The sample size allows 80% power to address specific aims for between and within group comparisons, including a between group difference of 2.8% in our primary outcome, MPR.

Present Accrual: 0

Target Accrual: 90

Contact information: Emily Douglas, MD; edouglas@wakehealth.edu

Table 1: Study Procedures

Table 1: Study procedures

Evaluation/Procedure	Baseline	Year 1	Year 2
Vitals	X	X	X
Body measurements: (Height, Weight, BMI, Waist circumference)	X	X	X
Labs/Biomarkers	X		X
CMR	X	X	X
CCTA	X		X
EKG	X		X
Patient questionnaires: race, co-morbidities, etc.	X	X	X

Disclosure(s):

Emily Douglas, MD: No financial relationships to disclose

Nathaniel O'Connell, PhD: No financial relationships to disclose

Mary Hackney, MD: No financial relationships to disclose

Wendy Bottinor, MD: No financial relationships to disclose

John Grizzard, MD: No financial relationships to disclose

Igor Klem, MD: Bayer: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

Carolyn Park, MD: No financial relationships to disclose

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12/7/2022

5:00 PM - 6:15 PM

OT2-01-06

Phase II trial of palbociclib plus endocrine therapy followed by combination of pembrolizumab, palbociclib and endocrine therapy in patients with hormone receptor positive metastatic breast cancer

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Background: The combination of CDK4/6 inhibitors (CDK4/6i) and endocrine therapy (ET) is standard-of-care for patients with hormone receptor positive (HR+) HER2- metastatic breast cancer (MBC). Immune modulatory effects of CDK4/6i are well documented preclinically but poorly understood in the clinical setting. Our previous study combining letrozole, palbociclib and pembrolizumab in patients with HR+ MBC (NCT02778685) showed a promising complete response rate of 31%. Dynamic changes in peripheral blood mononuclear cell (PBMC) subpopulations indicated that palbociclib may increase CD8+ TEMRA (terminally differentiated effector memory cells) and CD4+ TEM (effector memory cells) and enable immune activation. The current cohort 3 was designed to study the immune modulatory effect of palbociclib as an immune-priming agent with a biomarker enriched design. Methods: Women with ECOG 0-1, HR+ HER2- MBC, RECIST 1.1 measurable disease, no prior therapy for MBC were enrolled. Patients with endocrine therapy, including aromatase inhibitor +/- ovarian suppression or fulvestrant, were eligible. A palbociclib + ET lead-in design was used, starting on day -28 followed by combination therapy with pembrolizumab added on C1D1. Peripheral blood and tumor biopsy at baseline and on-treatment were collected to allow in-depth analysis of biomarkers predicting response to the combination. The primary endpoint was to evaluate if the palbociclib potentiated immune responses as a "priming" agent through PBMC analysis and on treatment tumor biopsy. Secondary endpoints included other immune cell subsets and changes that follow the combination with pembrolizumab. With 25 patients, assuming a standard deviation of 0.51 in the relative change in classic monocytes in PBMCs, there is 90% power to detect a relative change of log(C1D1/baseline) of 34.5% with a type I error (two-sided) of 0.05. Results: Between August 2020 and April 2022, 16 patients were enrolled in cohort 3. Currently 11 patients have adverse event (AEs) and 16 patients have response data. Median age was 57 years (39-72). 8/11 (73%) were non-Hispanic white, 1/11 (9%) Hispanic, 1/11 (9%) Asian, and 1/11 (9%) African American. 87% patients had grade 3 AEs, and 30% had grade 4 AEs. Grade 3 AEs were 9/11 (82%) neutropenia, 5/11 (45%) leukopenia, 1/11 (9%) elevated LFTs, and 1/11 (9%) each lymphopenia, hot flashes, febrile neutropenia, and pneumonitis. Grade 4 AEs

were 1/11 (9%) lymphopenia. 8/16 (50%) patients achieved a partial response (PR), 5/16 (31%) had stable disease (SD), and 1/16 (6%) had progression of disease (PD) by RECIST 1.1. Additionally, 2/16 (13%) patients were too early to determine best overall response. Response rate (CR+PR) was 50%. PBMCs and tumor microenvironment profiling are ongoing. Conclusion: The combination of palbociclib, pembrolizumab and ET is well tolerated, and a response rate of 50% was identified in HR+ MBC patients who received this combination as front-line therapy. Dynamic changes in peripheral blood mononuclear cells and tumor microenvironment profiling are ongoing.

Disclosure(s):

Yuan Yuan, MD PhD: AstraZeneca: Speaker's bureau (Ongoing); Celgene: Contracted Research (Ongoing); Daiichi Sankyo: Speaker's bureau (Ongoing); Eisai: Contracted Research (Ongoing), Speaker's bureau (Ongoing); Genentech: Contracted Research (Ongoing), Speaker's bureau (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), Speaker's bureau (Ongoing); Merck: Contracted Research (Ongoing); Novartis: Contracted Research (Ongoing), Speaker's bureau (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Puma: Consulting Fees (e.g., advisory boards) (Ongoing)

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Niki Tank, MD: No financial relationships to disclose

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5:00 PM - 6:15 PM

OT2-01-07

evERA Breast Cancer: A phase III study of giredestrant (GDC-9545) + everolimus vs exemestane + everolimus in patients with estrogen receptor+, HER2- locally advanced or metastatic breast cancer

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BACKGROUND Endocrine therapy (ET) modulates estrogen synthesis and/or estrogen receptor (ER) activity and is the mainstay of ER+ breast cancer (BC) treatment. ET + a cyclin-dependent kinase 4/6 inhibitor (CDK4/6i) is the standard of care in patients (pts) with ER+, HER2– metastatic BC (mBC) in the first-line setting. Fulvestrant ± a CDK4/6i, and everolimus + exemestane, are the current regimens approved for use in the second-line setting. However, therapeutic resistance to some ETs, such as aromatase inhibitors, can arise from ESR1 mutations driving estrogen-independent transcription and proliferation. Current post-CDK4/6i treatment options are suboptimal. New therapy options are therefore needed to reduce this risk and to improve outcomes, tolerability, quality of life, and adherence to treatment. Giredestrant is a highly potent, nonsteroidal oral selective ER antagonist and degrader (SERD) that achieves robust ER occupancy and is active regardless of ESR1 mutation status. While phase I SERD combination data in the post CDK4/6 setting is encouraging, there is no randomized combination data. Combining giredestrant and everolimus may potentially improve outcomes after CDK4/6is and in pts with ESR1-mutated tumors; evERA BC is investigating this combination to address the unmet need in the post-CDK4/6i setting. **TRIAL DESIGN** This phase III, global, randomized, open-label, multicenter study will evaluate the efficacy and safety of giredestrant + everolimus vs exemestane + everolimus in pts with ER+/HER2– locally advanced (LA)/mBC who had previous treatment with a CDK4/6i and ET in the LABC/mBC or adjuvant setting. Pts will be randomized to either giredestrant (30 mg) + everolimus (10 mg) by mouth (PO) every day (QD) on Days 1–28 of each 28-day cycle, or exemestane (25 mg) + everolimus (10 mg) PO QD on Days 1–28 of each 28-day cycle. Pts will receive treatment until disease progression or unacceptable toxicity. Pts will use a dexamethasone mouth rinse four times QD for 8 weeks, started concurrently with study treatment. **ELIGIBILITY** Female/male pts ≥18 years with ER+/HER2– LA/mBC, an Eastern Cooperative Oncology Group Performance Status of 0–1, measurable disease defined per RECIST v.1.1 (or evaluable bone metastases with at least one predominantly lytic bone lesion confirmed by computed tomography or magnetic resonance imaging), disease progression ≥6 months after initiating ET + CDK4/6i in the LABC/mBC setting (and ≥4 months on most recent ET, if ET + a CDK4/6i was not the most recent therapy received), or relapsed either while taking or within 12 months of exposure to combination adjuvant ET (≥12 months) and a CDK4/6i (≥6 months). Availability of a baseline blood sample to determine ESR1 mutation status by circulating tumor DNA assay for testing at a central laboratory. Men and pre-/perimenopausal women will receive a luteinizing hormone-releasing hormone agonist on Day 1 of each 28-day cycle. **AIMS** Primary endpoint: investigator-assessed progression-free survival (PFS; per RECIST v1.1). Secondary endpoints: investigator-assessed PFS in pts with detectable ESR1-mutated tumors in circulating tumor DNA at baseline; overall survival; objective response rate; duration of response; clinical benefit rate; patient-reported outcomes; safety; pharmacokinetics. **STATISTICAL METHODS** The primary endpoint analysis will use a stratified log-rank test at an overall 0.05 significance level (two-sided). An independent data monitoring committee will be in place for safety. **ACCRUAL** Target enrollment is 224 pts globally, and this study is currently recruiting. **CONTACT INFORMATION** For more information or to refer a patient, email global.roche.genentechtrials@roche.com or call 1-888-662-6728 (USA only). [Clinicaltrials.gov](https://clinicaltrials.gov) number NCT05306340.

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OT2-01-08

SEQUence of Endocrine therapy in advanced Luminal Breast cancer (SEQUEL-Breast): A phase 2 study on fulvestrant beyond progression in combination with alpelisib for PIK3CA-mutated, HR+ HER2- advanced breast cancer.

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Goal To investigate the efficacy of alpelisib added to fulvestrant beyond progression in patients with HR+ HER2- advanced breast cancer (ABC). Background The SOLAR-1 study (Andre et al, 2019) has shown that the addition of alpelisib, an alpha-specific PI3K-inhibitor to fulvestrant led to a PFS-benefit of 5.3 months in patients with PIK3CA-mutated HR+ HER2- ABC. In this study, patients were fulvestrant-naive, and only 6% of this population was previously treated with a CDK4/6 inhibitor (CDK4/6i). Nowadays, most patients have been treated with a CDK4/6i, either combined with an aromatase-inhibitor (AI) in 1st line, or with fulvestrant in the 1st or 2nd line setting. Results of the ongoing Dutch SONIA-trial (NCT03425838) will show whether the addition of CDK4/6i to an AI in 1st line is superior to the addition of CDK4/6i to fulvestrant in 2nd line. Patients who have progressed on a CDK4/6i in either line and fulvestrant may be treated with fulvestrant and alpelisib. However, the efficacy of fulvestrant beyond progression combined with alpelisib is unknown. Aim of this study The aim is to determine if treatment with fulvestrant beyond progression and alpelisib results in a clinically meaningful median PFS of ≥ 6 months. Primary endpoint: Progression-free survival (PFS). Secondary endpoints: 'On treatment' PFS Overall survival Objective Response Rate Clinical Benefit Rate Duration of response Safety Risk factors for alpelisib-induced hyperglycemia Quality of life Pharmacokinetics Prognostic value of ctDNA Mechanisms of resistance Trial design The SEQUEL-Breast trial is a nationwide Dutch investigator-initiated phase 2 trial. 25 centers are expected to participate in the SEQUEL-Breast. Clinicaltrials.gov identifier: NCT05392608 Intervention: fulvestrant beyond progression combined with alpelisib. Population Patients must be adults with HR+ HER2- ABC with an activating PIK3CA-mutation. Prior treatment with an AI and fulvestrant is mandatory, as well as prior treatment with a CDK4/6i in either line. Patients must have progressed on fulvestrant (+/- CDK4/6i), and fulvestrant must be the most recent line of therapy. Patients with ECOG performance score 0,1 or 2 are eligible, as well as those with

controlled (HbA1C < 8.4%) diabetes mellitus type 2. Patients with uncontrolled diabetes, visceral crisis, symptomatic CNS metastases or clinically relevant heart disease are ineligible. Patients with diseases or previous surgery that might affect the bioavailability of alpelisib, those in need to use CYP3A4 inhibitors or BRCP inhibitors, as well as patients with any other conditions that would put them at particular risk when partaking in the study, are also ineligible. Accrual Start: June 2022 Accrual, June 27: 3 patients Target: 105 patients (minimum) to 130 patients (maximum) Estimated accrual time: 2-3 years Statistical considerations For sample size calculation, H1 (median PFS \geq 6 months) is weighed against H0 (median PFS \leq 4 months) in a one sample log rank test. $\alpha=0.05$ $\beta=0.1$. 71 events are needed. We estimated that inclusion of 79 patients is required to reach 71 events, given an accrual time of 36 months and a minimum follow-up time of 6 months. To ensure that also PFS 'on treatment' has the desired accuracy, we accounted for 25% non-persistence due to toxicity, hence 105 patients. On top of these 105 patients, another 25 patients may be included, if they harbor rare PIK3CA mutations. Further information Corresponding author: sequel@nki.nl BOOG Study Center acts as sponsor for this trial. This trial is funded by Novartis.

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ABEMACARE: Abemaciclib in Combination with Endocrine Therapy as First Line Therapy in Metastatic Breast Cancer Patients with Symptomatic Visceral Metastases or High Tumor Burden – A prospective multicenter observational study

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ABEMACARE: Abemaciclib in Combination with Endocrine Therapy as First Line Therapy in Metastatic Breast Cancer Patients with Symptomatic Visceral Metastases or High Tumor Burden – A prospective Multicenter Observational Study Sophia Ramsperger, Franziska Kotzur, Lothar Müller, Stephan Seitz, Peter A. Fasching, Stefanie Jilg, Dorothea Fischer, Silvia Egert-Schwender, Victoria Kehl, Ute Reuning, Lukas Rief, Romina Rösch, Holger Bronger, Christof Winter, Marion Kiechle, Johannes Ettl Background: Combined endocrine therapy with Cyclin-dependent kinase 4 and 6 (CDK 4/6) inhibitors and aromatase inhibitor (AI) or Fulvestrant has become standard of care in first line therapy of estrogen receptor (ER) positive, HER2 negative metastatic breast cancer. Numerical trials have shown excellent results regarding disease control and survival while maintaining quality of life for patients. In the MONARCH 2 and MONARCH 3 trials, patients with liver metastases derived a particularly large benefit from the use of Abemaciclib. Nevertheless, in real world many patients with endocrine sensitive metastatic breast cancer are still being treated with chemotherapy in first line. Symptomatic visceral disease and/or high tumor burden are often seen as reasons for upfront chemotherapy even in the absence of visceral crisis. In this specific patient population Abemacare aims at determining the efficacy of Abemaciclib in combination with endocrine therapy as first line treatment. Further, the question is addressed, whether circulating tumor DNA might serve as a predictive biomarker for early tumor response. Study Design: Abemacare is a prospective multicenter noninterventional, observational study. 96 patients in 10 German cancer centers who receive first line Abemaciclib in combination with AI or Fulvestrant are planned to be enrolled. Recruitment started in December 2020. As of July 1st 2022, 51 patients have been included in six study sites. Patients with documented ER-positive, HER2-negative metastatic breast cancer and measurable visceral disease are eligible if they fulfill one of the following inclusion criteria: Presence of clinical signs or symptoms of visceral disease (e.g. pleural effusion, ascites, abdominal pain from liver or peritoneal metastases, dyspnea from pleural effusion or lymphangiosis of the lung, elevated liver enzymes or bilirubin level (> 2x ULN)) or signs of high tumor burden (e.g. LDH > 399 U/l with K+ in normal range, abnormal CEA or CA 15-3 level (> 2x ULN), radiographic signs of lymphangiosis of the lung, cytologically proven bone marrow infiltration). Patients with prior therapy with a CDK 4/6 inhibitor in any setting or first line therapy for metastatic disease are excluded from the trial. Primary endpoint is best objective response rate (ORR) defined by the proportion of patients who are evaluated using RECIST V1.1 as having partial (PR) or complete response (CR) while being on study treatment. ORR will be analyzed using the one group χ^2 test at the 5% significance level. The test hypotheses are as follows: H0: ORR = 0.43, HA: ORR \neq 0.43. In addition, ORR will be reported with a 95% CI. Several additional endpoints regarding disease control and patient reported outcomes will also be evaluated. Plasma samples for ctDNA are being collected at d1 and d15 of cycle 1 and d1 of cycle 2 and 3. Contact information: For further information please contact the leading physician Dr. Johannes Ettl via johannes.ettl@tum.de This study is supported by Eli Lilly and Company. NCT04681768

Disclosure(s):

Johannes Ettl, n/a: Amgen, Celgene, Eisai, Myriad, Teva.: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer, Pierre Fabre, Lilly, Roche, AstraZeneca, Daiichi, Gilead, Seagen: Consulting Fees (e.g., advisory boards) (Ongoing)

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WinPro: A window of opportunity study of endocrine therapy with and without prometrium in postmenopausal women with early-stage hormone receptor-positive breast cancer

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WinPro: A window of opportunity study of endocrine therapy with and without prometrym in postmenopausal women with early-stage hormone receptor-positive breast cancer Authors Teesha Downton^{1,2,3}, Davendra Segara³, Andrew Ong⁴, Janne Bingham⁵, Emma-Kate Carson⁴, Julia Chen^{1,2,3}, Kate Middleton³, Geoffrey Lindeman⁶, Andrew Parker³, Elgene Lim^{1,2,3}. Affiliations ¹Garvan Institute of Medical Research, Darlinghurst NSW, Australia; ²School of Clinical Medicine, St Vincent's Healthcare Clinical Campus, Faculty of Medicine and Health, University of New South Wales Sydney, Australia; ³St Vincent's Hospital Sydney, Darlinghurst NSW, Australia; ⁴Campbelltown Hospital, Campbelltown NSW, Australia; ⁵Royal Adelaide Hospital, Adelaide SA, Australia; ⁶Walter & Eliza Hall Institute of Medical Research, Parkville VIC, Australia Disclosures T. Downton: None. D. Segara: None. A. Ong: None. J. Bingham: None. E. Carson: None. J. Chen: None. K. Middleton: None. G. Lindeman: None. A. Parker: None. E. Lim: Advisory Board for Pfizer, Astra Zeneca, Lilly, Roche, Novartis, Gilead Australia. Research Funding from Pfizer, Novartis, Bayer. Abstract Background: Preclinical studies have observed that progesterone has inhibitory effects on the estrogen-stimulated growth of estrogen receptor (ER)-positive, progesterone receptor (PR)-positive breast cancer. Mohammed H et al. (Nature 2015) identified that activated PR associates with the ER and modulates the interactions of the ER with chromatin, with a shift towards the transcription of genes associated with apoptosis and differentiation, and away from genes associated with proliferation. We hypothesize that the addition of prometrym, a microionized progesterone, may enhance the anti-proliferative effects of standard endocrine therapy in women with ER-positive PR-positive breast cancer. Trial Design: WinPro (NCT03906669) is an ongoing multicenter, phase II, randomized, open-label, window of opportunity study comparing the effect on standard endocrine therapy with or without prometrym on breast cancer cell proliferation. The study population is postmenopausal women with early-stage operable breast cancer where the tumor is $\geq 5\text{mm}$ on imaging, ER $\geq 10\%$, PR $\geq 10\%$, and HER2-negative. Patients currently on hormone replacement therapy or the oral contraceptive pill, or who have a history of endometrial cancer or venous thromboembolism are not eligible. Patients are randomized 1:1:1 to letrozole 2.5mg daily, letrozole 2.5mg + prometrym 300mg daily, or tamoxifen 20mg + prometrym 300mg daily. Allocated treatment is taken for 14 days prior to surgery. Primary surgery and adjuvant treatment is as per standard of care. Objectives: The primary objective is to compare the geometric mean suppression of centrally assessed Ki67 between the diagnostic biopsy sample (pre-treatment) and the surgical sample (post-treatment). The secondary objective is to evaluate safety and tolerability. Tertiary objectives include defining genes predictive of a reduction in Ki67, and evaluating the changes in ER, PR, AR, FoxA1, Cyclin D1, and apoptotic markers in breast tumors post-intervention. Accrual: This study opened in February 2018 and as of 13 July 2022, 164 patients have been enrolled. Target accrual is 200 patients. Contact information: This study is led at St Vincent's Hospital Sydney, Australia, and funded by the Cancer Council of NSW and the NHMRC Translational Breast Cancer Project grant. Contact: Elgene Lim MBBS FRACP PhD at e.lim@garvan.org.au.

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ctDNA-guided Adaptive Therapy Escalation in ER+ MBC: A Phase 1b Study with Letrozole, Palbociclib and Onapristone ER

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ctDNA-guided Adaptive Therapy Escalation in ER+ MBC: A Phase 1b Study with Letrozole, Palbociclib and Onapristone ER Background: Extended release onapristone (onapristone ER) is a progesterone receptor (PR) antagonist that inhibits hormone-mediated PR activation and stabilizes PR association with corepressors, resulting in an antineoplastic effect when applied alone or in combination with antiestrogen therapy to breast cancer cells in vitro. Recent preclinical studies further suggest that onapristone adds to inhibition of cell proliferation when combined with CDK4/6 inhibitors and fulvestrant. Elevations in ctDNA can precede overt disease progression by a matter of months in metastatic breast cancer and may represent an opportunity for proactive therapeutic intervention. Trial Design: This is an investigator initiated open-label, single institution phase 1b study of onapristone ER added as escalation therapy in patients with ER+, PR+, HER2 negative MBC, who have detectable ctDNA after six months of treatment with letrozole and palbociclib in the first line. The study is supported by Context Therapeutics and involves two stages. Stage 1 is a dose escalation/de-escalation phase of 18 patients maximum, in which the safety and recommended phase 2 dose (RP2D) will be established for onapristone ER when used in combination with letrozole and palbociclib. In

stage 2, the dose expansion phase, the RP2D of onapristone will be combined with letrozole and palbociclib in 10 patients to further explore the tolerability of the regimen. ctDNA will be collected serially while patients are on this triplet therapy. Eligibility Criteria: This study is enrolling patients with radiologically measurable or evaluable metastatic or unresectable ER+/PR+/HER2-negative MBC in whom a tumor-derived somatic mutation can be detected in ctDNA at a variant allele fraction of 0.5% or greater after 6 months (+/- 4 weeks) of treatment with first line letrozole and palbociclib without progression, using our in house CLIA certified MSK-ACCESS assay. Adequate organ function and functional status for enrollment are stipulated in the protocol. Specific Aims: The primary objective of this study is to define the safety, tolerability, and recommended phase 2 dose of onapristone ER used in combination with letrozole and palbociclib. Secondary objectives include to investigate ctDNA response rate of the triplet therapy regimen, to gather early data regarding the 6-month clinical benefit rate , overall response rate , and progression free survival of this triplet escalation therapy regimen in high risk ctDNA+ patients, and to evaluate the pharmacokinetics of Onapristone ER when used in combination with letrozole and Palbociclib. Exploratory objective include to describe ctDNA dynamics during antiprogesterin therapy escalation in ER+ MBC, as well as the molecular features present in responders vs. non-responders using ctDNA and pre-treatment tissue. Target Accrual: The total planned cohort for the phase I dose escalation is a maximum of 18 patients across 3 dose levels, and the total planned cohort for the dose expansion is 10 patients, with an anticipated maximum total of 28 patients. We will allot for 5 additional patients to account for inevaluability during the dose escalation and expansion portions of the trial. The trial is currently open to enrollment at MSKCC. Contact Information: Dragoj@mskcc.org; Jhaverik@mskcc.org

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heredERA Breast Cancer: Phase III study of first-line, fixed-dose combination of pertuzumab and trastuzumab for subcutaneous injection ± giredestrant (GDC-9545) for estrogen receptor+, HER2+ advanced breast cancer

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BACKGROUND Giredestrant is a highly potent, nonsteroidal, oral selective estrogen receptor antagonist and degrader (SERD) that was found to be well tolerated and active as a monotherapy and in combination therapy in Phase I/II studies in early BC and pretreated locally advanced/metastatic BC (LA/mBC). Dual HER2 blockade with pertuzumab + trastuzumab (PH) + a taxane (induction therapy) followed by maintenance PH is the first-line standard of care for most patients (pts) with HER2+ LA/mBC. Despite HER2–ER blockade synergy, paucity of Phase III data evaluating maintenance PH + endocrine therapy (ET) vs. PH in pts with

ER+/HER2+ LA/mBC leads to variable use of ET in this setting. Adding giredestrant to the maintenance phase could improve outcomes. TRIAL DESIGN This is a Phase III, randomized, two-arm, open-label, multicenter study evaluating the efficacy and safety of giredestrant + the fixed-dose combination of PH for subcutaneous injection (PH FDC SC) vs. PH FDC SC after induction therapy with PH FDC SC + a taxane in pts with ER+/HER2+ LA/mBC. In the induction phase, pts will receive 4–6 PH FDC SC cycles (1200 mg P/600 mg H in the first cycle, followed by 600/600 mg every 3 weeks) + a taxane (investigator choice of docetaxel/paclitaxel). Pts deriving clinical benefit may receive two additional cycles per investigator's discretion. Pts completing ≥ 4 induction therapy cycles, achieving at least stable disease, and with a left ventricular ejection fraction (LVEF) $\geq 50\%$ will be randomly assigned 1:1 to maintenance giredestrant 30 mg/day + PH FDC SC every 3 weeks or PH FDC SC only, until disease progression (PD). ET (aromatase inhibitor/tamoxifen) will be allowed in the PH FDC SC-only arm. Study treatment will continue until PD, limiting toxicity, death, or consent withdrawal. ELIGIBILITY Enrolled pts must have ER+/HER2+ LA/mBC, disease-free interval from completion of (neo)adjuvant non-ET ≥ 6 months, Eastern Cooperative Oncology Group performance status 0/1, LVEF $\geq 50\%$, and adequate organ function. Pts with prior SERD treatment or presence of symptomatic central nervous system metastases will be excluded. All men and pre-/perimenopausal women must be eligible for a luteinizing hormone-releasing hormone agonist. AIMS The primary endpoint is investigator-assessed, maintenance progression-free survival. Secondary endpoints include overall survival (OS), objective response rate, duration of response, clinical benefit rate, pt-reported outcomes, and safety. STATISTICAL METHODS The primary endpoint analysis will use a stratified log-rank test at an overall 0.05 significance level (two-sided). An interim OS analysis is planned, and an independent data monitoring committee will be in place. ACCRUAL The study is open for enrollment. Approximately 812 pts will be enrolled in the induction phase, to allow for approximately 730 pts to be randomized in the maintenance phase. CONTACT INFORMATION For more information or to refer a patient, email global.roche.genentechtrials@roche.com or call 1-888-662-6728 (USA only). Clinicaltrials.gov number: NCT05296798.

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lidERA Breast Cancer: A phase III adjuvant study of giredestrant (GDC-9545) vs physician's choice of endocrine therapy in patients with estrogen receptor+, HER2-early breast cancer

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BACKGROUND Endocrine therapies (ETs) that target estrogen receptor (ER) activity and/or estrogen synthesis are the mainstay of ER+ breast cancer (BC) treatment. Despite best management, $\leq 20\%$ of patients (pts) with ER+/HER2- early BC (eBC) develop resistance (in some cases due to acquisition of tumor mutations in ESR1 that can drive estrogen-independent transcription and proliferation) and still have high recurrence rates on standard ETs. New treatment alternatives for ER+/HER2- eBC are needed to reduce risk of recurrence and improve survival, tolerability, quality of life, and adherence. Giredestrant, a highly potent, nonsteroidal oral selective ER antagonist and degrader (SERD), achieves robust ER occupancy and is active against tumors that retain ER-sensitivity or have ESR1 mutation(s). It has been demonstrated to be more potent in vitro and achieves higher ER occupancy in vivo than fulvestrant, the only currently approved SERD. Early-phase clinical studies have demonstrated that single-agent giredestrant (30 mg daily) has promising clinical and pharmacodynamic activity and is well tolerated in the ER+/HER2- eBC and metastatic BC settings. **TRIAL DESIGN** This is a phase III, global, randomized, open-label, multicenter study evaluating efficacy and safety of adjuvant giredestrant vs physician's choice of adjuvant ET (PCET) in pts with medium- and high-risk stage I-III histologically confirmed ER+/HER2- eBC. Pts are randomized 1:1 to oral 30 mg daily giredestrant or PCET (tamoxifen, anastrozole, letrozole, or exemestane, given according to prescribing information). Stratification factors are risk (medium vs high, based on anatomic [tumor size, nodal status] and biologic features [grade, Ki67, gene signatures if available]); geographic region (US/Canada/Western Europe vs Asia-Pacific vs rest of the world); prior chemotherapy (no vs yes); and menopausal status (pre-/perimenopausal vs postmenopausal). Beginning on Day 1 of Cycle 1, pts will be treated with giredestrant or PCET for ≥ 5 years. Continuing PCET after 5 years is at discretion of the investigator and per local standard of care. **ELIGIBILITY** Female/male pts with medium-/high-risk stage I-III ER+/HER2- eBC; prior curative surgery; completion of (neo)adjuvant chemotherapy (if administered) and/or surgery < 12 months prior to enrollment; no prior ET (≤ 4 weeks of [neo]adjuvant ET is allowed). For men and pre-/perimenopausal women, a luteinizing hormone-releasing hormone agonist will be given per local prescribing information (mandatory for pts in the giredestrant arm). **AIMS** Primary endpoint: Invasive disease-free survival (IDFS). Secondary endpoints: Overall survival; IDFS (STEEP definition, including second non-primary BC); disease-free survival; distant recurrence-free survival; locoregional recurrence-free interval; safety; pharmacokinetics; pt-reported outcomes. In addition, this study aims to improve health equity in research and expand clinical trial access. The study will also use/develop digital healthcare solutions, which will enable better understanding of pts' needs and their adherence

to ET. STATISTICAL METHODS The primary endpoint analysis will use a stratified log-rank test at an overall 0.05 significance level (two-sided). An interim analysis and a futility analysis are planned, and an independent data monitoring committee will be in place. ACCRUAL 1018/4100 pts have been recruited globally. CONTACT INFORMATION For more information or to refer a patient, email global.roche.genentechtrials@roche.com or call 1-888-662-6728 (USA only). Clinicaltrials.gov number NCT04961996. AB, PS and CG contributed equally. This abstract was originally presented at SABCS 2021 (OT2-11-09).

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5:00 PM - 6:15 PM

OT2-04-01

A Video Intervention to Improve Patient Understanding of Tumor Genomic Testing in Patients With Metastatic Cancer

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Background: Tumor genomic testing (TGT) has become increasingly adopted as part of standard cancer care for many cancers. Despite national guidelines around patient education prior to TGT, available evidence suggests that most patients' understanding of genomics remains limited, particularly lower income and minority patients, and most patients are not informed regarding potential incidental germline findings. Purpose: The primary object of this ongoing clinical trial is to evaluate the effectiveness of concise, animated videos to provide patient pre-test education prior to TGT as a supplement to patient-provider discussion. Trial Design: This prospective observational cohort study will enroll a total of 150 cancer patients in three clinical cohorts: Cohort 1: breast cancer (n=50); Cohort 2: lung cancer (n=50); Cohort 3:

cancer patients of any tumor type (n=50). The primary objective is to assess change in patient knowledge of TGT following exposure to the video to evaluate the hypothesis that exposure to a brief educational video will increase patient knowledge about tumor genomic testing. Secondary objectives include assessing changes following exposure to the video, including: 1) genomic knowledge 2) trust in Physician 3) comparison of results between the three patient cohorts. Methods: Based on published guidelines around pre-TGT provider-patient education and patient focus groups and interviews, content for a series of videos was developed to standardize patient pretest education of TGT. A base animated video was created to be applicable to any cancer type; additional tumor type content was added for the breast and lung cancer-specific videos. Participant recruitment is occurring at The Ohio State University's Comprehensive Cancer Center. Eligibility criteria include: age 18 years or older, biopsy-confirmed cancer, and provider plan to undergo TGT. This study requires participants to complete surveys at three timepoints: before video viewing (T1), immediately after video viewing (T2), and after provider communicates TGT results to the patient (T3). Four survey instruments are completed at T1/T2/T3: video message-specific recall, objective genomic knowledge/understanding, the 11-item Trust in Physician, and attitudes around genetic/genomic testing. TGT intention surveys are captured at T1 and T2. Participant evaluation of the video is collected at T2. For the primary objective, we will use a two-sided Wilcoxon signed-rank test with alpha of 0.05, giving us 90% power to detect an effect size of 0.47 in change of recall accuracy from pre- to post- video intervention. All secondary outcomes will be summarized using descriptive statistics and compared pre-/post-video using Wilcoxon signed-rank test. For comparisons of MBC and MLC, endpoints will include 1) baseline and pre-/post-video intervention change in genomic knowledge/understanding in MBC versus MLC patients; 2) baseline and pre-/post-video intervention change in trust in provider. The baseline and the change from pre- to post-video intervention in the secondary outcomes will be compared between MBC and MLC patients using Wilcoxon rank sum test. Conclusions: The long-term goal of this project is to test this broadly applicable, modular video-based intervention to be administered prior to tumor NGS to ensure equitable access to informed care. The use of a short video in this setting is innovative and we are demonstrating capacity to complete such a project. Study enrollment began March 30, 2022 and to date, 33 participants have enrolled (n=18 breast cancer; n=9 lung cancer; n=6 other cancer types). ClinicalTrials.gov NCT05215769.

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FLEX: 30K Full Transcriptome, Real-World Evidence Database for Early-Stage Breast Cancer, and Investigator-Initiated Protocols

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FLEX: 30K Full Transcriptome, Real-World Evidence Database for Early-Stage Breast Cancer, and Investigator-Initiated Protocols BACKGROUND: Genomic signatures, such as the 70-gene MammaPrint, provide additional prognostic information for early-stage breast cancer (EBC), such as tumor metastatic potential, and expand the available information clinicians and patients require for shared treatment decision making beyond the standard clinicopathologic factors. EBC tumors are further stratified into clinically actionable subtypes by molecular assays such as the 80-gene molecular profiling assay BluePrint, improving pathological complete response rates (pCR) and outcomes as evidenced by a number of recent trials. The ongoing FLEX Study (NCT03053193) is designed to expand the genomic information available for EBC cases, and to increase the speed of data generation for rare and underserved research areas. To date, FLEX is the largest international multicenter real-world evidence (RWE) EBC registry, with more than 10,000 patients enrolled in fewer than five years since opening. FLEX pairs full genome data with more than 800 clinical data points collected over 10 years of follow up to provide the most comprehensive big data database available for early-stage breast cancer. The FLEX enrollment has a goal of a minimum of 30,000 patients within 10 years. METHODS: The FLEX study is a multicenter, prospective, observational trial for patients ≥ 18 years old with histologically proven stage I-III invasive breast cancer that is node negative or positive (up to three nodes) who receive MammaPrint, with or without BluePrint as standard of care management. Patients consent to the collection of clinically annotated full transcriptome data. Additionally, this study protocol allows physicians to investigate targeted populations or clinical trial investigator-initiated studies (IIS) upon approval by a peer-driven Scientific Review Committee. As patients enrolled in the FLEX study meet all eligibility criteria for inclusion no additional consent is required. The FLEX enrollment has already surpassed 1/3 of set target goal. As of April 2022, the trial has surpassed 10,000 patients enrolled at nearly 100 trial sites across the US and Europe, Middle East and Africa (EMEA). To date, there have been 36 publications in international scientific congresses with 39 FLEX IIS and in progress. With over 250 active and collaborating physicians leveraging the shared infrastructure, the IIS have enabled the ability to address disparities in treatment to underrepresented populations, rare subtypes, age, and patient centered specific topics. Current and future questions investigated via this platform will continue to strive to improve outcomes for early-stage breast cancer patients.

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Breast Cancer Cohort of the Comprehensive Outcomes for After Cancer Health (COACH) Study: Study Protocol

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Background: Women with breast cancer account for the largest cohort (23%) of over 18 million cancer survivors in the United States. Of the nearly 4 million breast cancer survivors, many, including individuals with metastatic breast cancer, will require lifelong treatment for chronic conditions. As part of a multi-site study including diverse tumor types, breast cancer survivors are being recruited to explore the feasibility and outcomes of a digital health coaching (DHC) program following the completion of primary therapy to support self-management of symptoms and general wellness. Trial design: A randomized-wait list control design will evaluate outcomes related to engagement in a DHC program following completion of primary therapy. Participants will be enrolled in a 6-month DHC program delivering evidence-based content via weekly calls, text, and email, in addition to usual support from their respective healthcare teams. The

intervention group will receive coaching upon enrollment. The control group will receive coaching after a 6-month monitoring period. Twelve months of longitudinal clinical, patient-reported outcomes, activity tracking (via Fitbit), and microbiome data will be collected from both groups. Eligibility criteria: The breast cancer cohort will consist of individuals with both localized and metastatic disease within 1 year of completion of primary therapy, defined as treatment of curative intent, first-line or later, from which the individual is advancing to active surveillance or follow-up, with or without maintenance therapy. All study participants must be >18 years old, able to read and speak English, have access to mobile technology, and agree to wear and have data collected from an activity tracker. Specific aims: 1) Assess the feasibility and acceptability of a DHC program and its effect on participant health self-efficacy; 2) characterize associations between participant symptoms, physical/psychosocial well-being, and health self-management and gut microbiota changes; and 3) explore patient-generated health data outcomes among participants (patient reported and wearable biometrics outcomes). Statistical methods: Feasibility and acceptability will be assessed through descriptive statistics. Feasibility for this study is defined as a retention rate $\geq 70\%$, and acceptability is defined as $\leq 20\%$ scoring "not at all helpful." Secondary aims will be assessed using linear mixed models. Cross-cohort analysis of physical function, measured by the PROMIS Physical Function 10a, will be conducted. Assuming a power of 0.8 and significance level of .05, we will be able to detect a 2.51 difference in PROMIS score means between the control and intervention group (SD 10) with a sample of 500 total participants. Sub-group analysis will be conducted with the anticipated 250 participants in the breast cancer cohort with a focus on feasibility, acceptability, and descriptive and exploratory endpoints for this population as a whole and comparing early stage and metastatic participants. Target and present accruals: 500 individuals with diverse tumor types will be enrolled across 5 collaborating sites, of which 4 will include individuals with breast cancer. An estimated 250 breast cancer participants (approximately 50% of the total study population), including 150 with de novo or progressive metastatic breast cancer, are planned to be recruited. To date, 1 Midwestern site has enrolled the first 7 breast cancer survivors. Two additional sites plan to enroll in July 2022, with the remaining 2 sites to begin enrollment by the end of 2022.

Disclosure(s):

Robin M. Lally, PhD, MS, BA, RN, AOCN, FAAN: Daiichi Sankyo: Contracted Research (Ongoing); Optum: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Pack Health: Contracted Research (Ongoing); Pfizer: Contracted Research (Terminated, December 30, 2020)

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12/7/2022

5:00 PM - 6:15 PM

OT2-07-01

Feasibility study to evaluate performance of the LUM Imaging System for intraoperative detection of residual tumor in breast cancer patients receiving and not receiving neoadjuvant therapy

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Background: Microscopically tumor-free lumpectomy margins are critical for safe breast conserving surgery. With current tools, 15%-25% of lumpectomies have positive margins that require second surgical procedures and increase cost and patient discomfort. Additionally, current lumpectomy margin assessment techniques show poor performance in predicting residual disease at re-excision, with a PPV of 35%. Better detection tools are needed to identify residual cancer during the initial lumpectomy and reduce second operations. LUM015 is a

protease-activated fluorescent imaging agent that accumulates in tumor cells and tumor associated macrophages after preoperative intravenous injection. The LUM Imaging System visualizes activated LUM015 in the lumpectomy cavity via a hand-held wide field detector and proprietary tumor detection software. This system has been tested in multiple single-site studies and two prospective multi-site studies enrolling >600 patients, and demonstrated successful detection of residual lumpectomy cavity tumor. Initial studies excluded the approximately 20% of patients receiving neoadjuvant therapy. Patchy tumor cell death with preoperative therapy can leave small, multifocal deposits of tumor invisible on pre-operative imaging and not palpable or visible during surgery. We now evaluate the LUM Imaging System in patients with and without neoadjuvant therapy. Trial Design and Specific Aims: This prospective, multi-center study at 6 US sites tests the LUM Imaging System in lumpectomy surgery after neoadjuvant therapy to evaluate potential impact of treatment-related tissue changes and tumor cell death on tumor detection algorithms. An initial cohort of 10 patients address the objective of algorithm development. A second cohort of 104 patients will further evaluate the feasibility of the LUM Imaging System after neoadjuvant therapy. A third cohort will enroll 208 patients who have not received neoadjuvant therapy. All cohorts are evaluated for safety and for reduction in residual tumor after LUM Imaging System guidance compared to standard of care lumpectomy. After excision of the main lumpectomy specimen, patients are randomized 3:1 to device or control arms. In the device arm, the cavity is imaged and margins with LUM015 signal are excised. Final comprehensive shaved margins are removed in both arms to evaluate extent of residual disease after the use of the LUM Imaging System or after standard lumpectomy. No LUM Imaging is performed in the control arm, however, all patients are injected with LUM015 to evaluate drug safety. Patient reported outcomes assessing re-excision concerns, breast appearance and preferences for treatment type are collected. Eligibility Criteria: This study seeks to enroll women 18 and older with histologically confirmed primary invasive breast cancer (IBC), ductal carcinoma in situ (DCIS) or a combination of IBC/DCIS undergoing a lumpectomy for their breast malignancy who have received any form of neoadjuvant treatment prior to surgery (cohorts 1 and 2) or who have not received any therapy prior to lumpectomy (cohort 3). Patients allergic to polyethylene glycol or intravenous contrast agents are excluded. Use of blue node mapping dyes before imaging with the LUM015 is not allowed per study protocol. Accrual and Study Progress: Cohort 1 has completed enrollment and interim analysis. No new risks specific to the neoadjuvant population were identified. LUM015 fluorescent signals measured in neoadjuvant patients were within the expected range, and no changes to the tumor detection algorithm were required. Cohorts 2 and 3 have enrolled a total of 38 patients. This trial is registered as NCT04440982. The NIH funds this study through a R01 grant issued to Massachusetts General Hospital.

Disclosure(s):

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5:00 PM - 6:15 PM

OT2-08-01

A prospective phase 2 study on efficacy and safety of AK105, anlotinib combined with nab-paclitaxel (nab-P) as a first-line therapy in patients(pts) with advanced triple-negative breast cancer(TNBC).

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Background: PD-1/PD-L1 inhibitor plus chemotherapy have shown tolerability and significant clinical benefits in pts with advanced TNBC. As antiangiogenic agent could remodel tumor blood vessels and increase the response to immune-checkpoint inhibitors (ICIs), we designed an investigator initiated trial (IIT) to investigate the efficacy and safety of AK105 (anti-PD-1 antibody), anlotinib (antiangiogenic, multi-target tyrosine kinase inhibitor) combined with nab-P as a first-line therapy in pts with advanced TNBC. Method: In this multicenter, prospective, single arm, phase 2 study, eligible pts were female aged 18-75 years, with ECOG PS 0-1, who had locally advanced or recurrent/metastatic triple-negative (estrogen receptor-, progesterone receptor- and HER2-) breast cancer. The main exclusive criteria were previous use of PD-1/PD-L1 antibody, cytotoxic T lymphocyte-associated antigen-4 (CTLA-4) antibody or antiangiogenic agent, and central nervous system (CNS) metastases. Eligible pts were treated with intravenous AK105(200mg on day 1), oral anlotinib(12mg once daily on days 1-14) and intravenous nab-P (125mg/m² on days 1 and 8) . The triplet combination regimen repeated every 21 days until disease progression, death or intolerable toxicity. The primary endpoint is overall response rate (ORR), and the secondary endpoints are disease control rate (DCR), progression-free survival (PFS), overall survival (OS) and safety. Simon's two-stage design were used to calculate the sample size assuming ORR is improved from 45.9% (nab-P alone) to 65% (AK105, anlotinib combined with nab-P) with the power (1- β) taken as 0.80 and the type I error (α) taken as 0.05 (two-sided). Enrollment began in June 2022 with a total goal of 42 pts at 7 sites in China. Clinical trial information: NCT05244993. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

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Liang Zhang, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

OT2-08-02

SOLTI-1907 ATREZZO: Targeting hormonal receptor negative (HR-) or PAM50 non-luminal disease with atezolizumab in combination with trastuzumab and vinorelbine in HER2-positive metastatic breast cancer (MBC)

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Background Today, there is no clear therapeutic algorithm for patients with metastatic HER2-positive (HER2+) breast cancer (BC) who have progressed to trastuzumab, pertuzumab, tyrosine kinase inhibitors and antibody-drug conjugates (ADC). Among the emerging strategies, the use of immune checkpoint inhibitors in combination therapy is showing promising clinical

benefit in the advanced setting of HER2+ BC by overcoming immune resistance and enhancing antitumor cellular immunity. The intrinsic subtypes Basal-like and HER2-enriched (i.e PAM50 non-luminal tumors) represent approximately the 60% of HER2+ BC and are associated with higher expression of immune-related genes, tumor-infiltrating lymphocytes (TILs) presence and high tumor mutational burden (TMB), compared to luminal subtypes. Additionally, immune infiltration and TMB in HER2+ BC are associated with chemo/antiHER2 responsiveness and with potential benefit from anti-PD-1/PD-L1 inhibitors. We hypothesize that combining atezolizumab with trastuzumab and vinorelbine may improve outcomes in HR- or PAM50 non-luminal/HR-positive (HR+) disease within HER2+ MBC. Methods ATREZZO is an open-label, single-arm, Simon 2-stage, multicenter phase II study. The trial will include 55 pre- or post-menopausal female or male patients with unresectable locally advanced or metastatic HR- or PAM50 non-luminal/HR+ HER2+ BC and progressed to trastuzumab-based chemotherapy and anti-HER2 ADC. Prior pertuzumab is allowed, but not required. Treatment consists of atezolizumab IV 1200 mg every 3 weeks combined with trastuzumab and vinorelbine. Patients with stable, progressing, or untreated brain metastasis not requiring immediate local therapy are eligible. The primary objective is to evaluate the Overall Response Rate (ORR) according to RECIST v 1.1 and secondary endpoints include ORR in patients with PD-L1 positive breast cancer, clinical benefit rate, overall survival and progression-free survival. The final recruited population will contain no more than 60 % of patients with PD-L1 negative tumors. Tumor assessments will be performed every 9 weeks. Incidence, duration and severity of adverse events, and further correlative molecular analyses will be also evaluated. An interim analysis will be conducted when 19 patients are evaluable for ORR and if the number of responses is ≥ 3 , 36 additional patients will be included. As of July 15th, 2022, 48 patients were screened and 15 were included in sixteen Spanish sites. This study was funded by Roche Farma SA. Trial identification: NCT04759248

Disclosure(s):

Eva Ciruelos, MD, PhD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer,: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Travel, accommodations, expenses (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Travel, accommodations, expenses (Ongoing)

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12/7/2022

5:00 PM - 6:15 PM

OT2-08-03

Immunogenicity of pembrolizumab and doxorubicin in a phase I trial for patients with metastatic triple negative breast cancer

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Background: Combination of immune checkpoint inhibitor pembrolizumab and chemotherapy are standard of care therapy for patients with programmed death-ligand 1 positive (PD-L1+) metastatic triple negative breast cancer (mTNBC). However, a greater understanding of how immune checkpoint inhibitors and chemotherapies synergize to yield anti-tumor T cell responses is needed. The current phase I study evaluated the immunogenicity of doxorubicin plus pembrolizumab in patients with mTNBC. Patients and Methods: Patients with mTNBC, no prior anthracycline use, and 0-2 lines of prior systemic chemotherapies received pembrolizumab 200 mg IV and doxorubicin 50-60 mg/m² IV every 3 weeks for 6 cycles followed by pembrolizumab maintenance until disease progression or intolerance. Patients were not selected based on PD-L1 expression. The primary objectives were safety and objective response rate per RECIST 1.1. Peripheral blood samples were collected at baseline, Cycle 2 Day 1 (C2D1), and post Cycle 3 for analysis by high parameter flow cytometry. Results: Ten patients were enrolled between March 2016 and November 2019. Best responses included one patient with complete response (CR), five with partial responses (PR), two with stable disease (SD), and one with progression of disease (PD). Flow cytometry showed increased CD3⁺ T cells (p=0.03) from pre-treatment to C2D1 with substantial inter-patient variation in CD3⁺ T cells. The expansion of proliferative exhausted-like PD-1⁺ CD8⁺ T cell population was identified in 8/9 patients, and exhausted CD8⁺ T cells were significantly expanded from pre-treatment to C2D1 in the patient with CR (p=0.01). Notably, frequencies of PD-1^{hi} proliferative CD8⁺ T cells contracted significantly from C2D1 to post Cycle 3 (p=0.005), with a return to near baseline frequencies in the majority of the patients. In the context of all identified T cell subsets, PD-1^{hi} proliferative CD8⁺ T cells demonstrated the greatest increase in fold change from pre-treatment to C2D1. In contrast, PD-1^{lo} proliferative CD8⁺ T cells demonstrated the greatest decrease in fold change from pre-treatment to C3D1. Conclusion: Anthracycline-naïve patients with mTNBC treated with the combination of pembrolizumab and doxorubicin yielded robust peripheral blood T cell responses. Further studies dissecting the dynamics and durability of anti-tumor T cell responses and concurrent tumor immune microenvironment changes are needed to optimize combined immune checkpoint inhibitor and chemotherapy treatment for patients with mTNBC.

Disclosure(s):

Colt A. Egelston, PhD: No financial relationships to disclose

Weihua Guo, PhD: No financial relationships to disclose

Susan E. Yost, PhD: No financial relationships to disclose

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12/7/2022

5:00 PM - 6:15 PM

OT2-09-01

TBCRC-055: A Phase II Study of NirAparib, Dostarlimab, and Radiotherapy in Metastatic, PD-L1 Negative or Immunotherapy-Refractory Triple-Negative Breast Cancer (NADiR) – NCT04837209

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Background: Metastatic triple negative breast cancer (mTNBC) is associated with high recurrence and mortality rates. Prior studies have shown an immune checkpoint inhibitor (ICI) + chemotherapy improves progression-free survival for patients with PD-L1 positive mTNBC. There remains a need for treatment options in patients who do not respond to ICI or are PD-L1 negative. Preclinical data suggests that a PARP inhibitor (PARPi) may promote innate immune signaling, and combination with an ICI has shown a positive response in patients with mTNBC.

Radiotherapy (RT) is a potent immune stimulator and used for local control in the setting of metastatic breast cancer. This phase II study (NCT04837209) proposes combination of PARPi, ICI, and RT to combat ICI resistance and improve response rates in patients with mTNBC who are PD-L1 negative or who have progressed on prior ICI. Methods: 32 patients with mTNBC defined as ER< 1%, PR< 1%, HER-2-neu 0-1+ by IHC or non-FISH-amplified or patients with metastatic HR+/HER2- breast cancer are anticipated to participate. Eligibility criteria for mTNBC patients includes those who are PD-L1 negative or have progressed on prior ICI. Eligibility criteria for HR+/HER2- patients is specific to those who harbor a deleterious BRCA1 or BRCA2 mutation with or without high tumor mutational burden (TMB). All trial patients should have at least 1 lesion amenable to RT and at least 1 measurable lesion that will not be radiated. Study treatment consists of 3-week cycles, with 500mg dostarlimab given on day 1 of each cycle through cycle 5, then 1000mg given every 6 weeks. RT (24 Gy) is delivered in 3 consecutive fractions starting day 1 of cycle 1. Niraparib (200mg) is dosed orally daily. Tumor biopsies are taken within 28 days pre-treatment, and at C3D1-8. Blood samples are taken at baseline and every odd cycle for cfDNA and PBMC analysis. The primary endpoint is to assess overall response rate as measured by RECIST v1.1 of the combination of niraparib, dostarlimab, and RT. Secondary objectives include assessing safety and toxicity, overall survival, progression free survival, and quality of life. Results: To date, this study has accrued 4 subjects, including 3 with mTNBC, and 1 with HR+/HER2-/BRCA mutant + TMB high mBC. The study is currently open at MGH and Sibley, and the addition of UPenn, Johns Hopkins, and Duke are in progress. Funding for this study was provided by GSK. GSK was provided the opportunity to review a preliminary version of this abstract for factual accuracy, but the authors are solely responsible for final content and interpretation. People with specific interest in the trial should reach out to Elizabeth Scott, Clinical Research Coordinator, at escott@mgh.harvard.edu.

Disclosure(s):

Elizabeth Scott, n/a: No financial relationships to disclose

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12/7/2022

5:00 PM - 6:15 PM

OT2-10-01

A phase 2, randomized study of magrolimab combination therapy in adult patients with unresectable locally advanced or metastatic triple-negative breast cancer

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Background: Improving outcomes for patients (pts) with triple-negative breast cancer (TNBC) remains a high unmet need. Immune checkpoint inhibitors (ICIs) + chemotherapy (chemo) and single-agent sacituzumab govitecan, a trophoblast cell-surface antigen 2–targeted antibody-drug conjugate coupled to SN38 via a proprietary, hydrolysable linker, are approved in newly diagnosed pts with programmed death-ligand 1 (PD-L1)–positive tumors and pts who received ≥ 2 prior systemic therapies (≥ 1 for metastatic disease), respectively. However, additional options are urgently needed, particularly for pts with tumors that do not express PD-L1 and for those with progression on chemo \pm ICI. Magrolimab is an antibody blocking CD47, a “don’t eat me” signal overexpressed on cancer cells, including TNBC, inducing tumor phagocytosis by macrophages. Magrolimab has shown preclinical activity and promising clinical efficacy in hematologic and solid tumors. Chemo agents, including taxanes, can enhance prophagocytic signals on tumor cells, leading to the potential for synergistic antitumor activity with magrolimab. This study is evaluating the safety/tolerability and efficacy of magrolimab in combination with nab-paclitaxel/paclitaxel or with sacituzumab govitecan in unresectable locally advanced/metastatic TNBC. Trial Design: This open-label, 2-cohort (C) study consists of safety run-in and phase (ph)2 portions evaluating nab-paclitaxel/paclitaxel (choice) + magrolimab (safety run-in) or \pm magrolimab (ph2, randomized 1:1) in pts with untreated, advanced/metastatic TNBC ineligible for ICI (C1) and magrolimab + sacituzumab govitecan

(safety run-in and ph2) in pts with advanced TNBC who received 1 prior systemic treatment in the metastatic setting (C2). Stratification factors for C1 are neoadjuvant and/or adjuvant taxane therapy, liver metastases, and nab-paclitaxel vs paclitaxel. In both cohorts, magrolimab will be administered intravenously (IV) in de-escalating doses to establish the recommended ph2 dose (RP2D). Nab-paclitaxel/paclitaxel and sacituzumab govitecan will be administered IV per standard of care. Eligibility Criteria: Eligible pts are ≥ 18 y with PD-L1–negative, untreated, unresectable locally advanced/metastatic TNBC (C1) or unresectable locally advanced/metastatic TNBC who received 1 prior line of therapy in the advanced setting, including a taxane and an ICI if PD-L1 positive (C2), with measurable disease per RECIST v1.1. Exclusion criteria include active central nervous system disease, red blood cell transfusion dependence, or prior treatment with CD47/signal regulatory protein α –targeting agents for both cohorts. Additional exclusions are disease progression within 6 months of (neo)adjuvant therapy or rapid visceral progression and/or symptomatic disease, for which single-agent chemo would not be appropriate (C1); chronic inflammatory bowel disease and a history of bowel obstruction or gastrointestinal perforation within 6 months of enrollment, prior treatment with topoisomerase I inhibitors or antibody-drug conjugates containing a topoisomerase inhibitor, and receipt of high-dose systemic corticosteroids within 2 weeks of cycle 1 day 1 (C2). Specific Aims: The primary objectives are safety/tolerability and magrolimab RP2D (safety run-in) and efficacy (ph2: C1, progression-free survival [PFS]; C2, objective response rate [ORR]; both by investigator). Secondary objectives include ORR, PFS, and duration of response by investigator and independent central review, overall survival, and magrolimab concentration vs time and antidrug antibodies. Present and Target Accrual: The study is enrolling in the US, Australia, and Hong Kong. Target accrual is 144 pts. Contact Information: ClinicalTrials.gov: NCT04958785.

Disclosure(s):

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Ownership Interest (stocks, stock options, patent or other intellectual property or other
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5:00 PM - 6:15 PM

OT2-10-02

Phase I trial of an alpha-lactalbumin vaccine in patients with operable triple-negative breast cancer (TNBC)

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Background: Triple-negative breast cancer (TNBC) is the subtype of breast cancer with the worst prognosis and is the subtype most often associated with germline mutations of BRCA1 as well as other genes. Alpha-lactalbumin (aLA) is a milk protein expressed in lactating breasts but not at other times or in other normal tissues. Expression of aLA is found in approximately 70% of TNBC (Cancers PMID: 27322324) so is an attractive immunologic target for TNBC based on the “retired protein hypothesis” (Semin Immunol PMID: 31926646). Pre-clinical studies have shown that vaccination with aLA inhibits the growth of established breast tumors and provides potent protection from development of autochthonous tumors in transgenic murine models of breast cancer and against 4T1 transplantable breast cancer in BALB/c mice (Nat Med PMID: 20512124). **Specific Aims:** We are conducting a Phase I trial of vaccination with an aLA vaccine in patients with early stage TNBC to demonstrate the safety of this approach and to document the ability to produce a relevant immunologic response to aLA. **Trial Design:** Patients are being entered into a Phase I trial of alpha-lactalbumin with GMP-grade zymosan adjuvant in Montanide ISA 51 VG vehicle. Subjects receive a total of 3 vaccinations administered once every 2 weeks. Toxic events of Common Terminology Criteria for Adverse Events (CTCAE) grade 2 or greater are considered dose-limiting. Dose levels being tested in the current protocol are alpha-lactalbumin/zymosan 0.01/0.01, 0.1/0.01, 0.5/0.01, 0.5/0.03, and 0.5 mg/0.06 mg. Patients are being monitored for toxicity until 84 days after the first vaccination or resolution of toxicity, whichever is later. Blood is being drawn prior to therapy and 14, 28, and 56 days after the first vaccination to assess cellular response using enzyme-linked immunosorbent spot (ELISpot) assays of interferon-gamma and interleukin-17 production in response to aLA. Humoral response to aLA vaccination is being assessed by enzyme-linked immunosorbent assay (ELISA). **Eligibility Criteria:** Patients with ER-negative, PR-negative, HER2-negative breast cancer of pathologic stage II-III or who had residual disease after standard pre-operative systemic therapy. Participants must be within 3 years of initiation of treatment and have no evidence of recurrence. **Dose Selection:** Doses are being escalated using a 3+3 trial design to determine the maximum tolerated dose, the lowest immunologic dose and the optimal immunologic dose **Present Accrual and Target Accrual:** Dependent on toxicity, 18-30 patients will be treated. **Future Plans and Contact Information:** After identification of the maximum tolerated dose and expansion of the dose levels associated with effective tumor immunity we plan to enroll 2 additional cohorts of patients: 1) patients who have completed pre-operative chemo-immunotherapy and are receiving pembrolizumab as standard of care therapy, and 2) patients without cancer planning to undergo prophylactic bilateral mastectomy. Interested parties may contact Dr. Budd at buddg@ccf.org. **Funding Source:** Department of Defense (W81XWH-17-1-0592 and W81XWH-17-1-0593)

Disclosure(s):

George Budd, MD: ambrx: Contracted Research (Ongoing); ayala: Contracted Research (Ongoing); daiichi: Contracted Research (Ongoing); deciphera: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); roche: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); salarius: Contracted Research (Ongoing); tracon: Contracted Research (Ongoing)

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5:00 PM - 6:15 PM

OT2-10-03

HCRN BRE 19-433: A Multi-institutional Phase II Study to Evaluate Efficacy and Safety of TALazoparib, Radiotherapy and Atezolizumab in gBRCA 1/2 negative Patients with PD-L1+ Metastatic Triple Negative Breast Cancer (TARA)

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Background Although immunotherapy (IO) in combination with chemotherapy has improved progression free and overall survival in patients with PD-L1+ metastatic triple negative breast cancer (mTNBC), prognosis remains poor. A potential therapeutic strategy to restore sensitivity to IO in patients with progressive disease is to introduce agents that re-sensitize the immune system to IO leading to a more tumor-specific and less toxic treatment in the second-line setting or beyond. Both talazoparib, a PARP inhibitor, and radiation (XRT) independently increase PD-L1 expression on the tumor cell surface resulting in heightened sensitivity to IO agents like atezolizumab, a PD-L1 inhibitor. Although a local treatment, XRT has the ability to produce an abscopal effect resulting in systemic shrinkage of non-irradiated tumors outside/distant to the

XRT field, a phenomenon observed in patients receiving concurrent IO. While talazoparib is standard treatment in patients with gBRCA1 and 2 mutations, it is also a potent radiosensitizing agent that suppresses homologous recombination and PARP-1-dependent nonhomologous end joining (NHEJ) repair while promoting error-prone alt-NHEJ. When combined with IO, talazoparib can amplify immune responses by generating immunogenic neo-antigens independent of gBRCA1/2 status. We, therefore, hypothesize that the combination of talazoparib, XRT, and atezolizumab will re-sensitize mTNBC tumors to IO and promote a durable tumor-specific response that spares patients from toxicities associated with traditional chemotherapy regimens. Methods This is a Phase II multi-institutional study designed to assess efficacy and safety of talazoparib, high dose XRT, and atezolizumab given in the second-, third-, or fourth-line settings to patients with mTNBC that is PD-L1 positive. A total of 23 patients with mTNBC who do not carry gBRCA pathogenic variants will be enrolled. All patients will be treated with induction talazoparib of 1mg PO daily starting Day 1 of a 28-day cycle. Patients will then receive 8 Gy x 3 fractions to 1-4 metastatic lesions QOD beginning Day 12, 13, or 14. Atezolizumab will be given intravenously (840 mg) on Day 15 of the 1st cycle and then on Day 1 and Day 15 of the subsequent cycles. Talazoparib and atezolizumab treatment will continue until progression or severe toxicity. The primary endpoint is objective response rate (ORR) in non-irradiated lesions 8 weeks after the first dose of atezolizumab. Key inclusion criteria include biopsy proven mTNBC (ER< 10%, PR< 10%, Her2-) with at least 2 extracranial metastatic lesions. Patients must have at least 1 extracranial metastatic lesion amenable to high dose radiotherapy and at least one additional extracranial lesion of measurable disease by Response Evaluation Criteria in Solid Tumors (RECIST v1.1) that will not receive radiotherapy. Tumors must be PD-L1 positive as defined as >1% on IHC using the SP142 Ventana Assay. Key exclusion criteria include patients with germline BRCA pathogenic variants, more than three previous lines of chemotherapy treatment in the advanced setting with or without IO, and breast cancer progression within the first 3 months of previous IO treatment for non-metastatic or metastatic breast cancer. Sample size was determined using Simon's 2-stage Minimax design to detect a 20% increase in ORR. The null hypothesis that the true response rate among gBRCA1/2 negative patients of 10% will be tested against a one-sided alternative. Inflammatory cytokines, circulating B cells, and ctDNA will be collected for correlative analysis. Enrollment began in April 2021. The study is managed by the Hoosier Cancer Research Network and is open to accrual at Emory University and University of Alabama at Birmingham. Clinical trial information: NCT04690855

Disclosure(s):

Mylin A. Torres, MD: Genentech: Contracted Research (Ongoing); OncoHealth: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Varian: Presenter on indications for breast cancer radiation (Ongoing)

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OT2-10-04

Treatment of advanced or metastatic triple-negative breast cancer with adoptive therapy of PD1+ tumor-infiltrating lymphocytes (TILS001 trial).

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Background Metastatic triple-negative breast cancer (mTNBC) exhibits a particularly poor clinical outcome, generally with rapid progression and worse overall survival (OS) than other BC subtypes. Among the few therapeutic options, chemotherapy-based combinations are associated with increased toxicity and limited survival benefit, being treatment with sequential single agents, such as paclitaxel considered an appropriate first-line regimen for the metastatic setting for PDL-1 negative patients. Herein, there is an urgent need for clinically active agents for the mTNBC. Adoptive cell transfer (ACT)-based immunotherapy using ex vivo activated and expanded tumor-infiltrating lymphocytes (TILs) has shown promising therapeutic outcomes in some patients with metastatic tumors. The identification, selection, and enrichment of tumor-reactive lymphocytes at the early stages of the ACT generation could enhance their clinical activity. Thus, the selection of reactive T cells, such as PD1-positive (PD1+) TILs, could improve the responses achieved in those settings. TILS001 trial aims to explore the safety, tolerability and efficacy of selected PD1+ T-cell infusion with a previous pre-selection of mRNA PD1-high expression in patients with mTNBC. Study design: TILs001 trial is an open-label, single-arm, multicenter phase I/II prospective study with a two-stage design evaluating treatment with PD1+ TILs infusion in advanced or mTNBC, defined as HER2 negative and Hormonal Receptor < 10%. The study involves three different parts before PD1+TILs treatment. Tumor samples evaluable for PD1 mRNA expression and life expectancy ≥ 6 months are mandatory for part 1. Patients with high levels of PD1 mRNA, defined by the pre-specified cutoff, candidates for receiving a first-line taxane-based containing regimen and with at least 1 accessible target lesion to generate TILs are eligible for part 2. Finally, once the complete expansion of PD1+TILs is reached, patients will receive the non-myeloablative lymphodepleting chemotherapy regimen followed by PD1+TIL infusion and IL-2 treatment. Allogeneic hematopoietic stem cell transplantation, immune system-related disease or clinically active cerebral metastasis are not allowed. The primary objectives are to evaluate the safety and tolerability of the PD1+ TIL product, as per incidence of grade 3-5 adverse events (AE) or any grade AE that leads to treatment discontinuation and to assess the efficacy of ACT therapy with selected PD1+ TILs in mTNBC in terms of progression-free survival (PFS) at 6 months. The secondary endpoints are clinical benefit rate at 6 months (CBR6), overall response rate, duration of response (DoR), PFS and OS. Further translational research including immunophenotyping, TCR sequencing and mutational analysis will also be performed. The first 3 patients will be included in a safety run-in phase where safety will be evaluated 24h after PD1+/TILs infusion (before IL-2 treatment) and a phase II stage where efficacy will be evaluated, which will include up to 20 patients. Patients will be enrolled in 4 sites in Spain. Recruitment is expected to start by July 2022 and to be completed within 24 months. This study is financially supported by the Asociación Española Contra el Cáncer (GCAEC19010PRAT). NCT05451784

Disclosure(s):

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HER2Pro: A Phase 1b dose de-escalation study of high dose prochlorperazine added to paclitaxel, trastuzumab and pertuzumab in patients with previously untreated HER2-positive metastatic breast cancer

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HER2Pro: A Phase 1b dose de-escalation study of high dose prochlorperazine added to paclitaxel, trastuzumab and pertuzumab in patients with previously untreated HER2-positive metastatic breast cancer Authors Teesha Downton^{1,2}, Emma Karlsen¹, Katharine Cuff^{3,4}, Euan Walpole^{3,4}, Fiona Simpson^{3,4}, Elgene Lim^{1,2}. Affiliations ¹Garvan Institute of Medical Research, Darlinghurst NSW, Australia; ²School of Clinical Medicine, St Vincent's Healthcare Clinical Campus, Faculty of Medicine and Health, University of New South Wales Sydney, Australia; ³Diamantina Institute, University of Queensland, Woolloongabba QLD, Australia; ⁴Princess Alexandra Hospital, Brisbane QLD, Australia Disclosures T. Downton: None. E. Karlsen: None. K. Cuff: None. E. Walpole: None. F. Simpson: None. E. Lim. Advisory Board for Pfizer, Astra Zeneca, Lilly, Roche, Novartis, Gilead Australia. Research Funding from Pfizer, Novartis, Bayer. Abstract Background: The anti-emetic prochlorperazine reversibly inhibits dynamin-mediated endocytosis. Preclinical studies have demonstrated that through this mechanism, high dose prochlorperazine can temporarily increase tumor cell antigen presentation, enhance interaction of tumor antigens with therapeutic monoclonal antibodies, and improve antibody-dependent cellular cytotoxicity (Chew H et al. Cell 2020). High dose

prochlorperazine has been well tolerated and proof of mechanism demonstrated in a pilot study (ACTRN12619001051134), and in a phase Ib trial (ACTRN12619001527156) of prochlorperazine with cetuximab in patients with EGFR-expressing advanced head and neck squamous cell carcinoma or breast cancer. Prochlorperazine potentially offers a novel approach to improve the efficacy of a range of therapeutic antibodies. This study HER2Pro (ACTRN12622000016730) aims to evaluate the feasibility and safety of high dose prochlorperazine in combination with paclitaxel, trastuzumab, and pertuzumab in patients with HER2-positive metastatic breast cancer. Trial Design: In this phase Ib single-arm trial, patients receive standard of care trastuzumab and pertuzumab 3-weekly and paclitaxel weekly. From cycle 2, patients in addition receive de-escalating doses of prochlorperazine weekly for 6 weeks, though an additional 6 weeks may be given if there are no treatment associated serious adverse events. Dose de-escalation will be evaluated using a 3+3 design, commencing at a prochlorperazine intravenous dose of 0.8mg/kg weekly. Eligibility: Eligible patients must have previously untreated HER2-positive metastatic breast cancer, Eastern Cooperative Oncology Group performance status 0-1, and baseline left ventricular ejection fraction \geq 50%. Key exclusion criteria include current daily treatment with corticosteroids at a dose $>$ 10mg prednisolone or equivalent, blood pressure $<$ 90/50 mmHg, prolonged QT interval, and Parkinson's disease. Objectives: The primary objective is to determine the recommended phase 2 dose. Secondary objectives include determining the frequency and severity of adverse events, rates of cardiotoxicity, objective response rate, duration of response and progression free survival. Tertiary objectives include analysis of receptor trafficking and immune system activation on paired tumor biopsies obtained before and after first prochlorperazine dose. Accrual: 6-12 patients will be enrolled across 2 Australian sites. Enrollment for this trial is expected to commence late 2022.

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5:00 PM - 6:15 PM

OT2-10-06

Phase III study to evaluate the efficacy and safety of GLSI-100 (GP2 + GM-CSF) in breast cancer patients with residual disease or high-risk pCR after both neo-adjuvant and postoperative adjuvant anti-HER2 therapy, Flamingo-01

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Background: GP2 is a biologic nine amino acid peptide of the HER2/neu protein delivered in combination with Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF) that stimulates an immune response targeting HER2/neu expressing cancers, the combination known as GLSI-100. In a prospective, randomized, single-blinded, placebo-controlled, multicenter Phase IIb study, no recurrences were observed in the HER2+ population after 5 years of follow-up, if the patient was treated with GLSI-100, survived and was followed for more than 6 months ($p = 0.0338$). Immunotherapy elicited a potent response measured by skin tests and immunological assays. Of the 146 patients that have been treated with GLSI-100 over 4 clinical trials, GLSI-100 was well-tolerated and no serious adverse events were observed considered related to the immunotherapy. Method: This Phase III trial is a prospective, randomized, double-blinded, multi-center study. After 1 year of trastuzumab-based therapy, 6 intradermal injections of GLSI-100 or placebo will be administered over the first 6 months and 5 subsequent boosters will be administered over the next 2.5 years for a total of 11 injections over 3 years. The participant duration of the trial will be 3 years treatment plus 1 additional year follow-up for a total of 4 years following the first year of treatment with trastuzumab-based therapy. Patients will be stratified based on residual disease status at surgery, hormone receptor status and region. Study Size – Interim Analysis: Approximately 498 patients will be enrolled. To detect a hazard ratio of 0.3 in invasive breast cancer free survival (IBCFS), 28 events will be required. An interim analysis for superiority and futility will be conducted when at least 14 events have occurred. This sample size provides 80% power if the annual rate of events in placebo patients is 2.4% or greater. Up to 100 non-HLA-A*02 subjects will be enrolled in an open-label arm. Eligibility Criteria: The patient population is defined by these key eligibility criteria: 1. HER2/neu positive and HLA-A*02 2. Residual disease or High risk pCR (Stage III at presentation) post neo-adjuvant therapy 3. Exclude Stage IV 4. Completed at least 90% of

planned trastuzumab-based therapy Trial Objectives: 1. To determine if GP2 therapy increases IBCFS 2. To assess the safety profile of GP2 3. To monitor immunologic responses to treatment and assess relationship to efficacy and safety Contact information: Snehal Patel Greenwich LifeSciences, Inc. Stafford, TX Email: snehal.patel@greenwichlifesciences.com Website: greenwichlifesciences.com Funding: This trial is supported by Greenwich LifeSciences.

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OT2-11-01

A phase 1 study of the novel immunotoxin MT-5111 in patients with HER2+ tumors: interim results

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MT-5111 is a 55kD engineered toxin body targeting HER2 in solid tumors that binds to an epitope distinct from trastuzumab and pertuzumab, offering potential combination strategies with other HER2-targeting agents. MT-5111 works by internalizing, self-routing through intracellular compartments to the cytosol, and inducing potent cell-kill via the enzymatic and permanent inactivation of ribosomes.

This is a phase 1 study in adults with advanced HER2+ solid tumors. MT-5111 is dosed weekly IV over 30 min in every 21-day cycle until disease progression, unacceptable toxicity, death, or withdrawn consent. The study has dose escalation (Part A) cohorts enrolling patients (pts) with any HER2+ cancer (CA) and expansion (Part B) cohorts for HER2+ breast cancer (BC), Gastric or Gastroesophageal junction adenocarcinoma (GEA), or other HER2+ solid CA.

As of 30 June 2022, 42 total pts had enrolled (36 in Part A on 0.5-23 µg/kg/dose, 6 pts with BC in Part B1 on 10 µg/kg/dose). Median age 65 years, 28 (66.78%) pts were female, median of 4 prior systemic and 2 prior HER2-targeting treatment (tx). 17 pts with BC, 6 with biliary CA, 9 with GEA, and 10 with other solid CA have enrolled. Of the 17 BC pts, 15 received ≥ 10 µg/kg/dose.

Tx emergent adverse events (TEAEs) have been reported in 40 (95%) pts, and tx-related AEs (TRAE) occurred in 23 (55%) pts. No pt experienced G4-G5 TRAE. G1 troponin elevations were noted in 5 pts without clinical signs of cardiotoxicity (1 pt 6.75 µg/kg, 2 pts 10 µg/kg, 1 pt 17 µg/kg, 1 pt 23 µg/kg). Reversible G1/G2 infusion-related reactions were reported in 2 pts. Tx-related G1-G3 rash was observed in 5 pts (4 pts ≥ 10 µg/kg/dose); maculopapular in 2 pts, acneiform in 1 pt and associated with pruritus in 3 pts. The G3 rash developed one wk after first dose of 23 µg/kg, was declared a DLT, improved with systemic steroid therapy and the pt continued tx at the same dose without recurrence.

Best overall response per RECIST thus far is stable disease (SD) in 17 pts, non-CR/non-PD in 1 pt, and progressive disease (PD) in 14 pts. 1 pt had non-CR/non-PD for 30 wks (1 µg/kg, BC); 1 pt had SD for 24wks (10 µg/kg, pancreatic); 1 pt is on tx with SD through 8 cycles (10 µg/kg, BC). Of the 10 BC pts who received ≥ 10 µg/kg/dose, the best response was 5 SD.

The mean serum concentration of MT-5111 has increased in a dose-proportional manner starting at 6.75µg/kg/dose (Table 1). The soluble HER2 (sHER2) levels at end of tx were higher compared to baseline in cohorts that received ≤ 4.5µg/kg/dose, but similar or lower in cohorts that received ≥ 6.75µg/kg/dose. Higher MT-5111 doses have been well tolerated and may saturate circulating sHER2, leading to more predictable serum concentrations and tumor penetration. The C_{max} in humans at doses ≥6.75 µg/kg/dose is above the in vitro IC₅₀ for high HER2+ cell lines (0.029nM) and at 17 µg/kg/dose, above the IC₅₀ for moderate HER2+ cells (1.6nM).

In conclusion, the dose proportionate increase in serum concentration with levels above the in

vitro IC50 and the leveling off/reduction of sHER2 indicate exposure to MT-5111 is at clinically therapeutic levels. Skin toxicity at higher doses may indicate on-target effect as observed in other EGFR-targeted therapies where it is associated with clinical response and a better prognosis. sHER2 biomarker data is expected for all cohorts with PK correlation and 23µg/kg safety and efficacy data.

PK profile of MT-5111, C1D1 values

Dose (µg/kg)	N	C _{max} (ng/mL)	C _{max} (nM)*	t _{1/2} (hr)
6.75	5	33 (± 12)	0.6 (±0.22)	3.9 (± 2.0)
10.0	11	54 (± 24)	0.98 (±0.44)	6.9 (± 6.3) ^
13.0	3	81 (± 46)	1.47 (±0.84)	5.3 (± 4.0)
17.0	4	93 (± 27)	1.69 (±0.49)	6.6 (± 4.0)

C_{max} = maximum serum concentration; C_{max} and t_{1/2} values are mean (± SD).
 *nM= (ng/mL)/(molecular weight of MT-5111) ^Data available for 10 pts.
 Note: PK values for doses 0.5, 1, 2, 3, and 4.5 µg/kg are not presented. C_{max} values were below or just above IC₅₀ for cell lines with high HER2+ and below that for moderate HER2+.

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5:00 PM - 6:15 PM

OT2-12-01

Clinical Application of LFSPRO: A Prospective Study

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Background: Individuals with Li-Fraumeni Syndrome (LFS) have increased risk of developing cancers of several types, such as early-onset breast cancer, soft-tissue/bone sarcoma, leukemia, brain tumors, and more, throughout their lifetime. LFS is primarily caused by autosomal dominant germline mutations in the TP53 tumor suppressor gene. It is difficult to identify TP53 mutation carriers because of the overlap in the occurrence of multiple cancer types in LFS with other inherited cancer syndromes. In order to improve the accuracy of risk assessment for these families, the LFSPRO risk model was created to predict the likelihood of

a proband having LFS based off detailed patient and family history information, as well as predict cancer-specific risks for patients who have already been identified as having LFS. Specific Aims: The primary aim of this study is to evaluate the concordance of LFSPRO and clinical criteria in predicting TP53 mutation status in patients undergoing germline TP53 testing. Trial Design: After receiving standard genetic counseling, patients identified as concerning for a potential TP53 mutation by a MD Anderson genetic counselor (GC) are run through LFSPRO. LFSPRO TP53 mutation carrier risk, whether the patient meets Chompret and/or Classic criteria, decision to test, and genetic test results are collected. Select GCs are then asked to complete a survey regarding their experience with LFSPRO. Eligibility Criteria: Through standard genetic counseling practice, MD Anderson GCs identify patients with a clinical suspicion for a TP53 germline mutation. All patients identified are run through LFSPRO. Out of these identified patients, select GCs that participated in the initial genetic counseling session are asked to complete a survey over their experience using the LFSPRO. Statistical methods: We will evaluate the concordance in the prediction of TP53 mutation carrier status between LFSPRO and current clinical criteria as compared to the outcome of genetic testing results. We will cross-tabulate the predicted TP53-mutation status (positive vs. negative) with the carrier status in a 2x2 table and calculate the sensitivity and specificity of each prediction tool separately (LFSPRO, clinical criteria), with 95% confidence interval. Accrual: Currently, 72 patients have been run through LFSPRO. Select GCs have completed the survey regarding their experience with LFSPRO on 20 of these patients. Data collection began in December 2021 and is currently ongoing. Funding: This research is supported by the Cancer Research and Prevention Institute of Texas. Contact: Jacynda Woodman-Ross, MS, CGC, The University of Texas MD Anderson Cancer Center, jawoodman@mdanderson.org

Disclosure(s):

Jacynda Woodman-Ross, MS, CGC: No financial relationships to disclose

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BMS: Consulting Fees (e.g., advisory boards) (Ongoing); Notable Labs: Consulting Fees (e.g., advisory boards) (Ongoing); Servier: Consulting Fees (e.g., advisory boards) (Ongoing)

Wenyi Wang, PhD: Curis Inc: Contracted Research (Ongoing)

Banu K. Arun, MD: AstraZeneca: research paid to the MD Anderson Cancer Center (Ongoing)

12/7/2022

5:00 PM - 6:15 PM

OT2-13-01

Willingness to Participate in a Trial Comparing Standard Genetic Counseling versus Genetic Counseling with Personalized Cancer Risks Estimates in Patients with Li-Fraumeni Syndrome

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Background: Individuals with Li-Fraumeni Syndrome (LFS) have increased risk of developing breast cancer, sarcomas, brain tumors, leukemia, and other cancers throughout their lifetime. LFS is primarily caused by autosomal dominant germline mutations in the TP53 tumor suppressor gene. Due to the large number of cancers caused by LFS, and their variable age of presentation, each LFS family often presents very differently. Currently, standard genetic counseling for patients with LFS often involves general lifetime risk predictions for developing several primary cancers. At present, there are no standard tools available to help genetics providers obtain a personalized risk assessment for a patient with LFS based on their unique personal and family history data. To address this, the LFSPRO risk model was developed to estimate the likelihood of a proband having LFS, to provide cancer-specific risks of a first primary cancer, and to estimate risk of time to second primary cancer diagnosis by utilizing

detailed personal and family history information. Specific Aims: This study aims to understand patients' willingness to participate in a randomized trial comparing standard genetic counseling practice to personalized genetic counseling via LFSPRO risk estimates. Trial Design: Eligible patients or parents/guardians are invited via email to complete a survey assessing interest in a hypothetical clinical trial scenario where patients are randomized to receive one of two types of post-disclosure genetic counseling approaches: standard genetic counseling for TP53 results, involving generic risk predictions for developing cancers, or personalized risk information provided from LFSPRO. Following the hypothetical scenario, participants are asked about their perceived benefits and barriers to this research scenario and interest in receiving personalized risk results. Demographic information is also collected. Eligibility Criteria: Individuals who receive genetic counseling through MD Anderson Cancer Center genetics clinics specifically for TP53 genetic testing and who consent to undergo TP53 genetic testing or individuals who genetic testing already indicates a TP53 germline mutation are offered this survey. Patients must be 13 years or older to complete the survey, otherwise a parent/guardian may complete the survey on their behalf. Patients must have English fluency. Statistical methods: Descriptive statistics will be used to analyze the data and summarize the opinion of the participants. Accrual: Enrollment is set to open in July 2022. Currently, 157 patients have been identified to be invited to participate in the study. Funding: This research is supported by the Cancer Research and Prevention Institute of Texas. Contact: Jacynda Woodman-Ross, MS, CGC, The University of Texas MD Anderson Cancer Center, jawoodman@mdanderson.org

Disclosure(s):

Jacynda Woodman-Ross, MS, CGC: No financial relationships to disclose

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Wenyi Wang, PhD: Curis Inc: Contracted Research (Ongoing)

Banu K. Arun, MD: AstraZeneca: research paid to the MD Anderson Cancer Center (Ongoing)

12/7/2022

5:00 PM - 6:15 PM

OT2-14-01

Pyrotinib after trastuzumab-based adjuvant therapy in high-risk early human epidermal growth factor receptor 2-positive breast cancer: a multicenter phase 2 trial

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Objective: Trastuzumab-based adjuvant therapy was demonstrated to improve the prognosis of early human epidermal growth factor receptor 2 (HER-2) positive breast cancer, while about 10% of patients showed primary resistance. ExteNET study showed that 1 year of neratinib, an irreversible pan-HER tyrosine kinase inhibitor, after trastuzumab-based adjuvant therapy significantly improved invasive disease-free survival (iDFS) in women with HER2-positive breast cancer. Besides, for patients with early hormone receptor positive breast cancer within 1 year of prior trastuzumab with residual disease after neoadjuvant therapy, extended adjuvant neratinib showed prolonged overall survival, which suggested the potential benefit of extended adjuvant therapy for high-risk patients. Pyrotinib is an oral irreversible pan-HER receptor tyrosine kinase inhibitor targeting epidermal growth factor receptor, HER2, and HER4, which showed promising efficacy and manageable safety profiles in the treatment of HER-2 positive advanced breast cancer. In this study, we aimed to evaluate the efficacy and safety of extended adjuvant pyrotinib following trastuzumab-based adjuvant therapy in patients with high-risk early HER-2 positive breast cancer.

Methods: In this ongoing multicenter, open-label, phase II trial at 23 centers in China, women with operable high-risk early HER-2 positive breast cancer and known hormone receptor status, who have completed trastuzumab-based adjuvant therapy within 6 months were enrolled. High-risk patients must meet one of the following criteria: N stage ≥ 1 ; T stage ≥ 2 ; did not achieve pathological complete response (pCR) after neoadjuvant therapy; had pCR after neoadjuvant therapy but with tumor size ≥ 5 cm or N stage ≥ 2 ; or tumor size less than 2cm but with high Ki67, histologic grade 3 or with lymph node micrometastasis. Eligible patients were assigned to receive 6 month or 1 year of oral pyrotinib 400mg/day. The primary endpoint was the 2-year iDFS rate.

Results: Between January, 2019 and February, 2022, a total of 142 eligible women were enrolled and assigned to receive pyrotinib, with a median age of 50 (range: 25-72) years old. Ninety-seven patients had a T stage ≥ 2 . A total of 108 patients (76.1%) had node-positive disease, and 64 (45.1%) were hormone receptor positive. Twenty-five patients used neoadjuvant therapy previously, and all of them did not receive pCR (Table 1). After a median follow-up of 20 (range: 0.25-41) months, the 2-year iDFS rate was not available. Two and four patients reported invasive disease events after 6-month and 1-year of follow-up, with the 6-month and 1-year iDFS rates of 98.6% and 97.2%, respectively. The most common adverse events reported was diarrhea (78.2%), followed by fatigue (36.6%), lymphocyte count decreased (36.6%), nausea (33.1%) and hand-foot syndrome (33.1%). Forty-three patients experienced grade 3 diarrhea, and no grade 4 or higher adverse event was reported (Table 2). Adverse event leading to treatment discontinuation occurred in 12 (8.5%) patients.

Conclusion: Extended adjuvant pyrotinib administrated after trastuzumab-based adjuvant therapy was well-tolerated and showed potential efficacy in high-risk early HER-2 positive breast cancer. The follow-up is ongoing to determine the long-term benefit of extended adjuvant pyrotinib.

Table 1. Baseline characteristics of patients

Variables	All (n=142)
Age (years), median (range)	50 (25-72)
T stage, n (%)	
T1	43 (30.3%)
T2	84 (59.2%)
T3	11 (7.7%)
T4	2 (1.4%)
Unable to determine	2 (1.4%)
Nodal status, n (%)	
Negative	34 (23.9%)
1-3 positive nodes	50 (35.2%)
>3 positive nodes	58 (40.8%)
Hormone receptor status, n (%)	
Negative (ER and PR negative)	78 (54.9%)
Positive (ER positive, PR positive, or both)	64 (45.1%)
ER positive, PR negative	20 (14.1%)
ER negative, PR positive	3 (2.1%)
ER positive, PR positive	41 (28.9%)
Ki67, n (%)	
≥20%	119 (83.8%)
<20%	23 (16.2%)
Previous neoadjuvant therapy, n (%)	25 (17.6%)

ER: estrogen receptor; PR: progesterone receptor.

Table 2. Treatment-emergent adverse event occurring in at least 10% of the patients

Events, n (%)	All (n=142)	
	Any grade	Grade 3
Diarrhea	111 (78.2%)	43 (30.3%)
Fatigue	52 (36.6%)	0
Lymphocyte count decreased	52 (36.6%)	0
Nausea	47 (33.1%)	0
Hand-foot syndrome	47 (33.1%)	0
Hyperuricemia	33 (23.2%)	0
White blood cell count decreased	26 (18.3%)	0
Dizziness	26 (18.3%)	0
Anemia	24 (16.9%)	0
Vomiting	22 (15.5%)	0
Headache	19 (13.4%)	0
Creatinine increased	17 (12.0%)	0
Neutrophil count decreased	16 (11.3%)	0

Disclosure(s):

Feilin Cao, Master of Medicine: No financial relationships to disclose
Zhaosheng Ma, Master of Medicine: No financial relationships to disclose
Guinv Hu, Bachelor of Medicine: No financial relationships to disclose
Xiaotao Zhu, Master of Medicine: No financial relationships to disclose
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12/7/2022

5:00 PM - 6:15 PM

OT2-15-01

Continue the SaMe systemic therapy after local ablative therapy for Oligoprogression in metastatic breast cancer - the COSMO study

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Background

Patients with metastatic breast cancer (MBC) are usually treated with palliative systemic therapy until progression or unacceptable toxicity. When progression occurs, clinicians typically switch to the next line of systemic therapy. However, this strategy might be suboptimal in case of mixed response or oligoprogression.

Oligoprogression refers to a situation in which inter-lesion heterogeneity causes one or few metastatic lesions to progress while the vast majority of the metastatic burden responds to the treatment. Locally ablative treatment of the progressive lesion(s) with radiotherapy, resection or radiofrequency ablation may enable continuation of otherwise effective systemic treatment. Solid data to support this approach, however, is lacking at this moment.

Study design

The COSMO study is an investigator-initiated single-arm phase 2 study. It is intended to be a multicenter study.

Eligibility criteria

Patients with MBC and oligoprogression, defined as 1-2 progressive lesions while the majority of the metastatic burden remains stable or in remission, are eligible. Current systemic therapy must be 1st or 2nd line and patients must have responded to this systemic therapy for at least

six months prior to the occurrence of oligoprogression. The aberrant lesion must be amenable to locally ablative therapy.

All eligibility criteria may be found in table 1: eligibility criteria.

Aim

To investigate efficacy of local ablation of aberrant lesions combined with continuation of the same systemic therapy in patients with oligoprogression of MBC.

Primary endpoint:

Progression-free survival rate at six months (PFS-6).

Secondary endpoints:

- PFS
 - Overall survival
 - Time to next line of systemic therapy
- Primary and secondary endpoints will also be stratified by localization of progressive lesion and BC subtype (ER+/HER2- vs. HER2+ vs. TN).

- Local control rate of lesion treated with LAT at 12 months
- Complications due to LAT
- Quality of life
- Incidence of visceral crisis

Exploratory endpoints:

- Biomarkers, including receptor (ER/PR/HER2), PD-L1 and gene expression patterns in biopsies from progressive and responding lesions
- Prognostic value of ctDNA at oligoprogression and during the course of treatment

Statistical methods

An A'hern design was chosen to conduct this study. As null-hypothesis (H0), PFS-6 rate $\leq 25\%$ is set. The alternative hypothesis (H1) is PFS-6-rate $\geq 40\%$. Hypotheses were set to meet criteria for clinical significance, as stated by experts in the field. Setting one-sided $\alpha = 0.05$ and a desirable power=95%, 107 evaluable patients are needed. To account for 10% of the patients to be unevaluable, 118 included patients are needed. An early stopping rule for safety is applicable: if out of the first 45 patients ≥ 4 of these patients have developed visceral crisis, the study will be closed early.

Accrual

Start: July 2022

Target: 118 patients

Estimated accrual time: 2-3 years

Further information

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Clinicaltrials.gov identifier: NCT05301881

This study is funded by the Maarten van der Weijden foundation.

This study was developed during the 21st EORTC/ESMO/AACR workshop on methods in

clinical cancer research (MCCR).

Eligibility criteria

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> • Adults with MBC according to TNM-staging • Oligoprogression, defined as: 1-2 distant metastatic progressive lesions, limited to one organ, OR progression of primary tumor (+/-lymph nodes) while distant metastases remain stable/responding • Patients are currently receiving 1st or 2nd line systemic therapy • SD/PR/CR for at least six months prior to occurrence of oligoprogression under one systemic treatment regimen • Oligoprogression is detected by same imaging modality as used at start of systemic therapy, and confirmed six weeks after its first detection • WHO performance status 0 or 1 • Willingness and ability to comply with study procedures • Signed informed consent. 	<ul style="list-style-type: none"> • Having received >2 lines of systemic therapy for MBC • Diagnosis of any other malignancy with an influence on general prognosis of the patient • Current pregnancy or breastfeeding. Women of childbearing potential must use adequate contraceptive protection • Any other condition that would pose an unacceptable risk, when partaking in the study, or potentially hamper patient's ability to comply with the protocol.

Table 1. Eligibility criteria.

Disclosure(s):

Cornelia AM Almekinders, MD: No financial relationships to disclose

Tessa G Steenbruggen, MD: No financial relationships to disclose

Ingrid A. Mandjes, n/a: No financial relationships to disclose

Marta Lopez-Yurda, PhD: No financial relationships to disclose

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Gabe S. Sonke, MD, PhD: Agendia: Contracted Research (Ongoing); AstraZeneca: Contracted Research (Ongoing); Biovica: Consulting Fees (e.g., advisory boards) (Ongoing); Merck: Contracted Research (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Roche: Contracted Research (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing)

12/7/2022

5:00 PM - 6:15 PM

OT2-16-01

ONCX-NAV-G201: A phase 2, basket study of navicixizumab monotherapy or in combination with chemotherapy in patients with select advanced solid tumors: Triple-negative breast cancer cohort (trial in progress)

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Objective: The objective of this Phase 2, open-label, multicenter study is to investigate the antitumor activity of navicixizumab monotherapy or in combination with chemotherapy in patients with advanced solid tumors. Cohort C will enroll triple-negative breast cancer (TNBC) patients. Background: Navicixizumab is a bispecific humanized monoclonal immunoglobulin G2 kappa antibody directed against human delta-like ligand 4, a critical ligand of the NOTCH pathway, and human vascular endothelial growth factor (VEGF). Aberrant NOTCH signaling is associated with chemotherapy resistance, tumor plasticity, enhanced metastatic potential, promotion of a cancer stem cell phenotype, and immune evasion. In TNBC, aberrant NOTCH expression is associated with poor prognosis, making targeting of this pathway an attractive therapeutic strategy. Additionally, NOTCH may mediate resistance to angiogenesis inhibition. While VEGF inhibitors are approved for the treatment of multiple solid tumors, observed anti-tumor activity is limited in breast cancer. Pre-clinical data show that co-inhibition of NOTCH and angiogenesis have superior antitumor activity compared to individual pathway targeting. We postulate that navicixizumab will demonstrate anticancer efficacy against TNBC. Methods: Eligible TNBC patients will have locally advanced or metastatic disease and have received at

least 2 and no more than 4 prior lines of standard therapy for metastatic disease, including immunotherapy (for PD-L1 positive TNBC patients), and sacituzumab govitecan. TNBC is defined as ER and PR < 1%, and HER2-negative (IHC 0, 1+, or 2+ and negative fluorescence in situ hybridization [FISH]). Formalin-fixed paraffin-embedded tissue from an archival or a core tumor sample must be available for biomarker analysis. Samples will be tested using Oncomap™ ExTra with the Xerna TME Panel™ to classify patient samples into one of four tumor microenvironment (TME) subtypes based on angiogenic and immune gene expression signatures. Up to 30 patients will be enrolled to each TNBC cohort from approximately 8 sites in the US and will receive 3 mg/kg navicixizumab alone (Cohort C1) or in combination with paclitaxel (80 mg/m² on Days 1, 8, and 15 of a 28-day cycle) (Cohort C2). Patients will have radiologic tumor assessments every 8 weeks and will continue to receive treatment until disease progression per RECIST v1.1 (as assessed by the investigator), unacceptable toxicity, withdrawal of consent, another protocol-defined discontinuation criterion is met, or the sponsor terminates the study, whichever occurs first. The primary endpoints of the study are objective response rate (ORR) and progression-free survival (PFS). The historical benchmarks for this patient population are estimated at an ORR of < 5% and a 20% PFS rate at 4 months, with targets of 15% and 40% respectively considered promising for this study. Interim efficacy assessments will be at 10-patient increments following the time patients have had at least 1 post-baseline scan. Cohort continuation and future evaluation decisions will be guided by the boundaries identified by a sequential monitoring procedure. Secondary efficacy endpoints include overall survival, time to response, disease control rate, duration of response, and the relationship between antitumor activity of navicixizumab and Xerna TME Panel™ biomarker subtypes.

Disclosure(s):

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12/7/2022

5:00 PM - 6:15 PM

OT2-16-02

Open-label, phase 3b/4 study of trastuzumab deruxtecan (T-DXd) in patients with or without baseline brain metastasis with advanced/metastatic human epidermal growth factor receptor 2–positive breast cancer: DESTINY-Breast12

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Background: Patients (pts) with human epidermal growth factor receptor 2–positive breast cancer (HER2+ BC) have a high incidence (up to 50%) of brain metastasis (BM) despite advances in treatment (Zimmer AS et al. *Cancer Rep (Hoboken)*. 2020;e1274; Hurvitz SA et al. *Clin Cancer Res*. 2019;25:2433-2441). Although several agents have been studied in pts with HER2+ BC with BM, an unmet medical need remains. In DESTINY-Breast01, T-DXd demonstrated efficacy in the overall population and preliminary efficacy in a pt subgroup with

stable BM (n=24), with a confirmed objective response rate (ORR) of 61.4%, an extracranial confirmed ORR by independent central review (ICR) of 58.3%, respectively, and median progression-free survival (PFS) of 19.4 and 18.1 months, respectively (Modi S et al. Cancer Res. 2021. Abst PD3-06; Jerusalem G et al. Ann Oncol. 2020. Abst 138O). T-DXd also demonstrated preliminary efficacy in a subgroup of pts with BM in the DESTINY-Breast03 trial, with an extracranial ORR of 67.4%, intracranial ORR of 63.9%, and median PFS of 15.0 months (Hurvitz S et al. SABCs 2021. Abst GS3-01). However, both trials excluded pts with active/progressive BM. Here we describe a trial evaluating T-DXd in a real-world setting in pts with stable or active BM and pts without BM with previously treated advanced/metastatic HER2+ BC. The data generated by this study will complement previous and ongoing studies, providing a more robust understanding of T-DXd treatment in patients with and without BM. Trial design: DESTINY-Breast12 (NCT04739761) is an open-label, multicenter, international (91 sites in the US, Europe, Australia, Canada, and Japan), phase 3b/4 study assessing the efficacy and safety of T-DXd 5.4 mg/kg every 3 weeks in pts with HER2+ BC ± BM. As part of prescreening, all pts will provide informed consent for tumor tissue samples (archival tumor tissue or fresh biopsy) to be collected and tested for HER2 status. Pts will be enrolled in 1 of 2 cohorts (250 pts each): cohort 1 (no BM at baseline) and cohort 2 (BM at baseline). Pts must have previously treated HER2-positive BC that has progressed on or after ≥1 prior anti-HER2-based regimen (including disease progression ≤6 months after adjuvant treatment with HER2-targeted therapies) and received ≤2 lines of therapy in the metastatic setting (excluding pts with prior tucatinib). Cohort 1 will be limited to include ≤25% third-line pts. Pts with BM must have untreated BM not needing immediate local therapy or previously treated stable or progressing BM. Primary endpoints are ORR in cohort 1 and PFS in cohort 2 (both by Response Evaluation Criteria in Solid Tumors [RECIST] version 1.1 per ICR). Secondary endpoints in both cohorts are overall survival, DOR, time to progression, duration of subsequent therapy, PFS2, safety, and changes in symptoms, functioning, and quality of life. Incidence of new symptomatic central nervous system (CNS) metastasis is a secondary endpoint in cohort 1, and ORR and CNS ORR by RECIST 1.1 per ICR, CNS PFS and DOR, and time to new CNS metastasis are secondary endpoints in cohort 2.

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Phase 3 study of tucatinib or placebo in combination with trastuzumab and pertuzumab as maintenance therapy for HER2+ metastatic breast cancer (HER2CLIMB-05, trial in progress)

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Background: The current first-line (1L) standard of care (SOC) for human epidermal growth factor receptor 2-positive (HER2+) metastatic breast cancer (MBC) is trastuzumab (T) plus pertuzumab (P) and a taxane. Despite advances in 1L SOC, most patients (pts) progress during maintenance therapy with T+P. Tucatinib is a tyrosine kinase inhibitor (TKI) approved in combination with T and capecitabine for adults with HER2+ MBC, with and without brain metastases (BM). In HER2CLIMB, the addition of tucatinib significantly prolonged progression-

free survival (PFS) and overall survival (OS) in pts with HER2+ MBC and was well tolerated. Adding tucatinib also reduced the risk of disease progression or death in pts with untreated and/or active BM (Murthy et al. 2020, Curigliano et al. 2021). HER2CLIMB-05 investigates whether adding tucatinib to 1L SOC as maintenance therapy will extend PFS while maintaining quality of life (QOL). Methods: HER2CLIMB-05 (NCT05132582) is a phase 3, randomized, double-blind study evaluating tucatinib plus T+P as maintenance therapy for HER2+ MBC. Approximately 650 pts will be enrolled. Eligible pts will have advanced HER2+ disease, no progression on 4–8 cycles of prior 1L SOC, ECOG Performance Status of 0 or 1, and no or asymptomatic BM. Exclusion criteria include prior treatment with anti-HER2 and/or anti-epidermal growth factor receptor TKI (prior SOC for early BC is permitted) or inability to undergo contrast magnetic resonance imaging of the brain. Pts will be randomized 1:1 to receive either tucatinib or placebo twice daily, with T+P once every 21 days. Pts with HR+ disease may receive endocrine therapy. The primary endpoint is investigator-assessed PFS. Secondary endpoints include OS (key endpoint), time to deterioration of health-related QOL, central nervous system PFS, safety, and pharmacokinetic (PK) parameters. PFS and OS will be compared using a 2-sided stratified log-rank test between treatment groups. Time-to-event endpoints will be summarized using the Kaplan–Meier method. PK and safety data will be summarized using descriptive statistics. Enrollment is ongoing in the US, with additional sites planned.

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KN026 in combination with docetaxel as neoadjuvant treatment for HER2-positive early or locally advanced breast cancer: A single arm, multicenter, phase 2 study

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Background: Despite the use of targeted therapy has revolutionized the treatment in the neoadjuvant setting for early, locally advanced, HER2-positive breast cancer, these approaches still have limited efficacy, which calls for persistent exploration for optimized treatment strategy. KN026 is a bispecific monoclonal antibody that targets the distinct extra-cellular domains II (Pertuzumab binding site) and IV (Trastuzumab binding site) of HER2. KN026 has better anti-tumor activity than either Trastuzumab or Pertuzumab used alone, and also aimed to demonstrate similar or better anti-tumor response than Trastuzumab in combination with Pertuzumab. Here we report the preliminary results of KN026 and docetaxel as neoadjuvant treatment in patients with HER2-positive early or locally advanced breast cancer (LABC). Methods: Treatment naive patients with HER2-positive early (T1c or 2, N1, M0; T2 or 3, N0, M0) or locally advanced breast cancer (T1c or 2 or 3, N2, M0; T3N1M0; T1c or 2 or 3, N3a or 3b, M0) were enrolled to receive 4 cycles of KN026 (30mg/kg, ivgtt d1, q3w) and docetaxel (75 mg/m² ivgtt d1, q3w) neoadjuvant treatment. The primary endpoint was total pCR rate (tpCR;

defined as absence of any residual invasive cancer in the breast and lymph nodes) [ypT0/is, ypN0]). Secondary endpoints were pCR in the breast (bpCR, defined as absence of any residual invasive cancer in the breast [ypT0/is]), ORR (objective response rate), safety · PK (pharmacokinetics) and immunogenicity. The study is still ongoing, and the planned enrollment number is 30. This study is registered in ClinicalTrials.gov, number NCT04881929. The data cutoff date was April 15, 2022. Results: Between August 8, 2021, and April 15, 2022, a total of 15 patients were enrolled from 5 sites. 7 (46.7%) patients were stage II, and 8 (53.3%) patients were stage III; 12 (80%) patients with lymph node metastases, and 3 (20%) patients without lymph node metastases; 7 (46.7%) patients were hormone receptor positive, and 8 (53.3%) patients were hormone receptor negative. As of April 15, 2022, 4 patients are still under neoadjuvant therapy, 1 patient withdrew from the study earlier due to AE during neoadjuvant treatment period, and 10 patients completed the surgery. Of the 10 patients who completed surgery, tpCR rate were 50% (5/10, 95% CI: 18.7%-81.3%), bpCR rate were 50% (5/10, 95% CI:18.7%-81.3%), and ORR were 100% (10/10, 95% CI: 69.2%-100%). The incidence of TRAE and Grade ≥3 TRAEs were 100% (15/15) and 53.3% (8/15) respectively. The most common TRAE were alopecia (14/15, 93.3%), white blood cell decreased (10/15, 66.7%), anemia (10/15, 66.7%), diarrhea (9/15, 60.0%), neutrophil count decreased (9/15, 60.0%), alanine aminotransferase increased (8/15, 53.3%) and hypoalbuminemia (8/15, 53.3%). The Grade ≥3 TRAE include neutrophil count decreased (8/15, 53.3%), white blood cell decreased (5/15, 33.3%), alanine aminotransferase increased (1/15, 6.7%), and lymphocyte count decreased (1/15, 6.7%). No Grade 5 TRAEs occurred. 3 TRAEs (Alanine aminotransferase increased, blood bilirubin increased and neutrophil count decreased) leading to KN026 interruption, and no TRAE leading to KN026 discontinuation. 1 SAE (hepatitis E-not TRAE; outcome: recovered) occurred in 1 patient, without other SAE or death throughout the study. Conclusions: KN026 and docetaxel as neoadjuvant treatment has shown promising clinical benefit for patients with HER2-positive early or locally advanced breast cancer with an acceptable and manageable safety profile. Further validation in a large-scale randomized controlled trial is warranted.

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Safety Analyses of NRG BR004: A Randomized, Double-blind, Phase III Trial of Taxane/Trastuzumab/Pertuzumab with Atezolizumab or Placebo in First-line HER2-Positive Metastatic Breast Cancer (MBC)

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Background: The CLEOPATRA trial established trastuzumab, pertuzumab and a taxane (THP) as a standard of care for first line metastatic, HER2-positive breast cancer with median progression-free survival (PFS) of 18.7 months and median OS of 57 months. NRG BR004 was a phase III, placebo-controlled trial designed to determine whether the addition of the PD-L1 inhibitor, atezolizumab, to THP would improve progression-free survival (PFS), relative to THP/placebo in patients with newly documented HER2-positive measurable metastatic breast cancer.

Methods: BR004 was designed to detect an improvement in the primary endpoint of PFS in patients with measurable disease from 16.5 to 22.5 months with addition of atezolizumab (HR 0.733). A sample size of 600 would provide 80% power with a type I error rate of 0.05 to detect such an improvement when 326 PFS events had been reported. Monthly accrual was projected at 30 patients per month with completion of accrual in 24 months. In addition to routine monitoring of safety data by the IDMC every 6 months, a formal analysis of the toxicity data was to be performed 16 weeks after the 100th patient had been randomized with review by the IDMC.

Results: First patient was randomized on May 1, 2019, and after 37 months 190 patients had

been randomized. Several amendments were not successful in addressing the low accrual rate. The IDMC began regular monitoring of safety and accrual data in July 2020 and reviewed the formal safety analysis in February 2022. As of the February 2022 IDMC meeting, four Grade 5 adverse events (AEs) had been reported (2 occurring in 2020 and 2 in 2021), one of which occurred in a patient with evolving liver failure due to rapid disease progression at the start of therapy. The recommendation was to continue without modification, but notice was given the Grade 5 AEs had occurred on the same treatment arm without unblinding. When additional Grade 5 AEs occurred on 3/4/2022 and 4/27/2022 both on the same study arm with none reported on the other arm, accrual was held until the IDMC could review updated safety data, narratives of the Grade 5 AEs and the overall context of the trial. There was no evidence of clinically important imbalances between Grade 3 and Grade 4 AEs between the arms., Based on an uncertain but material safety signal, the ongoing accrual challenges, and determination that the clinical question being addressed was no longer sufficiently compelling, the IDMC recommended that the trial should be permanently closed to further enrollment. Summary safety data from 187 treated patients are provided in the Table. A decision was made to discontinue atezolizumab/placebo in patients receiving the investigational component of the trial therapy and unblind investigators and patients. The study will continue to collect information on PFS events, deaths and late immune AEs through April of 2024 when PFS and OS will be analyzed.

Conclusions: The imbalance in Grade 5 AEs which occurred on BR004 coupled with continued poor accrual and the changing landscape in HER2+ MBC resulted in early closure of enrollment and unblinding of patients. Follow-up continues to assess PFS, OS and monitor for delayed immune AEs.

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	Placebo % (n=91)				Atezolizumab % (n=96)			
	Grade 2	Grade 3	Grade 4	Grade 5	Grade 2	Grade 3	Grade 4	Grade 5
Overall highest grade	41.8	42.9	12.1	0	26.0	47.9	14.6	6.1
LV dysfunction/HR	6.6	0	1.1	0	4.2	1.0	0	1.0
Hypothyroid	1.1	0	0	0	8.3	0	0	0
Hyperthyroid	0	0	0	0	2.1	0	0	0
Adrenal insufficiency	1.1	0	0	0	2.1	0	0	0
Hypophysitis	1.1	0	0	0	0	0	0	0
Colitis	4.4	0	0	0	2.1	0	1.0	0
Diarrhea	27.5	5.5	0	0	24	9.4	0	0
Infusion reaction	17.6	0	0	0	19.8	3.1	0	0
CRS	0	0	0	0	0	0	1.0	0
ALT increase	4.4	3.3	0	0	7.3	3.1	0	0
AST increase	2.2	3.3	0	0	3.1	3.1	0	0
Tot bilirubin increase	0	1.1	0	0	5.2	0	0	0
Hepatobiliary disorder	0	1.1	0	0	1.0	0	0	1.0
Creatinine increase	1.1	1.1	0	0	7.3	1.0	0	0
Acute kidney injury	0	2.2	0	0	0	2.1	2.1	0
Pneumonitis	0	1.1	0	0	2.1	4.2	0	0
Lung infection	1.1	3.3	0	0	1.0	2.1	2.1	0
Respiratory failure	0	0	0	0	0	0	2.1	1.0
Febrile neutropenia	0	2.2	0	0	0	5.2	1.0	0
Sepsis	0	2.2	0	0	0	0	1.0	2.1
Sudden death NOS	0	0	0	0	0	0	0	1.0
Cutaneous toxicities	8.8	1.1	0	0	13.6	2.1	0	0
Sensory neuropathy	26.4	1.1	0	0	20.8	3.1	0	0
Venous thrombosis	1.1	2.2	0	0	4.2	2.1	0	0

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Phase 1 trial of anthracycline chemotherapy in combination with CD40 agonist and Flt3 ligand in metastatic triple-negative breast cancer

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Background: Only a subset of patients with metastatic triple-negative breast cancers (TNBC) demonstrate response to FDA approved PD-1 immune checkpoint blockade (ICB), and few have durable responses. Data suggests that breast cancers have defects in antigen presentation and that antigen presenting cells especially the DC1 subtype of dendritic cells (DCs) are required for response to ICB. CD40 agonists activate antigen presenting cells including DCs and B cells and also repolarize macrophages to an anti-tumor phenotype. Flt3 ligand is a growth factor that increases differentiation and expansion of DCs. We recently demonstrated in pre-clinical TNBC models that the combination of liposomal-doxorubicin chemotherapy, a CD40 agonist, and a Flt3 ligand improves outcomes compared to alternate combinations. Methods: This is a single arm phase I pilot study of liposomal-doxorubicin, CDX-1140 (CD40 agonist), and CDX-301 (Flt3 ligand) combination therapy in patients with metastatic or unresectable locally advanced metastatic TNBC. Patients will be randomized to 3 lead-in arms (triplet therapy, doublet immunotherapy only, or liposomal-doxorubicin only) for 1 cycle prior to receiving triplet therapy with fresh tissue biopsies before and after the lead-in treatment. CDX-301 will be discontinued after 2 cycles; liposomal-doxorubicin and CDX-1140 will be continued until disease progression or clinically limiting toxicities. Primary endpoint is determination of a recommended phase 2 dose based on treatment-related adverse events including dose-limiting toxicities. Secondary endpoints include anti-tumor immune response after triplet therapy, after immunotherapy alone, and after liposomal-doxorubicin alone; median progression-free survival, overall response rate, duration of response, and clinical benefit rate. Key eligibility criteria are unresectable stage III or stage IV TNBC (ER \leq 10%, PR \leq 10%, HER2/neu negative), 1st to 3rd line metastatic treatment setting (1st line patients need to be PD-L1 negative by 22C3 assay), measurable disease by RECIST 1.1 criteria, consent for pre-treatment and on-treatment biopsies of amenable soft tissue tumor lesions, no prior treatment with an anti-CD40 antibody or a Flt3 ligand, no anthracycline treatment in the metastatic setting, no prior progression while on anthracycline-based therapy or within 6 months of completing neoadjuvant chemotherapy, and no history of non-infectious pneumonitis or current pneumonitis. This trial will enroll up to 45 patients across multiple sites (NCT05029999).

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5:00 PM - 6:15 PM

OT2-17-02

The ARETHA Study: A phase 2 randomized control trial of Eribulin with Evexomostat (SDX-7320) or placebo for patients with metastatic triple-negative breast cancer and metabolic dysfunction

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Background: The prognosis for advanced/metastatic triple negative breast cancer (TNBC) remains poor and novel therapeutic strategies are urgently needed to improve outcomes. Insulin resistance and obesity contribute to cancer progression and are independent predictors of worse survival after TNBC diagnosis. Chemotherapy worsens insulin resistance, body mass index, and multiple other metabolic parameters which can paradoxically limit treatment efficacy and survival. Methionine aminopeptidase 2 (MetAP2/p67) is overexpressed in many tumor types and MetAP2 inhibitors exhibit broad anti-tumor activity. Additionally, MetAP2 inhibitors improve insulin resistance, reduce adiposity, and normalize levels of adipokines, attenuating the effects of metabolic dysfunction on tumor growth. Evexomostat (SDX-7320) is a second-generation MetAP2 inhibitor designed to improve drug-like properties and minimize central nervous system toxicities. Evexomostat improved insulin sensitivity, reduced fat mass and normalized adipokine levels in preclinical models of obesity, and reduced tumor growth in preclinical models of TNBC. In phase 1 trials, MetAP2 inhibition combined with chemotherapy was safe and well tolerated, while evexomostat monotherapy partially restored insulin sensitivity, reduced angiogenic factors as well as adipokines and showed anti-metastatic effects in patients with advanced solid tumors. The goal of this phase 2 study is to test whether evexomostat in combination with eribulin chemotherapy prevents worsening of insulin resistance and augments tumor response in patients with metastatic TNBC and concomitant metabolic dysfunction. Methods: This is a single-center, placebo-controlled phase 2 randomized control trial of evexomostat, a MetAP2 inhibitor, in combination with eribulin chemotherapy. Eligible patients must have histologically confirmed metastatic TNBC, measurable disease or ≥ 1 predominantly lytic bone lesion, baseline metabolic dysfunction defined as hemoglobin A1c $> 5.5\%$ and/or BMI ≥ 30 kg/m², have received ≤ 2 prior lines of therapy in the advanced/metastatic setting, have ECOG performance status ≤ 1 , and adequate

organ function. Patients with uncontrolled or insulin-dependent type II diabetes, or who require combination antihyperglycemic therapy are excluded. During the safety run-in period, 15 patients will be assigned to receive evexomostat 49 mg/m² every 2 weeks in combination with eribulin 1.4 mg/m² administered on days 1 and 8 of a 21-day cycle. Upon safety confirmation, an additional 40 patients will be randomized 2:1 to receive evexomostat or placebo in combination with eribulin. The primary endpoint is metabolic efficacy assessed by change in Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) score. Secondary endpoints include objective response rate, progression-free survival, duration of response, safety and tolerability, patient-reported outcomes, changes in metabolic markers, and changes in body composition parameters. Historically, HOMA-IR scores double during chemotherapy, and this trial will test whether evexomostat will attenuate the expected rise in HOMA-IR. Specifically, the trial will have >90% power to detect a difference between a 1.5-fold change in HOMA-IR in the control arm versus no change in the investigational arm while controlling the Type I error at 5%. This trial opened to accrual in July 2022. A total accrual of 61 patients is planned with a goal of 55 evaluable patients. For any inquiries/questions, please contact Sherry Shen at shens1@mskcc.org. Clinical trial registry number: pending Funding, study drug evexomostat and other support provided by: SynDevRx, Inc.

Disclosure(s):

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5:00 PM - 6:15 PM

OT2-18-01

Nab-paclitaxel followed by dose-dense epirubicin/cyclophosphamide in neoadjuvant chemotherapy for triple-negative breast cancer: an open-label, single-arm phase II study

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Purpose: The anti-tumor activity of nab-paclitaxel followed by epirubicin/cyclophosphamide (EC) as neoadjuvant chemotherapy (NAC) in Asian patients remains unclear, particularly in the aggressive subtype triple-negative breast cancer (TNBC). This study aimed to evaluate the efficacy and safety of this NAC regimen in TNBC. **Methods:** In this Simon's two-stage, phase II study, treatment-naïve patients with resectable unilateral primary invasive TNBC were enrolled. Eligible patients received nab-paclitaxel 125 mg/m² weekly on day 1 for 12 weeks, followed by dose-dense EC (epirubicin 90 mg/m²; cyclophosphamide 600 mg/m²) on day 1 for four 2-week cycles. The primary endpoint was the total pathological complete response (tpCR, ypT0/is ypN0) rate. Secondary endpoints included breast pathological complete response (bpCR, ypT0/is) rate, objective response rate (ORR), the proportion of patients requiring breast-conserving surgery, and safety. **Results:** 55 eligible patients were enrolled and treated. After neoadjuvant therapy, tpCR and bpCR were respectively observed in 43.1% (95% CI, 29.3%-57.8%) and 49.0% (95% CI, 34.8%-63.4%) of 51 evaluable patients for pathological response evaluation. 44 had an ORR as their best response (80.0%; 95% CI, 67.0%-89.6%). No correlations between clinicopathological variables and pathological/clinical response were observed. Grade 3 or more AEs occurred in 63.6% of 55 patients. The most frequent AEs were alopecia. No treatment-related surgical delay or death occurred. **Conclusions:** Nab-paclitaxel followed by dose-dense EC as NAC demonstrates promising anti-tumor activity and acceptable tolerability for patients with TNBC.

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Yin Liu, n/a: No financial relationships to disclose

Lei Fan, n/a: No financial relationships to disclose

Zhi-Ming Shao, M.D. Ph.D: No financial relationships to disclose

Zhong-Hua Wang, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

OT2-18-02

OlympiaN: a phase 2, multicenter, open-label study to assess the efficacy and safety of neoadjuvant olaparib monotherapy and olaparib plus durvalumab in patients with BRCA mutations and early-stage HER2-negative breast cancer

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Background: In early breast cancer (BC), neoadjuvant therapy can promote de-escalation of surgery or treat micrometastases. Pathological complete response (pCR) is a standard primary endpoint in neoadjuvant BC studies, and correlates with long-term outcomes such as event-free survival (EFS). The poly(ADP-ribose) polymerase (PARP) inhibitors olaparib and talazoparib are approved in the metastatic setting for patients with BC and a germline BRCA1 and/or BRCA2 pathogenic/likely pathogenic mutation (gBRCAm). Following the phase 3 OlympiA trial primary analysis (data cut-off [DCO] Mar 2020), the PARP inhibitor olaparib was FDA approved for the adjuvant treatment of patients with gBRCAm and HER2-negative, high-risk early BC who have been treated with neoadjuvant/adjuvant chemotherapy. At the second pre-specified OlympiA analysis (DCO Jul 2021), olaparib treatment sustained improvements in invasive disease-free survival (IDFS HR 0.63, 95% CI 0.50–0.78) and distant disease-free survival (DDFS HR 0.61, 95% CI 0.48–0.77), and also significantly reduced the risk of death (overall survival [OS] HR 0.68, 98.5% CI 0.47–0.97) vs placebo. PARP inhibitors have also shown efficacy in the neoadjuvant setting in smaller studies. Durvalumab, a programmed death-ligand 1 inhibitor, has been studied as neoadjuvant therapy in triple negative BC and showed improved IDFS, DDFS and OS vs placebo (GeparNuevo). For BRCAm carriers at low risk of recurrence, olaparib monotherapy may provide adequate neoadjuvant treatment, allowing de-escalation or omission of chemotherapy. For those at high risk of recurrence, it is hypothesized that addition of the immune checkpoint inhibitor durvalumab will enhance immunogenicity provided through cell death following PARP inhibition. Feasibility for a larger study will be assessed. Methods: OlympiaN is a phase 2, international, multicenter, open-label trial examining the efficacy and safety of neoadjuvant olaparib monotherapy and olaparib plus durvalumab in adults with deleterious/suspected deleterious BRCAm and operable, early-stage,

HER2-negative, ER-negative or ER-low BC (immunohistochemistry nuclear staining < 10%). Patients will be enrolled in two cohorts: (A) patients at lower risk of recurrence: tumor size >5 to < 20 mm and nodal status N0 will receive olaparib 300 mg orally twice daily continuously in 28-day cycles; (B) patients at higher risk of recurrence: tumor size >20 to ≤50 mm and N0, or T1 and N1 will receive olaparib 300 mg orally twice daily continuously in 28-day cycles plus durvalumab 1500 mg IV infusion every four weeks. After four to six cycles, patients will undergo definitive surgery, then systemic and radiation therapy in accordance with local standard of care. Patients who achieve pCR at surgery will be able to receive adjuvant olaparib monotherapy in lieu of standard adjuvant systemic therapy for a total of twelve 28-day cycles of neoadjuvant and adjuvant olaparib therapy. The primary endpoint is the pCR rate after completion of neoadjuvant systemic therapy, assessed by central pathology review. Secondary endpoints include the pCR rate assessed by local pathology review, residual cancer burden, tumor volumetric analysis, EFS, safety and tolerability. Tumor tissue will be collected pre-treatment and at surgery to evaluate the mechanism of action of therapy. Baseline and longitudinal assessment of ctDNA and its association with clinical outcomes will also be performed. The primary pCR analysis will occur ~6 months after last participant enrollment; the final DCO will be 3 years after last participant dosed or once all participants have had an EFS event. No formal statistical analyses are planned, data will be summarized descriptively. Enrollment is planned to commence by late 2022, across ~65 sites in 10 countries; the target accrual is ~25 patients per cohort to ensure adequate precision in the estimated pCR rate. Funding: This study is funded by AstraZeneca UK Plc.

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5:00 PM - 6:15 PM

OT2-18-03

Neoadjuvant anlotinib plus nab-paclitaxel based chemotherapy in patients with HER2-negative breast cancer: A prospective, single-arm, single-center, phase II clinical study

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BACKGROUND: Antiangiogenic agent plus neoadjuvant chemotherapy confers an improvement in pathological complete response (pCR) rate among patients with HER2-negative breast cancer. Anlotinib is a novel multi-target tyrosine kinase inhibitor that effectively inhibit VEGFR, FGFR, c-KIT, c-MET, and RET. This phase II study aims to evaluate the efficacy and safety of anlotinib combined with chemotherapy as neoadjuvant treatment in HER2-negative breast cancer. **PATIENTS AND METHODS:** Eligible patients (pts) were women, aged 18-70 years, ECOG status 0-2, previously untreated HER2-negative breast cancer. The HER2-negative, defined as immunohistochemistry of 0, 1+, and 2+/*ISH*-. Pts were required to have a palpable primary tumor at least 200mm in diameter in the breast, as assessed by physical examination, and to be classified as having tumor stage T1c to T3, nodal stage N0 to N2a, and metastasis stage M0. Thirty pts will be enrolled and received 5 cycles of anlotinib (12 mg qd, d1-14; 21 days per cycle) plus 6 cycles of nab-paclitaxel (200 mg/m², once every 3 weeks), anthracycline (pirarubicin 50 mg/m²) and cyclophosphamide at 500 mg/m², followed by surgery. The primary endpoint is pCR rate (ypT0/Tis ypN0) and the secondary endpoints include disease-free survival (DFS), overall survival (OS), and safety. The study was initiated in August 2021. This study is currently open and 10 patients had been enrolled. The estimated primary completion date is October 1, 2023. Results: The trial is in progress. Conclusion: The trial is in progress.

Disclosure(s):

Jing Fan, n/a: No financial relationships to disclose

Ting Wang, n/a: No financial relationships to disclose

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OT2-19-01

Single cell characterization of longitudinal biopsies from breast cancer patients treated neoadjuvantly with the aromatase inhibitor letrozole and the CDK4/6 inhibitor ribociclib in concert

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Background The recent introduction of CDK4/6 inhibitors has been one of the most pivotal breakthroughs in breast cancer therapy during the last decades. A growing body of evidence proposes that CDK4/6 inhibitors influence the recruitment of immune cells in the tumor microenvironment with potential effects on the outcome. **Study design** The NeoLetRib-study is a multicenter, single-arm, open-label, neoadjuvant, phase II trial aiming at treating 100 locally advanced luminal-A and luminal-B breast cancer patients, defined as either large T2, or T3/T4, and/or N2-3. Patients receive neoadjuvant therapy for 6 months: ribociclib (600 mg daily, 21 days on / 7 days off) and letrozole (2.5 mg daily). Peri- and premenopausal women also receive therapy with goserelin 3.6 mg s.c every 28 days. **Methods** Three sequential tumor biopsies were collected: pre-treatment and on-treatment (cycle 1 - day 21 and cycle 6 - day 21 with ribociclib). These biopsies were subjected to single-cell transcriptome, T cell receptor and B cell receptor profiling using the Chromium Single-Cell v2 5' Chemistry (10x Genomics). Libraries were paired-end sequenced on a NovaSeq6000. Single cell gene expression matrices were analyzed with the Seurat package (v4.0.2). After filtering out stressed / dying cells or cells with low quality sequencing, gene expression of the remaining good quality cells was normalized and scaled to construct principal components and further cluster cells. **Results** In this planned interim analysis, we clustered 242315 cells from longitudinal tumor biopsies from 18 patients at pre-treatment, 18 at cycle 1 - day 21 and 9 at cycle 6 - day 21, respectively. We identified 8 main cell types: T cells, B cells, epithelial cells, fibroblasts, endothelial cells, macrophages, mast cells and dendritic cells. To further identify specific and specialized cell subtypes, we clustered the cells belonging to the above-mentioned cell types and annotated the clusters obtained using validated marker genes. Statistical methods and algorithms were then used to characterize how the proportion of different cell types changes in tumors under treatment pressure. We identified significant changes in immune cell proportions, including regulatory T cells, CD14 monocytes, SLC2A1-Macrophages among others. **Conclusions** In this unique patient cohort, we used single cell transcriptome profiling to obtain a high-resolution map of cell types found in tumor biopsies from the NeoLetRib trial. We characterized the effects of the combination of ribociclib and letrozole on the tumor microenvironment and identified cells sensitive and resistant to treatment. In this interim analysis, the observed longitudinal changes of immune cell types proportions in the tumor microenvironment might suggest immune related effects of the treatment combination.

Disclosure(s):

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5:00 PM - 6:15 PM

OT2-20-01

Neoadjuvant survivin immunotherapy maveropepimut-S (MVP-S) to increase Th1 immune response in Ki67-high hormone receptor positive (HR+) early-stage breast cancer.

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Background: HR+ early stage breast cancer (ESBC) is associated with suboptimal pathologic complete response rate (pCR, ~10%) following neoadjuvant cytotoxic chemotherapy. Neoadjuvant endocrine therapy with aromatase inhibitors (AI) may serve as an effective alternative as gauged using the surrogate Ki67 cell proliferation histologic marker. Patients with poor Ki67 response (defined as Ki67>10%) following neoadjuvant AI exhibit poor prognosis and therapeutic resistance to both endocrine therapy and chemotherapy. In a genomic analysis of Ki67-high HR+ tumors, we identified 8-fold upregulation of BIRC5 (survivin), a gene that regulates apoptosis and the cell cycle and is associated with poor clinical outcome. Maveropemiput-S (MVP-S) leverages the non-aqueous, lipid-based DPX delivery platform to educate a specific and persistent T cell-based immune response to 5 HLA-restricted peptides from Survivin. Treatment with MVP-S and intermittent, low-dose cyclophosphamide (CPA) has shown to increase tumor infiltration of survivin-specific T cells. Previous clinical trials have shown that MVP-S is well-tolerated, immunogenic, and could lead to clinical response in several cancer indications. Further exploration of the regimen in breast cancer could extend the application of this immunotherapy for the unmet medical need of improving clinical response in high ki67 HR+ ESBC prior to surgery. Trial Design: NCT04895761 is phase I trial evaluating the safety and immunologic effects of neoadjuvant MVP-S plus letrozole (arm A, n=6), with/without tumor-directed MR-guided radiotherapy (arm B, n=6), or intermittent low-dose cyclophosphamide (CPA, arm C, n=6). Postmenopausal patients with T1c+ HR+HER2- breast cancer with Ki67>10% will receive two doses of MVP-S and 7 weeks of neoadjuvant letrozole prior to surgery (all arms), arm B will be treated additionally with concurrent 10Gy x 2 tumor boost radiation to facilitate immunogenic cell death, and arm C (n=6) will be treated additionally with intermittent low-dose CPA (50mg BID) to facilitate regulatory T cell depletion. Specific Aims: The primary objective is safety. Biomarker objectives are to evaluate for each treatment arm: 1) systemic type I survivin-specific immune response, as measured by IFN- γ ELISPOT; 2) changes in immune environment by GeoMx digital spatial genomic profiling; 3) and changes in tumor infiltrating lymphocytes (TILs) and Ki67. These data will be used to identify the most immunogenic MVP-S combination therapy for study in phase II trial powered to assess clinical outcome (pCR). Accrual: 3 of 6 patients in the MVP-S+ letrozole arm have been enrolled. Arm B and C will enroll after completion of arm A.

Disclosure(s):

Sasha E. Stanton, MD PhD: IMV Inc: Contracted Research (Ongoing); Stanford Burnham Prebys: Consulting Fees (e.g., advisory boards) (Ongoing)

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12/7/2022

5:00 PM - 6:15 PM

OT2-21-01

Assessing Response to neoadjuvant Taxotere and TrAstuzumab in Nigerian women with HER2-positive breast cancer (ARETTA)

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Background: Populations of African ancestry are underrepresented in global oncology clinical trials resulting in paucity of data on safety and efficacy of cancer medicines in vulnerable Black populations. The ARETTA clinical trial was initiated by the Nigerian Breast Cancer Study Team in partnership with the University of Chicago Comprehensive Cancer Center to build local capacity for biomarker informed clinical trials and translational breast cancer research. ARETTA is a pragmatic single-arm, phase II clinical trial to optimize therapy and determine the safety and efficacy of neoadjuvant taxotere and trastuzumab in women with HER2-positive breast cancer. The study sought to 1) determine the pathological complete response (pCR) rate of patients with early stage breast cancer to neoadjuvant docetaxel and subcutaneous trastuzumab 2) develop the capacity of investigators in Nigeria to improve quality of care through participation in oncology clinical trials using upgraded facilities and trained personnel and 3) determine accrual rate and retention of participants. Methods: Inclusion criteria include treatment naïve women aged 18 years to 70 years with HER-2 positive breast cancer stages II-IIIC (AJCC). Eligible participants receive four cycles of docetaxel 75mg/m² and trastuzumab every 3 weeks. Those with incomplete clinical response by breast ultrasound volume measurements receive 3 additional cycles of chemotherapy; cyclophosphamide 600mg/m², epirubicin 90mg/m² and 5-fluorouracil 600mg/m² every 3 weeks before re-evaluation for surgery. All participants receive a fixed dose of sub-cutaneous Herceptin (600mg) every 3 weeks (total of 18 doses). The primary endpoint is pCR rate. Secondary objectives are to evaluate invasive disease-free survival (iDFS), the pattern of response and mechanisms of resistance to treatment based on genomic markers, the pharmacokinetics of Herceptin SC, quality of life, and adverse event rates, including cardiac toxicity. Planned enrollment is 47 evaluable patients, which will provide 90% power to test the null hypothesis that the pCR rate is 20% versus a 40% alternative (one-sided alpha=0.05). More protocol details can be found at ClinicalTRial.gov NCT03879577 and JCO Glob Oncol2020 doi: 10.1200/GO.20.00043
Progress: The study has met its primary endpoint and will be closed to accrual by the time of the meeting. Results will be submitting as Late Breaking before the meeting

Disclosure(s):

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5:00 PM - 6:15 PM

OT2-22-01

Epirubicin, cyclophosphamide and pyrotinib followed by docetaxel, trastuzumab and pyrotinib as neoadjuvant therapy for stage II-III HER2-positive breast cancer: a single-arm, multicenter phase 2 trial

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Background: Dual HER2 targeted therapy with pyrotinib (a tyrosine kinase inhibitor targeting HER1, HER2, and HER4) and trastuzumab plus chemotherapy has been approved as neoadjuvant therapy for patients with HER2-positive breast cancer in China based on the results from phase 3 PHEDRA study. However, the optimal chemotherapy partner still needs exploration. This multicenter phase 2 trial (ChiCTR1900022293) aimed to investigate the efficacy and safety of epirubicin, cyclophosphamide and pyrotinib followed by docetaxel, trastuzumab and pyrotinib (ECP-THP) as neoadjuvant therapy for patients with stage II-III HER2-positive breast cancer. Methods: Patients received intravenous epirubicin (90 mg/m²) and cyclophosphamide (600 mg/m²) on day 1 of each cycle for four 21-day cycles, followed by intravenous docetaxel (75 mg/m²) and trastuzumab (8 mg/kg loading dose, followed by 6

mg/kg) on day 1 for 4 cycles. Pyrotinib 400 mg was given orally once daily throughout the neoadjuvant therapy period. Surgery was performed within 16-20 days after the last neoadjuvant therapy. The primary endpoint was total pathological complete response (tpCR, ypT0/is ypN0) rate. Results: Between May 2020 and May 2022, a total of 175 patients enrolled. As of May 31, 2022, 144 patients had undergone surgery; the median age was 51 years (range, 26-67). Sixty-seven (46.5%) of 144 patients had hormone receptor (HR)-negative disease, and 77 (53.5%) had HR-positive disease. The tpCR rate was 67.4% (97/144; 95%CI, 59.3%-74.5%). Patients with HR-negative disease had numerically higher tpCR rate than those with HR-positive disease (73.1% [95%CI, 61.5%-82.3%] vs. 62.3% [95%CI, 51.2%-72.3%]), but without statistical significance (P=0.230). Miller-Payne grade 4 and 5 pathological responses were found in 22 (15.3%) and 97 (67.4%) of 144 patients, respectively. Regarding clinical response to neoadjuvant therapy before surgery, 31 (21.5%) of 144 patients achieved complete response and 99 (68.8%) achieved partial response, with an objective response rate of 90.3% (95%CI, 84.3%-94.1%). Of 161 patients with available safety data, the most common grade ≥ 3 adverse events included diarrhea (57.1%), white blood cell count decreased (8.7%), and neutrophil count decreased (5.6%). No treatment-related deaths occurred. Conclusions: Patients with stage II-III HER2-positive breast cancer show favorable clinical and pathological response to this ECP-THP neoadjuvant regimen, with an acceptable safety profile.

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OT2-22-02

Sequencing of anthracyclines and taxanes during neoadjuvant therapy of locally advanced HER2-negative breast cancer (NEOSAMBA Study / LACOG 0419)

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Background: Breast cancer (BC) is the most frequent cancer in women in Brazil, with more than 60,000 cases estimated annually. Forty percent of patients present with stages III and IV and neoadjuvant chemotherapy (NACT) remains the mainstay of treatment for locally advanced breast cancer (LABC). Taxanes usually follow anthracyclines in breast cancer neo/adjuvant treatment, likely because of their later introduction into clinical practice. However, the potential impact of alternative sequencing remains to be studied. A single-center phase II randomized clinical trial conducted in the Brazilian National Cancer Institute showed an improvement in overall survival with taxane-first compared with anthracycline-first sequencing in HER2-negative LABC (Bines J et al, *The Oncologist* 2020). As a taxane-before-anthracycline sequence carries neither an incremental cost nor increased toxicity, the optimal sequencing of these agents could have significant implications for clinical practice. To confirm this finding, we are currently conducting a multicenter randomized phase III trial comparing a taxane followed by an anthracycline-based regimen with the reverse sequence in the neoadjuvant setting. Trial Design: This randomized, open-label, phase III trial will be conducted in 15 research centers in

Brazil. It was approved by the local ethics committee in 2020 and is registered in ClinTrials.gov with the identifier NCT04540692. Women with HER2-negative LABC are randomized in a 1:1 ratio to anthracycline-before-taxane (AC-T arm) or taxane-before-anthracycline (T-AC arm), stratified by hormone receptor status (positive vs. negative) and axillary lymph node status (N0 vs. N+). The anthracycline-based therapy recommended in this trial is AC (doxorubicin 60 mg/m² and cyclophosphamide 600 mg/m²) every three weeks for four cycles, whilst the taxane-based therapy is either weekly paclitaxel 80 mg/m² weekly for 12 weeks, paclitaxel 175 mg/m² every three weeks, or docetaxel 75-100 mg/m² every three weeks. The use of carboplatin concomitantly with taxane for triple-negative tumors and dose-dense regimens is allowed following institutional guidelines. Further therapies (surgery, radiotherapy, and endocrine therapy) are performed according to the physicians' discretion. Tumor samples are collected and stored for translational studies. Eligibility: Inclusion criteria: women ≥18 years of age; histologically confirmed HER2-negative breast cancer (by ASCO/CAP guidelines); stage ≥ IIB (if TNBC) or ≥ III (if HR-positive); PS ECOG 0-2 and adequate organ function. Exclusion criteria: previous use of anti-cancer therapies; bilateral BC and pregnancy. Specific Aims: The primary objective is invasive disease-free survival (iDFS). Secondary objectives include pathological complete response (pCR) rates, overall survival (OS) and safety. Statistical Methods: Considering an uncausal type I error of 0.05, a type II error of 0.2, and an estimated iDFS of 50% in 5 years in the control arm, a total of 227 evaluable patients should be included per arm to demonstrate a HR of 0.7 favoring the taxane-first arm. Estimating a dropout rate of 10%, 494 patients will need to be included in the study. Present Accrual and Target Accrual: A total of 9 sites of 15 planned are activated. The first patient was enrolled on January 12, 2021, and as of June 24, 2022, a total of 113 patients have been accrued. The target goal of 494 patients is expected to be achieved by 2025 and initial study results will be reported by 2026. Funding: Brazilian Health Ministry, Programa Nacional de Apoio à Atenção Oncológica (PRONON), NUP 25000.183207/2019-50. Acknowledgements: CURA Project, SAS.

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5:00 PM - 6:15 PM

P3-01-03

Characterization of neutropenia in patients with hormone receptor–positive/human epidermal growth factor receptor 2–negative (HR+/HER2–) advanced breast cancer on palbociclib in a real-world setting: Results from POLARIS

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Background: The cyclin-dependent kinase 4/6 inhibitor palbociclib (PAL) is approved for the treatment of HR+/HER2– advanced breast cancer (ABC) in combination with an aromatase inhibitor (AI) as initial endocrine-based therapy or with fulvestrant (FUL) in patients whose disease progressed on prior endocrine therapy (ET). In clinical trials, the most common any-grade adverse event (AE) associated with PAL treatment was neutropenia. Here we evaluated the incidence of and risk factors for neutropenia by treatment cycle and line of therapy (LOT), as well as incidence of dose modification due to neutropenia, in patients with HR+/HER2– ABC receiving PAL in a real-world setting. **Methods:** POLARIS is a prospective, noninterventional, multicenter, real-world study of patients with HR+/HER2– ABC receiving PAL in routine clinical practice in the United States and Canada. Per protocol, sites were instructed to report absolute neutrophil count at baseline, anytime during the first 3 cycles, then at Day 1 (or before the start of a new cycle) of subsequent cycles per standard of care or as needed up to 6 months. The safety analysis set included all patients enrolled in the study who received at least one dose of study medication. **Results:** As of March 30, 2022, 1242 patients had enrolled in the study (median age, 64.0 years; 98.8% female; 94.8% stage IV; 39.1% visceral disease). Of these, 902 (72.6%) patients received PAL as first LOT and 340 (27.4%) as second LOT or greater. Among all patients, 722 received PAL + AI, 487 PAL + FUL, and 33 PAL + none or other ET (other than letrozole, anastrozole, fulvestrant, or exemestane); 90% of all patients started with 125 mg of PAL in the first cycle. Incidence of neutropenia among patients receiving PAL by cycle and LOT is shown in the Table. Percentages of patients experiencing on-treatment neutropenia were similar regardless of LOT. Over the course of treatment grade ≥ 3 neutropenia and febrile neutropenia were reported in 16.1% and 0.8% patients, respectively, and 19.2% of patients experienced a decreased neutrophil count. A total of 337 (27.1%) had a dose modification due to neutropenia. Of these 337 patients, 190 (56.4%) had a dose reduction associated with neutropenia. **Conclusions:** In this real-world study, incidences of treatment-related neutropenia associated with PAL were consistent with those reported in randomized clinical trials and were manageable by dose modification. Febrile neutropenia was uncommon. Incidences of neutropenia reported within the first 6 months were comparable among patients regardless of LOT. Further research is needed to understand the impact of the incidence of and risk factors for treatment-related neutropenia on therapy. **Clinical trial identification:** Pfizer; NCT03280303

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P3-01-04

A real-world evidence study of everolimus plus endocrine therapy beyond CDK4/6 inhibitors for HR+/HER2- advanced breast cancer.

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Introduction Since the approval a decade ago of everolimus in combination with endocrine therapy (ET), the treatment landscape of metastatic breast cancer (mBC) has changed dramatically. Endocrine monotherapy after progression to CDK4/6 inhibitors has shown a limited progression-free survival (PFS) below 3 months. Evidence of the efficacy of everolimus plus ET after CDK4/6 inhibitors is scarce. **Methods** We performed a retrospective observational study of patients with mBC treated with everolimus between September 2011 and April 2022 in 4 Spanish hospitals. Clinical and demographic data were collected from medical records. Our main objective was to estimate the median progression-free survival (mPFS) for everolimus + ET in patients previously treated with a CDK4/6 inhibitor. We also collected the adverse events (AE) related to everolimus. Quantitative variables were summarized with medians (range), and qualitative variables with proportions. We used the Kaplan-Meier method for survival estimates. **Results** We identified a total of 297 mBC patients treated with everolimus plus ET. The median follow-up time was 20 months (interquartile range: 1 – 97 months). In this cohort, the median age at diagnosis was 49 years (26 – 84 years). At the moment of starting everolimus, the median number of previous lines of treatment was 2 (0 – 12), 22% of patients were 'de novo' metastatic, 67% presented visceral involvement, 40% had received previous chemotherapy for advanced disease, and 51% (n=152) had received a previous CDK4/6 inhibitor. The ET combined with everolimus was exemestane (77%), fulvestrant (18%), and tamoxifen (5%). 45% of patients were alive at data cut-off. In patients previously treated with a CDK4/6 inhibitor, the estimated median PFS (mPFS) was 5.9 months (95%CI: 5.0 – 7.8 months). In patients without visceral involvement (n=52), mPFS was 7.2 months (95%CI: 5.5 – 11.0 months), and 5.6 months (95%CI: 3.9 – 7.8 months) in the presence of visceral metastasis (n=100). In patients without previous chemotherapy in the metastatic setting (n=109), mPFS was 7.2 months

(95%CI: 5.9 – 8.4 months), and 4.6 months (95%CI: 3.1 – 5.7 months) for patients who had received previous chemotherapy (n=43). For patients without a previous CDK4/6 inhibitor (n=145), the median PFS was 8.3 months (95%CI: 6.4 – 10.3 months). Everolimus starting doses were 10 mg (83%), 5 mg (15%), and 7.5 mg (2%). Dexamethasone mouthwash was used by 44% of patients. The most frequent AE were mucositis (51%; 3% grade 3), anemia (41%; 3% grade 3), hyperglycemia (34%; 2% grade 3), rash (28%; 2% grade 3), pneumonitis (21%; 2% grade 3), and diarrhea (17%; 1% grade 3). There were no grade 4-5 adverse events. Dose reduction was made in 35% of patients, and in 16% of patients the treatment was discontinued due to toxicity. Conclusions In our cohort, the use of everolimus plus ET in mBC patients previously treated with a CDK4/6 inhibitor showed a clinically significant benefit in terms of PFS, especially in patients without visceral metastasis, and no previous chemotherapy for advanced disease. In this real-world study, the toxicity profile of everolimus was manageable.

Disclosure(s):

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Laboratory monitoring in patients with hormone receptor–positive/human epidermal growth factor receptor 2–negative (HR+/HER2–) advanced breast cancer treated with palbociclib in a real-world setting: Results from POLARIS

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Background:

Palbociclib (PAL) is a cyclin-dependent kinase 4/6 inhibitor indicated for the treatment of HR+/HER2– advanced breast cancer (ABC) in combination with an aromatase inhibitor (AI) as initial endocrine-based therapy or with fulvestrant (FUL) in patients whose disease progressed on prior endocrine therapy (ET). Neutropenia was the most commonly reported adverse event in clinical trials. Per the prescribing information for PAL, complete blood counts (CBCs) should be monitored before initiation of PAL (Cycle 1, Day 1 [C1D1]), at the beginning of each subsequent cycle, on Day 15 of the first 2 cycles, and as clinically indicated for at least the first 6 cycles.

Methods:

POLARIS is a prospective, observational, multicenter, real-world study of patients with HR+/HER2– ABC who received PAL as deemed appropriate by the treating physician. CBC collected at baseline, anytime during the first 3 cycles, then on Day 1 (or before the start of a new cycle) of subsequent cycles as per standard of care were recorded. We analyzed the frequency of laboratory monitoring for patients with HR+/HER2– ABC receiving PAL in routine clinical practice. Lab collections outside these windows were also obtained (data not shown).

Results:

At data cutoff (March 30, 2022), 1242 patients were treated with PAL + ET; 902 patients as first-line (1L) and 340 as second-line or later ($\geq 2L$) therapies for ABC; 90% of all patients received 125 mg of PAL in the first cycle. The frequency of laboratory collection, overall and by site category (academic vs. community), within the first 6 months of treatment is reported in the Table. CBC collection reported by investigators and analyzed within the defined window of day 1 of each cycle (C1–C6). Day 1 CBC collection was 87% at C1D1, 69.4% at C2D1, 66.5% at C3D1, 63.2% at C4D1, 61.4% at C5D1, to 59.9% at C6D1. Reports of CBC collection on Day 15 for the first two cycles was 37.3% (C1D15) and 31.2% (C2D15). CBC collection pattern was comparable across the community and academic sites.

Conclusions:

In this real-world CBC monitoring data set analyzed in a defined cycle window, most sites reported CBC collection prior to PAL initiation, and over two thirds of sites in the subsequent cycles. Day 15 of Cycles 1 and 2 monitoring was conducted in one third of the patients. These results suggest that CBC collections in real-world clinical practice are performed less frequently than in clinical trials, which may reflect the sites' desire to reduce patient and/or clinic procedural burden, and treating physician's familiarity with PAL safety profile and their comfort level of managing patients in clinical practice.

Clinical trial identification: Pfizer; NCT03280303

Table

Site Category	CBC ^a Frequency, n (%)
C1D1 (N=1241) ^b	
Overall per cycle	1080 (87.0)
Site	
Academic (n=152)	130 (85.5)
Community (n=932)	808 (86.7)
Other ^c (n=138)	126 (91.3)
Missing (n=19)	16 (84.2)
C1D15 (N=1241) ^b	
Overall per cycle	463 (37.3)
Site	
Academic (n=152)	51 (33.6)
Community (n=932)	367 (39.4)
Other ^c (n=138)	36 (26.1)
Missing (n=19)	9 (47.4)
C2D1 (N=1152) ^b	
Overall per cycle	800 (69.4)
Site	
Academic (n=146)	89 (61.0)
Community (n=870)	628 (72.2)
Other ^c (n=118)	74 (62.7)
Missing (n=18)	9 (50.0)
C2D15 (N=1152) ^b	
Overall per cycle	359 (31.2)
Site	
Academic (n=146)	45 (30.8)
Community (n=870)	278 (32.0)
Other ^c (n=118)	29 (24.6)
Missing (n=18)	7 (38.9)
C3D1 (N=1087) ^b	
Overall per cycle	723 (66.5)
Site	
Academic (n=133)	86 (64.7)
Community (n=829)	560 (67.6)
Other ^c (n=109)	64 (58.7)
Missing (n=16)	13 (81.3)
C4D1 (N=998) ^b	
Overall per cycle	631 (63.2)
Site	
Academic (n=123)	72 (58.5)
Community (n=757)	489 (64.6)
Other ^c (n=102)	58 (56.9)
Missing (n=16)	12 (75.0)
C5D1 (N=932) ^b	
Overall per cycle	572 (61.4)
Site	
Academic (n=112)	61 (54.5)
Community (n=714)	444 (62.2)
Other ^c (n=91)	58 (63.7)
Missing (n=15)	9 (60.0)
C6D1 (N=880) ^b	
Overall per cycle	527 (59.9)
Site	
Academic (n=102)	47 (46.1)
Community (n=677)	420 (62.0)
Other ^c (n=86)	51 (59.3)
Missing (n=15)	9 (60.0)

C=cycle; CBC=complete blood count; D=day.

^aCBC collection interval spans -30 to +7 days from the cycle start date (C1D1); for all other cycles, the interval spans -7 to +7 days from the cycle start date.

^bN is the number of patients remaining on treatment at the corresponding visit; n is the number of patients remaining on treatment at respective site within the corresponding visit.

^cOther sites include Private Practices, Hospitals, Networks, Regional Cancer Centers.

Site	
Academic (n=112)	61 (54.5)
Community (n=714)	444 (62.2)
Other ^c (n=91)	58 (63.7)
Missing (n=15)	9 (60.0)
C6D1 (N=880) ^b	
Overall per cycle	527 (59.9)
Site	
Academic (n=102)	47 (46.1)
Community (n=677)	420 (62.0)
Other ^c (n=86)	51 (59.3)
Missing (n=15)	9 (60.0)

^cCycle: CBC=complete blood count; D=day.

^bCBC collection interval spans -30 to +7 days from the cycle start date (C1D1); for all other cycles, the interval spans -7 to +7 days from the cycle start date.

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^cOther sites include Private Practices, Hospitals, Networks, Regional Cancer Centers.

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12/7/2022

5:00 PM - 6:15 PM

P3-01-07

Phase II trial of palbociclib with fulvestrant in individuals with hormone receptor-positive, HER2-negative metastatic breast cancer with disease progression after palbociclib with an aromatase inhibitor

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Background: CDK4/6 inhibition (CDK4/6i) with endocrine therapy (ET) is a standard first line treatment for individuals with HR+, HER2- metastatic breast cancer (MBC). The anti-proliferative effect of CDK4/6i may reverse upon discontinuation, and the role of continuing CDK4/6i after progression on a CDK4/6i with aromatase inhibitor (AI) is not known. We examine the clinical activity of palbociclib and fulvestrant after disease progression on palbociclib with AI in a phase II trial in individuals with HR+, HER2- MBC (NCT02738866).

Methods: We conducted a prospective, phase II, multicenter, open-label study of palbociclib with fulvestrant in patients with HR+ HER2- MBC with disease progression after at least 6 months of first line palbociclib and AI. Previous chemotherapy was allowed. Eligible participants received fulvestrant and continued on the same palbociclib dose. Premenopausal women received a concomitant GnRH agonist. We obtained a baseline tumor biopsy, when accessible, for correlative studies, and serial blood samples for ctDNA and circulating tumor cells (CTCs) analysis. Participants received disease assessment with imaging every 2 cycles (8 weeks) for the first year, followed by every 3 cycles (12 weeks) for participants who had been on study for >12 months. The primary endpoint was progression-free survival (PFS), estimated using the Kaplan Meier method. Other key endpoints included objective response rate (ORR) and clinical benefit rate (CBR) per RECIST v1.1 .

Results: As of June 1, 2022, a total of 58 of 60 participants were enrolled, with median age 57.9 (range 28.2-82.1 years). 17 patients (29%) were premenopausal. 41 (71%) of participants were white and 12 (21%) of participants were black/African American. Median PFS (mPFS) among the entire cohort was 3.7 months; among pre-menopausal patients, mPFS was 2.5 months and among post-menopausal patients, mPFS was 4.0 months). 22 (38%) of patients were on treatment for 6 or more months, with 11 (19%) of patients experiencing long term response beyond one year (Table 1). 13/58 (22%) of participants required further dose reductions of palbociclib after initiating fulvestrant despite previously being on a stable dose of palbociclib with an AI; no unexpected treatment-related toxicities were noted . Updated results for the entire 60 patient cohort will be presented at the meeting.

Conclusions: Second line ET with palbociclib and fulvestrant following palbociclib and AI resulted in limited overall PFS. However, 38% of participants remained on therapy for greater than 6 months, suggesting clinical benefit in a subset of participants. Correlative studies, including of tissue, serial ctDNA and CTCs, are ongoing to further characterize this subset.

Table 1: Preliminary efficacy of palbociclib and fulvestrant

	Baseline (C1, D1)	3 mo	6 mo	12 mo	18 mo	24 mo
On Treatment - no. (%)	58 (100%)	33 (57%)	22 (38%)	11 (19%)	5 (9%)	3 (5%)

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novartis: Contracted Research (Ongoing); pfizer: Contracted Research (Ongoing); PUMA: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g.,

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12/7/2022

5:00 PM - 6:15 PM

P3-01-08

Metronomic chemo-endocrine treatment (FulVEC) for patients with advanced hormone-refractory ER+ breast cancer

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Introduction: The development of resistance to endocrine treatment (HTH) can result from various biological mechanisms not only related to ER function but also to activation of multiple signaling pathways, which make HTH insufficient to control cancer cells. The combination of HTH with CDK4/6 inhibitors, which largely resemble phase-specific antiproliferative cytotoxic agents, demonstrated a striking clinical activity and became a standard treatment in ER+ breast cancer. Therefore, we have hypothesized that combining HTH (ER degraded) with metronomic polychemotherapy might improve clinical outcomes in advanced, endocrine-resistant ER+ breast cancer patients. Material and methods: The treatment (FulVEC) combined fulvestrant (500 mg i.m. d 1, 14, 28, and q4w thereafter) with a VEC regimen (vinorelbine 40 mg p.o. 3x/week, capecitabine 500 mg p.o. tid, cyclophosphamide 50 mg p.o. qd). After local ethical committee approval, this treatment was initially offered as a salvage therapy for advanced ER+ BC patients who exhausted available treatment options, and latter also for patients who refused or were ineligible for standard intravenous chemotherapy. All patients were previously treated with at least 1 line of palliative systemic therapy (47% received 3+ lines and 21% 5+ lines). Most (53%) have previously failed fulvestrant, and 34%, 32%, and 29% have previously failed palliative treatment with capecitabine, vinorelbine, and cyclophosphamide, respectively. Almost half of the patients (47%) received CDK4/6i previously. Most patients presented with bone (82%) and liver (66%) metastases. Three patients (8%) had OUN metastases, and 5% showed only locally advanced disease. Results: Between 2017-2022 – 38 patients (median age 49.1 years) received the FulVEC regimen, and all data was prospectively collected. In the ITT administration of FulVEC led to at least disease stabilization in 87% of patients and was associated with median PFS and OS of 8.5 months and 21.5 months, respectively. Previous treatment with capecitabine and vinorelbine was associated with non-significantly shorter PFS of 6.5 and 6.3 months, respectively. However, previous utilization with fulvestrant or cyclophosphamide had no impact on patient outcomes. Surprisingly, previous treatment with CDK4/6 inhibitors did not impact either PFS or OS (8.5 and 20.8 months, respectively). Patients

with liver metastases had a higher (non-significant) risk of progression or death compared to other locations of metastases. Three patients with symptomatic OUN metastases (2 with leptomeningeal dissemination) treated with FulVEC responded to the treatment with median PFS and OS of 11.6 and 25.8 months, respectively. FulVEC regimen was generally well tolerated with no toxicity-related treatment cessation and temporary treatment interruption in 18% of patients due to G3-4 myelotoxicity, mainly neutropenia. Dose reduction, required in 47% of patients, was due to myelotoxicity, capecitabine-induced hand-foot-syndrome, and cyclophosphamide-induced cystitis. Conclusion: Chemo-endocrine therapy (FulVEC) comprising fulvestrant and metronomic polychemotherapy demonstrated surprisingly high activity in pretreated, endocrine-refractory breast cancer patients. Besides its significant antitumor activity and good safety profile, one of the most critical aspects of this therapy is its cost. FulVEC regimen consists of old, widely available, and inexpensive drugs and thus costs at least a level of magnitude less than any novel, targeted therapies considered for advanced ER+ BC. FulVEC and similar affordable strategies are critical for patients from low and middle-income countries. The activity of FulVEC proves that combining chemo- and hormone therapy in a palliative setting cannot be assumed as a no-go strategy. A phase III trial comparing FulVEC with physician treatment of choice in advanced BC patients who failed first-line HTH+CDK4/6i is warranted.

Disclosure(s):

Anna Buda-Nowak, n/a: No financial relationships to disclose

Lukasz Kwinta, n/a: No financial relationships to disclose

Pawel Potocki, n/a: No financial relationships to disclose

Joanna Streb, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

P3-01-09

Maintenance Therapy with ET and Ribociclib after 1st line Chemotherapy (CT) in Hormone Receptor (HR)-positive/HER2-negative Metastatic Breast Cancer (BC): a Phase II Trial (AMICA)

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Background: Approximately one third of HR-positive, metastatic BC patients receive CT as initial treatment. Longer duration of CT is associated with a better long-term outcome. However, the duration of CT is usually limited by toxicities and patients and physicians' preferences, resulting in treatment duration < 6 months. Replacing CT by maintenance endocrine treatment is an accepted treatment strategy in everyday clinical practice, but prospective data are lacking. Well tolerated maintenance treatments with the potential to prolong progression-free survival (PFS) and even overall survival (OS) are urgently needed. Methods: The AMICA trial (NCT03555877) is a multicenter, prospective, open-label phase II study to test the addition of the CDK4/6 inhibitor ribociclib to ET as maintenance therapy in patients with disease control after at least 4 cycles of 1st line mono- or poly-CT at investigator's discretion. Initially patients were randomized to receive ET +/- ribociclib. Due to slow accrual the study was amended after inclusion of 37 patients and all subsequent patients received ET+ribociclib. Treatment was given until disease progression, unacceptable toxicity, or withdrawal of consent. Maintenance ET could have already been started up to 6 weeks before enrolment. One previous line of ET including prior use of CDK4/6 inhibitor was allowed. The primary objective was to estimate the median PFS of patients treated with ET+ribociclib. Secondary objectives were median OS, safety, compliance, clinical benefit rate (CBR) and patient reported outcomes. The trial was closed prematurely due to slow recruitment. Results: Between March 2018 and December 2021, 56 patients were enrolled and started treatment (n=44 received ET+ribociclib, 12 ET alone). Median age of patients treated with ET+ribociclib was 60 years, 52.3% were overweight/obese, 88.6% were postmenopausal at study entry, 39.5% were M1 at primary diagnosis. Overall, 46.5% of the patients received letrozole, 14% anastrozole, 7.0% exemestane, 32.6% fulvestrant. A total of 10 (22.7%) patients in the ET+ribociclib arm had at least one serious adverse event, 2 at least one adverse event of special interest (N=1 hepatotoxicity, N=1 overdose). Conclusions: Results on the primary and secondary objectives will be presented at the meeting.

Disclosure(s):

Thomas Decker, n/a: Novartis: Consulting Fees (e.g., advisory boards) (Ongoing)

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12/7/2022

5:00 PM - 6:15 PM

P3-01-10

Going beyond the median: Estimating survival times for patients with hormone receptor positive, metastatic breast cancer commencing endocrine therapy

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Background: Oncologists are often asked to provide information about expected survival times for patients with metastatic breast cancer (MBC). We have previously demonstrated that using estimates of best-case, typical and worst-case scenarios for survival to explain life expectancy conveys more meaning and hope than simply providing single point estimates of the median overall survival (OS). Our aim was to assess whether using simple multiples of the median could accurately assess scenarios for survival for patients with estrogen receptor (ER) positive, MBC starting endocrine therapy (ET) using simple multiples of the median. Methods: We systematically searched for randomised trials of ET for ER positive MBC. We then recorded the following percentiles (representative scenarios) from the OS curve of each trial using UN-SCAN-IT® graph digitising software: 90th (worst-case), 75th (lower-typical), 50th (median) 25th (upper-typical), and 10th (best-case). We assessed the accuracy of estimating these percentiles for each OS curve by multiplying the median OS by four simple multiples: 0.25 (to estimate the 90th percentile), 0.5 (75th), 2 (25th) and 3 (10th). Estimates were deemed accurate if within 0.75 -1.33 times the actual value. Results: We identified 24 trials with 10,068 patients. The median OS (interquartile range [IQR]) was: 61.3 months (53.4-64.8) for first-line ET with cyclin-dependant kinase 4/6 inhibitors (CDK4/6i) (4 treatment groups); 42.6 months (40.9-50.4) for first-line ET alone (23 treatment groups) and 29.2 months (24.8-33.4) for subsequent line ET (21 treatment groups). The median OS (IQR) for each scenario for first-line ET with CDK4/6i was: worst-case 17.4 months (13.8-20.7); lower-typical 32.5 months (29.3-34.9); upper-typical and best-case percentiles were not available. Simple multiples of the median OS accurately estimated the 90th percentile in 79%; 75th percentile in 93%; and 25th percentile in 76% of curves. The 10th percentile was only available for four OS curves and could not be accurately assessed. Conclusion: Using simple multiples of the median OS to estimate and explain survival times to patients with MBC starting ET, is accurate and meaningful. Longer follow-up of trials is required to help clinician's estimate the best-case scenario for these patients.

Disclosure(s):

Andrew O. Parsonson, MBBS MMed FRACP: No financial relationships to disclose

Sunit Sarkar, MBBS FRACP: No financial relationships to disclose

Lauren Brown, MBBS FRACP: No financial relationships to disclose

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12/7/2022

5:00 PM - 6:15 PM

P3-01-12

Chidamide combined with fulvestrant in the treatment of HR-positive and HER2-negative advanced breast cancer after failure of previous endocrine therapy : A single-arm, single-center, phase 2 study

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Background: Chidamide is an oral subtype-selective histone deacetylase inhibitor. The ACE study demonstrated that chidamide plus exemestane improved progression-free survival compared with placebo plus exemestane in patients (pts) with advanced, HR-positive, HER2-negative breast cancer that progressed after previous endocrine therapy. This phase 2 study aims to evaluate the efficacy and safety of chidamide plus fulvestrant in the treatment of HR-positive and HER2-negative advanced breast cancer that had progressed after previous endocrine therapy.

Methods: Eligible pts were women aged 18-75 years with histologically confirmed HR-positive, HER2-negative, advanced invasive breast cancer, whose disease relapsed or progressed after at least one endocrine therapy with or without a CDK4/6i (either in the advanced or metastatic or adjuvant setting). Eligible pts were treated with oral chidamide (30mg twice a week for 4 consecutive weeks in a 4-week cycle) plus intramuscular fulvestrant (500 mg intramuscular injection; on days 0, 14, 28, then every 28 days thereafter) till disease progression or intolerant toxicity. Premenopausal women received a concomitant GnRH analogue. The primary endpoint is progression-free survival (PFS) and the secondary endpoints include overall response rate (ORR), duration of response (DoR), disease control rate (DCR), overall survival (OS), and safety.

Results: Between Mar 8, 2021 and May 20, 2022, a total of 18 pts were enrolled. Median age was 53.5 years (range 45-67), 18 (100%) pts had ECOG PS 1, 16 (89%) had visceral disease, 14 (78%) pts had prior treatments with the median lines of 2, including 12 (86%) received endocrine treatment, and 11 (79%) received chemotherapy in the metastatic setting. At data cutoff (Jul 3, 2022), 8 (44.4%) pts were still receiving the drug regimen. The median PFS was 7.2 (95% CI, 5.83-8.49) months. In the 17 efficacy evaluable pts, the ORR was 17.6% (95% CI, 3.8%-43.4%), DCR was 88.2% (95% CI, 63.6%-98.5%). Treatment related adverse events (TRAEs) of any grade occurred in 18 (100%) pts, in which 4 (22.2%) were \geq grade 3. The most common grade 3 or 4 TRAEs (incidence \geq 10%) were leucopenia (22.2%), and neutropenia (22.2%). No treatment-related deaths occurred. The trial is ongoing.

Conclusions: Chidamide combined with fulvestrant showed encouraging antitumor activity and tolerable toxicity in pts with HR-positive and HER2-negative advanced breast cancer that had progressed after previous endocrine therapy. Clinical trial information: ChiCTR2100044282. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd and Shenzhen Chipscreen Biosciences Co., Ltd.

Baseline characteristics

Baseline characteristics	N=18
Age, years	53.5 (45-67)
Menopausal status	
Premenopausal	7 (39%)
Postmenopausal	11 (61%)
ECOG performance status	
0	0 (0%)
1	18 (100%)
Sites of metastases	
Bone	10 (56%)
Bone only	2 (11%)
Visceral	16 (89%)
Lung	10 (56%)
Liver	6 (33%)
Number of previous treatments for metastatic disease	
0	4 (22%)
1	6 (33%)
2	7 (39%)
3	1 (6%)
Previous endocrine treatment for metastatic disease	
Yes	12 (67%)
Aromatase inhibitor	12 (67%)
No	6 (33%)
Prior chemotherapy	
No prior chemotherapy	1 (6%)
For metastatic disease	11 (61%)
For adjuvant disease	13 (72%)
Progesterone receptor status	
Positive	7 (39%)
Negative	11 (61%)

Baseline characteristics

Disclosure(s):

Wei Li, n/a: No financial relationships to disclose

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12/7/2022

5:00 PM - 6:15 PM

P3-01-13

Palbociclib , ribociclib and abemaciclib in real-world data: risk of disease progression on first-line treatment of metastatic breast cancer.

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Introduction and objectives

Cyclin dependent kinase (CDK) 4/6 inhibitors along with endocrine therapy (ET) is the standard first-line for endocrine receptor (ER)-positive HER2-negative metastatic breast cancer. Three CDK 4/6 inhibitors have the FDA and EMA approval: abemaciclib, palbociclib and ribociclib. They appear to have notable differences in their pharmacokinetic characteristics and ability to inhibit every cyclin. Nevertheless, the natural history of disease associated with each CDK 4/6 inhibitor remains unclear. The aim of this study is to establish a risk prediction model for disease progression under the different therapeutic regimes and assess whether there are differences in terms of efficacy between them.

Methods

This is a retrospective observational study in which patients treated with ET plus abemaciclib,

palbociclib or ribociclib as front line for metastatic breast cancer in Virgen del Rocio Hospital between April 2014 and April 2021 were selected. Patients in this population were followed for a period of 36 months. They were studied according to their clinical characteristics and disease outcome using descriptive analysis. The risk of progression was studied by a transversal method using a univariate logistic regression model. Moreover, Kaplan Meier curves were used to estimate progression-free survival (PFS) and the Breslow test to estimate the p value. All statistical analyses were performed with SPSS 28.0 (Statistical Package for the Social Sciences).

Results

A total of 189 patients were selected. 55(29.1%) of them received abemaciclib, 83(44%) palbociclib and 51(27%) ribociclib. 50(27%) patients had de novo metastatic disease, while 139(73%) were recurrences of previous disease. Almost half of the patients (45%) received fulvestrant and 104 (55%) patients received aromatase inhibitors. Table 1 represents the proportion of patients with visceral involvement and endocrine resistance in each arm. The univariate logistic regression model showed that patients treated with palbociclib had 2.36(CI95% 1.165-4.765) times the risk of progression compared to abemaciclib, while patients treated with ribociclib had 2.50(CI95% 1.139-5.475) times the risk of progression compared to abemaciclib. Overall PFS was 30.03 months. A tendency towards best PFS with abemaciclib in comparison with the other CDK 4/6 inhibitors was appreciated, but it did not reach statistical significance (abemaciclib-palbociclib p=0.289; abemaciclib-ribociclib; p= 0.293; palbociclib-ribociclib p=0.979).

Conclusions

In our sample of patients with ER-positive HER2-negative metastatic breast cancer treated with the different CDK 4/6 inhibitors as front line therapy, patients with abemaciclib achieved a lower risk of progression and a trend toward longer PFS. Further follow-up will be necessary to determine whether abemaciclib provides greater benefit in PFS.

Table 1. Proportion of patients with visceral involvement and endocrine resistance in each arm.

		CDK 4/6 Inhibitors		
		Abemaciclib	Palbociclib	Ribociclib
Metastasis site (N= 189)	Non-visceral	22 (40%)	41 (49.4%)	21(41.2%)
	visceral	33 (60%)	42 (50.6%)	30 (58.8%)
Endocrine resistance (N =188)	Non-endocrine resistance	35 (63.6%)	51 (62.2%)	31 (60.8%)
	Endocrine resistance	20 (36.4%)	31 (37.8%)	20 (39.2%)

Visceral metastases: Liver, Lung, central nervous System; Non-Visceral: Bone, skin, Lymph node.

Disclosure(s):

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5:00 PM - 6:15 PM

P3-01-14

Real-world treatment patterns of Palbociclib plus an aromatase inhibitor or aromatase inhibitor alone for metastatic breast cancer in the Flatiron database

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Background

CDK4/6 inhibitor in combination with an aromatase inhibitor (AI) or fulvestrant as initial endocrine therapy are standard of care for patients with HR+/HER2- advanced/metastatic breast cancer (mBC). This analysis describes treatment patterns including dosing patterns and time to subsequent treatment in patients receiving first line Palbociclib (PB)+AI therapy compared to AI alone, for HR+/HER2- mBC in the US routine clinical setting.

Methods

This was a retrospective analysis of Flatiron Health's nationwide longitudinal electronic health records from over 280 cancer clinics representing more than 3 million actively treated cancer patients in the US. Between February 2015 and March 2020, 2888 postmenopausal mBC women and men aged ≥ 18 years started first-line PB+AI or AI therapy. Patients were followed from start of therapy to September 2020, death, or last visit, whichever came first. PB treatment patterns were captured as starting dose and dose adjustments from medical records during the observation period. Comparative time to subsequent therapy (TTNT) or chemotherapy (TTC) was defined as length of time from the start of treatment to next line of anticancer therapy/chemotherapy, death from any cause, last visit, or end of study, whichever came first. Cox proportional-hazards models were used to estimate the relative effectiveness of PB+AI vs AI. Stabilized inverse probability treatment weighting (sIPTW) and propensity score matching

(PSM) statistical methods were used to balance of baseline demographics and clinical characteristics.

Results

Of the 2888 eligible pts (1324 with PB+AI and 1564 with AI), median age was 70.0 years, 67.8% were white, 34.8% had de novo mBC, 29.4% had lung or liver involvement, 38.7% had bone-only disease. Median follow-up was 25.0 months in the PB+AI arm and 23.3 months in the AI alone arm. Of the 1342 patients receiving PB, therapy was started at 125 mg, 100 mg, and 75 mg/day in 83.8%, 10.9%, 3.6%, respectively (1.7% undocumented PB dose) with dose changes in 41.1%, 36.8%, 31.3% of patients in each starting dose category with dosing information. After sIPTW median TTNT was 18.4 months (95%CI: 16.3-20.3) in the PB +AI group and 8.3 months (95%CI: 7.2-10.0) in the AI group; HR=0.56 (95%CI: 0.51-0.62), p< 0.0001. After sIPTW median TTC was 37.4 months (95%CI: 33.7-40.7) PB+AI group and 29.2 months (95%CI: 26.8-33.5) in the AI group; HR=0.77 (95%CI: 0.69-0.86), p< 0.0001. Results for the PSM analyses were similar. The table presents full results in detail.

Conclusions

These treatment patterns analyses in a heterogeneous mBC patients from real world US clinical practice, provide support for first line PB+AI treatment for HR+/HER2- mBC. The majority of patients initiated therapy at the 125 mg/daily dose (84%). Importantly, these analyses also report meaningful differences in the delay to next line of therapy and chemotherapy in the PB+AI compared to AI therapy arm.

Table. Median time to next line of therapy or chemotherapy

Variable	PB+AI (N=1324)	AI alone (N=1564)	HR
Months duration of follow-up, Median, 95% CI	25.0	23.3	--
Months TTNT, Median, 95%CI (unadjusted)	19.3 (95%CI 16.8-21.1)	8.2 (95%CI 7.1-9.8)	0.55 (95%CI 0.50-0.60) p<0.0001
Months TTNT, Median, 95%CI (sIPTW)	18.4 (95%CI 16.3-20.3)	8.3 (95%CI 7.2-10.0)	0.56 (95%CI 0.51-0.62) p<0.0001
Months TTNT, Median, 95%CI (PSM)	19.8 (95%CI 16.8-21.6)	9.8 (95% CI 15.8-21.6)	0.56 (95%CI 0.50-0.63) p<0.0001
Months TTC, Median, 95%CI (unadjusted)	38.1 (95%CI 35.0-41.1)	28.1 (95%CI 25.5-30.9)	0.74 (95%CI 0.66-0.82) p<0.0001
Months TTC, Median, 95%CI (sIPTW)	37.4 (95%CI 33.7-40.7)	29.2 (95%CI 26.8-33.5)	0.77 (95%CI 0.69-0.86) p<0.0001
Months TTC, Median, 95%CI (PSM)	37.8 (95%CI 33.7-41.3)	30.7 (95%CI 27.2-35.7)	0.78 (95%CI 0.68-0.89) p=0.0002

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P3-01-15

Real-world effectiveness of palbociclib plus aromatase inhibitors (AI) in African American (AA) patients with metastatic breast cancer (MBC)

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Background

Randomized clinical trials and a growing body of real-world evidence have demonstrated clinical benefit of cyclin dependent kinase 4/6 inhibitors (CDK4/6i) in combination with endocrine therapy for HR+/HER2- (MBC). In the National Comprehensive Cancer Network (NCCN) guidelines, CDK4/6i + AI or Fulvestrant is recognized as a preferred regimen for HR+/HER2- MBC. Disparities in survival and clinical outcomes between AA and white breast cancer patients are well documented, but AA patients were not well represented in CDK4/6i randomized clinical trials. We compared real-world progression free survival (rwPFS) and overall survival (OS) of palbociclib plus AI (PB+AI) vs AI alone in AA patients with HR+/HER2- MBC in US clinical practices.

Methods

The Flatiron Health longitudinal database contains electronic health records from >280 cancer clinics representing > 2.4 million actively treated cancer patients in the US. We conducted a retrospective analysis of 270 AA patients from the Flatiron database with HR+/HER2- MBC who started PB+AI or AI as first-line therapy between February 2015 and March 2020, Patients were evaluated from start of PB+AI or AI to September 30, 2020 (Data cutoff date), death, or last visit, whichever came first. OS was defined as months from start of PB+AI or AI to death. Patients were censored at the end of the study if they were living. rwPFS was defined as months from start of PB+AI or AI to death or disease progression, evaluated based on clinical assessment or radiographic scan/tissue biopsy. Cox proportional-hazards models were used to estimate the relative effectiveness of PB+AI vs AI without and with adjustment of baseline

demographics and clinical characteristics.

Results

Of the 270 eligible patients, 127 (47.0%) were treated with PB+AI and 143 (53.0%) were treated with AI. Median age was 64.0 years in PB+AI patients and 68.0 years in AI patients, respectively. Median follow-up was 24.0 months for PB+AI and 18.2 months for AI treated patients. Compared with AI patients, those treated with PB+AI were more likely to have de novo MBC (48.6% vs 30.8%) and to have ≥ 2 metastatic sites (41.7% vs 29.4%). Of the PB+AI patients, 82.7% started PB at 125mg/day and 30.7% experienced dose adjustment. Median OS was not reached (NR, 95%CI=(38.2-NR)) in PB+AI patients vs 28.2 months (95%CI=19.2-52.8) in AI patients (HR=0.46, 95%CI=0.31-0.68, $p < 0.001$; adjusted HR=0.56, 95%CI=0.36-0.89, $p=0.013$). Median rwPFS was 18.0 months (95%CI = 12.4 – 26.7) in PB+AI patients and 10.5 months (95%CI=7.0-13.4) in AI patients (HR=0.63, 95%CI=0.44-0.88, $p < 0.007$; Adjusted HR=0.74, 95%CI=0.47-1.17, $p =0.199$).

Conclusions

This comparative analysis of palbociclib plus AI vs AI alone provides evidence that first-line palbociclib in combination with endocrine is associated with improved effectiveness for AA patients with HR+/HER2- MBC in the real-world setting. Additional studies with larger cohorts are needed to provide additional evidence of outcomes and safety for AA patients in routine clinical practice.

Table. Patient characteristics and effectiveness outcomes

Variable	PB+AI (N=127)	AI alone (N=143)
Median age, years	64.0	68.0
Female sex, n (%)	126 (99.2)	141(98.6)
Metastatic sites ≥ 2 , n (%)	53 (41.7)	42 (29.4)
Lunge/liver involvement, n (%)	35 (27.6)	42 (29.4)
Bone only disease, n (%)	50 (39.4)	49 (34.3)
Interval from initial BC diagnosis to MBC		
De novo MBC	62 (48.8)	44 (30.8)
≤ 1 year	5 (3.9)	5 (3.5)
1–5 year	25 (19.7)	54 (37.8)
> 5 yr	35 (27.6)	40 (28.0)
OS rate at 12 months, %	91.7	70.3
OS rate at 24 months, %	75.9	53.2
OS rate at 36 months, %	61.2	44.3
Median OS (95%CI), months	NR (38.21-NR)	28.2 (19.2-52.8)
rwPFS rate at 6 months, %	78.4	66.9
rwPFS rate at 12 months, %	59.9	43.9
rwPFS rate at 20 months, %	46.6	30.1
Median PFS (95%CI), months	18.0(12.4-26.7)	10.5 (7.0-13.4)

AI= Aromatase inhibitor; PB+AI= Palbociclib plus AI; NR= Not reached; OS= Overall survival; rwPFS = real-world progression free survival

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P3-02-01

Chemotherapy plus immunotherapy in stage IV triple-negative breast cancer patient during pregnancy: a case report

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Introduction Cancer during pregnancy is uncommon but the incidence is increasing, particularly in breast cancer, the most common tumor diagnosed in this scenario. The treatment decision in pregnant patients with triple-negative breast cancer is challenging, even more so in cases with advanced disease. Clinical case A 36-year-old woman was referred to our hospital in January, 2020 with the diagnosis of an early (T2N0M0, stage IIA) invasive carcinoma of no special type triple-negative tumor on the left breast and germinative CHEK2 mutation. She received neoadjuvant treatment with four cycles of ACdd followed by nine weeks of paclitaxel and carboplatin, interrupted for local disease progression. The patient underwent a nipple-sparing mastectomy plus sentinel lymph node biopsy without complications. The pathology report showed gross residual disease, so we decided on adjuvant treatment with radiotherapy followed by capecitabine. Twelve months after the end of the treatment, she received the diagnosis of second-trimester pregnancy but also presented suspicion of pulmonary, nodal, and liver relapse. The liver biopsy confirmed triple-negative histology with CPS > 10. The first-line chemotherapy was liposomal doxorubicin, which showed hepatic disease progression after two cycles. As second-line, we started carboplatin, gemcitabine, and pembrolizumab. The radiologic evaluation after two cycles showed a partial response in the lung and liver, with the patient presenting excellent tolerability without fetal complications. The treatment plan is to wait until the term for delivery and continue treatment until progression or toxicity. Conclusion We report the first stage IV triple-negative breast cancer case in a pregnant patient treated with chemotherapy plus immunotherapy. This case indicates that the treatment is feasible and should be considered in this scenario.

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P3-02-02

Real-World Time-to-Treatment Discontinuation in Hormone-Receptor-Positive Metastatic Breast Cancer Patients following CDK4/6 Inhibitor Treatment, Based on Observational Data Collected Through Patient-Partnered Research

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Background: Cancer treatment decisions are often made without specific and representative information that can inform personalized treatment. The aim of this study was to determine if we can predict, based on clinical features, which treatment regimen may maximize real-world time-to-treatment discontinuation (rwTTD) after a hormone-receptor-positive (HR+) metastatic breast cancer (MBC) patient stops responding to a first CDK4/6 inhibitor in any line.

Methods: We used patient reported data (PRD) about diagnosis and treatment and medical records from 1,777 patients across the U.S. and Canada from Count Me In's Metastatic Breast Cancer Project (MBCproject). We interviewed 17 people, academic and community based medical oncologists and MBC patients, to inform the analysis plan. Patient eligibility criteria were prior HR+ MBC diagnosis, received exactly one prior CDK4/6 inhibitor (CDK4/6) containing regimen, start date of any subsequent regimen within four months of the end date of the CDK4/6-containing regimen, and completion of MBCproject's follow-up questionnaire at least one month after the start date of the subsequent regimen. We processed RWD from the follow-up questionnaire, performed chart review in ambiguous cases of patient eligibility, performed conformance, completeness, and plausibility verification checks to determine the dataset's fit-for-use, and described treatment variation seen in real-world settings. We designed a new user, active-comparator cohort study with rwTTD as the continuous outcome measure, used known and hypothesized confounders to control for treatment-by-indication bias, assessed covariate balance across cohorts, and conducted Cox proportional hazards (PH) outcome regressions to identify clinically relevant associations and estimate treatment effects across regimens. The analysis plan was publicly registered with the Center for Open Science prior to performing the analysis.

Results: 261 eligible HR+ MBC patients were identified, with 110 unique pairs of CDK4/6-containing and subsequent regimens. The most common CDK4/6-containing regimen was

Letrozole and Palbociclib (n=98) and subsequent regimen was Capecitabine (n=63). Three mutually exclusive and clinically relevant groupings of subsequent regimens chosen for analysis were chemotherapy only (n=99), fulvestrant-containing (n=53), and everolimus-containing (n=42). Among patients in these three groups, 93.9%+ are white race, 95%+ are non-hispanic, 2.7-9.4% live in a medically underserved area, 7.1-13.1% have HR+/HER2+ MBC, mean age at subsequent treatment was 52.6-53.8 years, 17-36% had bone-only metastasis and 14.3-25.3% had liver metastasis at MBC diagnosis, median number of past treatment regimens was one, and median time on CDK4/6-containing regimen was 9-14 months. The median rwTTD was 9, 15, and 5 months in the three groups, respectively. Out of 11 covariates, nine covariates failed to reject the null hypothesis that the distribution of values are the same across the three cohorts ($p>0.05$). Outcome regression Cox PH revealed rwTTD hazard ratio (HR) of 2.52 [1.53-4.15; 95% confidence interval (CI)] for presence of liver metastasis, HR of 1.09 [0.63-1.89; 95% CI] for presence of bone-only metastasis, HR of 2.00 [1.20-3.33; 95% CI] for everolimus-containing regimen vs. chemotherapy only, HR of 0.85 [0.50-1.46; 95% CI] for fulvestrant-containing regimen vs. chemotherapy only, and HR of 0.82 [0.65-1.00; 95% CI] for every six months rwTTD on previous CDK4/6-containing regimen.

Conclusion: In this cohort, chemotherapy was the most common treatment regimen following CDK4/6 even in second and third line settings and in patients with bone-only metastasis, which is a deviation from guideline-based treatment for many HR+ MBC patients. PRD helps develop hypotheses about patient response to treatment following CDK4/6 that can be further evaluated in larger, more diverse observational studies and clinical trials.

Table 1. Characteristics of eligible patients who received chemotherapy only, everolimus containing, or fulvestrant containing regimens.

	Chemotherapy	Everolimus_containing	Fulvestrant_containing	p	test
n	99	42	53		
age_at_nextline (mean (SD))	53.79 (11.01)	52.62 (10.14)	52.83 (11.16)		0.794
race_white (%)	93.9	100	94.3		
race_non_hispanic (%)	98.0	95.0	100		
ADI_mean (median [IQR])	33.00 [20.00, 47.50]	33.00 [18.00, 40.00]	34.00 [16.50, 52.50]		0.895 nonnorm
MUA = Yes (%)	9.4	2.7	5.9		0.375
De_novo_MBC = Yes (%)	20.2	21.4	35.8		0.088
CANCER_IDENTIFICATION_CLEAN (%)					0.996
IDC	56.6	57.1	60.4		
I LC	10.1	11.9	9.4		
NA	23.2	23.8	20.8		
Other	10.1	7.1	9.4		
HER2_POSITIVE (%)					0.16
NO	80.8	83.3	92.5		
YES	13.1	7.1	7.5		
Don't Know	6.1	9.5	0		
bone_only = Yes (%)	27.3	35.7	17		0.114
liver_mets = Yes (%)	25.3	14.3	17		0.252
num_past_regimens (median [IQR])	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]	1.00 [1.00, 2.00]		0.202 nonnorm
past_fulvestrant = Yes (%)	52.5	45.2	11.3		<0.001
firstline_TTD (median [IQR])	9.00 [4.00, 15.00]	12.50 [7.25, 22.00]	14.00 [8.00, 22.00]		0.002 nonnorm
nextline_iscensored = Yes (%)	41.4	23.8	45.3		0.074

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P3-02-03

A phase Ib trial of bintrafusp alfa and eribulin in patients with metastatic triple negative breast cancer (TNBC)

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Background: Metastatic TNBC is an aggressive breast cancer subtype with poor prognosis and limited systemic therapy options. While pembrolizumab in combination with chemotherapy is approved for PD-L1 positive TNBC, limited immunotherapy options exist for patients with progressive and/or PD-L1 negative disease. TGF β released by cancer cells and stromal fibroblasts attenuates the intrinsic antitumor potential of immune cells within the tumor microenvironment mediating resistance to immunotherapy. Consequently, inhibition of TGF β signaling could potentially enhance antitumor responses to anti-PD-L1/PD-1 therapies. Bintrafusp alfa is a bifunctional fusion protein composed of the extracellular domain of TGF- β receptor II (a TGF- β "trap") fused to a human IgG1 monoclonal antibody blocking programmed cell death ligand 1. Preclinical studies have shown that eribulin downregulates TGF β by phosphorylation of Smad proteins. Therefore, combining eribulin with bintrafusp alfa may have a synergistic effect. This study evaluated the combination of bintrafusp alfa with eribulin in patients with metastatic TNBC. Methods: This is a phase 1b, open label, single center study evaluating bintrafusp alfa in combination with eribulin in patients with metastatic TNBC who had relapsed/progressed on prior therapies. Patients with ER/PR \leq 10% with measurable disease were enrolled. Patients who received prior anti-PD-1/PD-L1 therapies in the metastatic setting were excluded. Patients received bintrafusp alfa 1200 mg intravenously every 2 weeks in combination with eribulin (1.4 mg/m² (dose level 1), 1.1 mg/m², or 0.7 mg/m²) on days 1, 8, 22, 29 on every 6-week cycle. Primary objectives were to determine the recommended phase II dose (RP2D) as well as to evaluate the safety and tolerability of eribulin in combination with the fixed dose of bintrafusp alfa. Secondary objective was to determine the overall response rate (ORR) according to RECIST 1.1. Bayesian optimal interval (BOIN) design was employed to identify the RP2D. Toxicities assessed using CTCAE v4.03. Tumor assessments were performed every 6 weeks. Results: A total of 25 patients were enrolled on the study. Twenty-one patients were evaluable (3 screen failures, 1 received only one dose of study treatment). Median age 59 (range 27-85). Median number of prior therapies 2 (range 0-8). The most common reason for protocol discontinuation was disease progression (n = 15, 71%). Four patients experienced dose limiting toxicities (DLTs); 3 with decreased neutrophil count and 1 with increased aspartate aminotransferase. Five patients (24%) experienced grade 4 toxicities (increased aspartate aminotransferase, hypokalemia, hypophosphatemia, neutropenia). Nine patients (43%) experienced grade 3 toxicities. Three patients (14%) discontinued study due to toxicity. Total of 2 deaths were observed, none related to treatment. Most common toxicities (any grade) include anemia (n = 13 patients), elevated aspartate aminotransferase (11), neutropenia (n = 10), elevated aminotransferase (9), headache (n = 9), hypokalemia (n = 8), hyperglycemia (n = 8), leukopenia (n = 8), and fatigue (n = 8). RP2D was eribulin 1.1 mg/m² with bintrafusp alfa 1200 mg. Six patients had PR (28.6%), 2 had SD (9.5%) and 12 had PD (57.1%) as the best response. One patient withdrew before response evaluation. Median PFS was 1.7 months (95% CI: (1.2, 5.9) and median OS was 11.1 months (95%CI: (5.2, 15.7). Conclusions: The combination of bintrafusp alfa with eribulin has manageable safety profile with meaningful clinical activity in patients with TNBC. Further studies evaluating TGF β inhibitors in breast cancer are warranted.

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P3-02-04

Phase II study of Pembrolizumab Maintenance treatment in patients with HER2-negative inflammatory breast cancer (IBC) and triple-negative breast cancer (TNBC) after response to chemotherapy

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Accumulating physical and hematologic toxicities make the indefinite use of chemotherapy unfeasible for many patients with metastatic/recurrent HER2- IBC or TNBC. Whether maintenance immunotherapy has a role in the treatment of these patients is unclear. We conducted a single-arm phase II trial of pembrolizumab monotherapy in patients with metastatic/recurrent HER2- IBC or TNBC (regardless of their PD-L1 expression status) and report here the clinical data from this trial. Methods: Eligible patients were enrolled between 2015 and 2022 and had had a CR, a PR, or SD after a minimum of 3 cycles of chemotherapy for metastatic/recurrent disease. PD-L1 expression status was not used to determine eligibility. Patients received 200 mg of pembrolizumab every 3 weeks (q3w) until disease progression, intolerable toxicity, or 2 years. In late 2021, the study was amended to allow patients who had received ≥ 8 cycles of q3w therapy to transition to q6w dosing (400 mg), based on the FDA's approval of both dosing regimens across all indications. The primary endpoint was the 4-month disease control rate (DCR); exploratory endpoints included safety and correlative biomarkers from tissue and blood to ascertain associations between clinical response and PD-L1 expression, T-cell clonality, and immune profiling. Results: Of 43 patients (median age, 54 years; range, 34-77 years), 11 had IBC (10 with triple-negative IBC and 1 with ER+ HER2-

IBC), and 32 had TNBC. The 4-month DCR was 58.1% (95% CI: 43.4%-72.9%). During a median follow-up of 11.4 months, 25 patients died. The entire cohort's median OS and PFS times were 26.0 months (95% CI: 11.0-33.5 months) and 4.8 months (95% CI: 3.0-7.1 months), respectively. The median OS times of the IBC and TNBC groups did not differ significantly, nor did those of the CR, PR, and SD groups. The median PFS times of the IBC group (2.2 months) and TNBC group (4.8 months) did not differ significantly ($p = .12$), but those of the CR, PR, and SD groups did (not reached, 10.3 months, and 3.4 months, respectively; $p = .01$). Among the 37 patients who are off study treatment, most patients (84%; $n=31/37$) discontinued treatment owing to disease progression rather than toxicities ($n=2$), and the toxicities overall were consistent with the known profile of single-agent anti-PD1. Five patients had grade 3 events; there were no grade 4 or 5 events. Three patients had irreversible endocrinopathies (thyroiditis and adrenal insufficiency) requiring hormone replacement, but only 1 patient discontinued pembrolizumab because of these events. One patient discontinued treatment because of optic neuritis requiring steroids. Four patients completed 2 years of treatment without disease progression. Conclusions: Pembrolizumab maintenance therapy achieves acceptable disease control after induction chemotherapy. The PFS in this trial compares favorably to the expected durations of response to later lines of therapy. The toxicity profile of pembrolizumab compares favorably with those of chemotherapy and ADCs, which may provide a rationale for the use of ICIs in this setting. However, whether pembrolizumab maintenance therapy is helpful in TNBC patients who have received concurrent pembrolizumab with neoadjuvant chemotherapy is unknown, as these patients were excluded from the trial. Acknowledgements: This trial was supported by Merck.

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Interim Analysis Results from a European Disease Registry Study Aimed to Prospectively Observe Treatment Patterns and Outcomes in Patients with HER2+ Unresectable Locally Advanced or Metastatic Breast Cancer

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BACKGROUND: Metastatic breast cancer (MBC) is incurable, with the primary goal of treatment being to extend survival while preserving quality of life. Treatment options available to patients (pts) with human epidermal growth factor receptor-2 positive breast cancer (HER2+ BC) may vary between countries, in terms of both the drugs used and the sequence in which they are used. There is limited data available on the clinical characteristics and outcomes in pts with unresectable locally advanced (LA) BC. This study aimed to capture real-world data on treatment patterns and clinical outcomes in HER2+ unresectable LABC and MBC.

METHODS: SAMANTHA (NCT02913456) is an ongoing, prospective, multicentre non-interventional study designed to observe pts with HER2+ unresectable LABC or MBC for a period of up to 8 years on study. The primary objectives are progression-free survival (PFS), assessed according to standard medical practice, and the treatment received. Secondary objectives included overall survival (OS), duration of response and safety. This pre-planned interim analysis reports baseline characteristics, treatment regimens received, first-line (1L) PFS by advanced BC status and the incidence of adverse events (AEs).

RESULTS: The study enrolled 647 pts from five European (EU) countries (Nov 2016-Nov 2019); 629 received 1L treatment and were included in data analysis. At data cut-off date (16 Nov 2021), median follow-up on study was 30.4 months (mo; range: 0.1; 60.0); 342 (54%) pts discontinued 1L treatments, of whom 170 (50%) pts received 2L treatments, 74 pts died, 49 pts were lost to follow-up, 35 pts withdrew consent and 14 pts withdrew due to physician decision. The full analysis set (FAS) included 222 (35%) LABC pts and 407 (65%) MBC pts [Table]. Pertuzumab/trastuzumab based regimens were given as 1L in the majority of pts [462 (73 %)]. The FAS Median (m) PFS in 1L was 41.3 mo (95% CI: 36.1, 54.1) for LABC and 23.5 mo (95% CI: 20.6, 27.6) for MBC. Median OS was not reached. In the FAS, any AEs were reported in 352 (56%) pts; of these 212 (34%) had a grade 3 or higher AE. Serious (S) AEs were reported in 135 (22%) pts; of whom, 36 (6%) pts had treatment related SAEs.

CONCLUSIONS: This interim analysis of SAMANTHA provides a snapshot of LABC/MBC treatment practices in five EU countries, where pertuzumab/trastuzumab based regimens appear to be the most used 1L treatment options, which aligns with the recommended standard of care. The mPFS is consistent with previous literature although higher than what was reported in the pivotal clinical trial CLEOPATRA. Given the good outcome observed in 1L and the current follow-up period of 30.4 mo, the data are not yet mature enough to provide complete insights into the treatment sequencing patterns and the clinical outcomes associated with these treatments.

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Table: Demographics and baseline disease characteristics of patients by status of advanced BC

[SABCS-Table.tif](#)

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5:00 PM - 6:15 PM

P3-02-06

Demographic and clinical features of patients with metastatic HER2 positive breast cancer: a retrospective multicenter registry study of the Turkish Oncology Group

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Background: Although HER2 is an aggressive subtype of BC, the outcomes have improved over the past two decades due to advances in targeted therapies. Here, we present data of HER2-positive subset from the multicenter registry study of the Turkish Oncology Group (TOG) for metastatic breast cancer with an evolving treatment landscape for over a decade (MBC). Methods: The study of TOG for MBC was a retrospective registry study aimed to collect the data of adult metastatic BC patients diagnosed between 2010-2019, at seven tertiary oncology clinics in Turkey. Patient and disease characteristics were recorded from chart reviews. HER2 (+) was defined as IHC scores of IHC3+ or IHC2+ and ISH (+). Overall survival (OS) and progression-free survival (PFS) were calculated by the Kaplan-Meier method. Correlations between demographic, prognostic variables and survival outcomes were carried out in database aggregates comprising of cohorts based on disease presentation (recurrent vs de-novo) and the diagnosis date of MBC (Cohort I: patient diagnosed between January 2010-December 2014 and Cohort II: between January 2015-December 2019). Results: Of the 1381 patients analyzed over the whole period, 333 (24.1%) HER2 (+) MBC patients were identified. 55.0% of the patients were in Cohort I. The majority (56.8%) had de novo MBC. Despite a decreasing frequency over time (63.4% in Cohort I vs 48.7% in Cohort II, $p=0.007$), this was the largest group with among all pathological subgroups presenting with de novo disease. 17 patients (2.4% of recurrent patients) demonstrated changes in HER2 receptor status from negative to positive between the primary tumor and subsequent metastasis. Recurrent BC patients were significantly younger than de novo MBC patients [44 (22-80) years vs 49 (20-91) years, $p=0.006$] and 43.1% ($n=62$) had relapsed within two years from initial diagnosis. Recurrent BC patients showed a higher frequency of brain metastasis as compared to de novo patients (13.2% vs 1.1%), whereas non-CNS visceral organ metastases were more common in de novo MBC patients (58.7% vs 47.9%, respectively, $p<0.001$). Following conditional approval of use in de novo visceral metastatic disease in 2016, dual-HER2 blockade including pertuzumab was more frequently used in Cohort II compared to Cohort I ($p<0.001$). Although overall median PFS was not statistically significant between the two cohorts (Cohort II vs I; 22 vs 17 months, respectively, $p=0.609$), there was a significantly higher PFS in the de novo group in Cohort II (29 vs 17 months, $p=0.037$). Furthermore, there was a significant improvement in median OS in Cohort II compared to Cohort I [not reached vs 48.0 (40.0-71.0) months, respectively; $p=0.017$]; mainly driven by the de novo group in alignment with the approval indication for dual blockade (Cohort I vs II; 3-year OS; 62.0% vs 84.7%; $p=0.009$); especially those with visceral metastatic presentation (59.4% vs 83.4%, $p=0.020$); HR (+) HER2 (+) disease (61.2% vs 89.2%; $p=0.013$) and age < 40 years (40.0% vs 94.7%; $p=0.009$). Conclusion: There was a significant survival benefit achieved in patients with metastatic HER2 (+) disease over time, regardless of high-risk factors such as visceral involvement or young age, mirroring advances in the timeline of anti-HER2 treatment.

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5:00 PM - 6:15 PM

P3-02-07

Combined Chemo-endocrine Therapy Maybe a New Option for HR+/HER2- Advanced Breast Cancer: A Prospective, Single-center Clinical Study of Fulvestrant plus Oral Vinorelbine

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Background Fulvestrant have demonstrated synergistic antitumor effect with chemotherapy regimen. This study evaluates the efficacy and safety of Fulvestrant with Vinorelbine in patients with hormone receptor positive (HR+)/ human epidermal growth factor receptor-2-negative (HER2-) recurrent or metastatic breast cancer. Methods In this prospective, single-arm and investigator-initiated clinical study, patients with recurrent or metastatic HR+/HER2- breast cancer after the first line adjuvant endocrine therapy for > 1 year were eligible, in which the subjects of the first line was defined as the patients with recurrence and metastasis after adjuvant endocrine therapy for over 1 year and did not receive treatment for the recurrence and metastasis and the second-line defined as the patients who had disease progression after receiving first-line endocrine therapy or first-line chemotherapy). Patients were administered i.m. Fulvestrant 500mg (day 1 per cycle for 28 days) and oral Vinorelbine (60 mg/m² on day 1, 8 and 15 of each cycle). The primary endpoint was progression-free survival (PFS). Secondary endpoints included overall survival (OS), objective response rate (ORR), disease control rate (DCR), duration of response (DoR), and safety. The Kaplan–Meier method and log-rank test were used to evaluate PFS and OS. Results Total 38 HR+/HER2- advanced breast cancer patients with median follow-up time (25.1 months) were enrolled in, and median PFS [9.86 months (95% CI: 7.2, 23.13)] were discovered. The median PFS of the first-line and the second-line treatment population were 20.73 months (95% CI: 9.82, NR) and 4.27 months

(95% CI: 3.68, NR), respectively. The median OS of the intent-to-treat (ITT) and the first-line treatment population were not reached, and the OS of the second-line treatment was 28.2 months (95% CI: 11.5, NR). The ORR of the ITT population was 39.47% (95% CI: 23.93, 55.01). The ORR of the patients receiving first-line and second-line treatments were 44.44% (95% CI: 25.70, 63.19) and 27.27% (95% CI: 0.95, 53.59), respectively. The DCR of ITT population was 92.11% (95% CI: 83.54, 100.00)], and the median DoR was approximately 15.33 months (95% CI: 7.23, 22.54)]. In the safety analysis, most of the adverse events were grade of 1/2, and none of grade 4/5 adverse events were reported. Conclusion This is the first exploratory study of Fulvestrant with oral Vinorelbine regimen in the treatment of HR+/HER2– recurrent and metastatic breast cancer conducted worldwide. The combinative chemo-endocrine therapy was efficacious, safe and promising for patients with HR+/HER2– advanced breast cancer.

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P3-03-01

The impact of the COVID19 pandemic on treatment practices for patients diagnosed with early breast cancer: a cross-sectional study from a large comprehensive cancer centre in Italy.

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The impact of the COVID19 pandemic on treatment practices for patients diagnosed with early breast cancer: a cross-sectional study from a large comprehensive cancer centre in Italy.

Introduction

The Coronavirus Disease 2019 (COVID19) has disrupted health services worldwide. The evidence on the impact of the pandemic on cancer care provision, however, is conflicting. Some reports found that management for patients diagnosed with early breast cancer (EBC) during the pandemic did not differ from pre-pandemic practices; other reports suggested that delays in breast cancer surgery may have occurred. We aimed to audit the management of patients diagnosed with EBC during the pandemic in a large, tertiary-level cancer centre in Italy.

Methods

We conducted a cross-sectional study to track the route to first treatment for patients diagnosed with EBC during 2019, 2020, and 2021. We abstracted data for all consecutive patients referred to the Veneto Institute of Oncology (Padua, Italy). We defined as point of contact (POC) the

date of the first consultation with a breast cancer specialist of the breast unit. We considered patients with a first POC in the 6 months preceding the multidisciplinary (MDT) meeting and initiating a treatment within 6 months from the POC. We chose the 3-month period April-June because in 2020 it was when health services were first acutely disrupted. We analysed the same period for 2019 and 2021. First treatment was defined as either upfront surgery or neoadjuvant chemotherapy (NACT). The time to first treatment was defined as the interval between the first POC and the first treatment. We used the median time to first treatment in 2019 to define the threshold for treatment delay.

Results

We reviewed medical records for 878 patients for whom an MDT report during 2019-2021 (April through June) was available. Of these, 431 (49%) were eligible: 144 in 2019, 127 in 2020 and 150 in 2021. Median age at first POC was 61 years. The proportion of screen-detected tumours was larger in 2019 and 2021 than in 2020 (59%). Conversely, the proportion of screen-detected tumours was offset by the proportion of palpable tumours in 2020 (44% versus 56%). These differences were statistically significant (chi-square test 11.12, $p=0.004$). Distribution of tumour and nodal stage was unchanged over time, but in-situ tumours were slightly fewer in 2020 than in 2019 or 2021. The odds ratio for treatment delay (45 days or more) was 0.87 for 2020 versus 2019 (95% CI, 0.5-1.53) and 0.9 for 2021 versus 2019 (95% CI, 0.52-1.55), after adjusting for type of POC, presentation with symptoms, treatment type, tumour stage, nodal stage, and EBC subtype (i.e., luminal, HER2-positive, triple-negative).

Conclusions

There was no evidence for major changes in the management of EBC patients during 2019-2021 and no treatment delays were observed. However, our results show a slight decrease in the absolute number of patients being treated in 2020, offset by an increase in 2021 to levels comparable to 2019. Our findings suggest that disruption of breast cancer screening programmes may have impacted on the characteristics of the patient population, with a larger proportion of women presenting with palpable nodules. Validation on a larger, population-based cohort of patients is warranted to robustly assess the impact of the COVID19 pandemic on treatment practices and outcome for EBC patients.

Characteristics of the population

	Apr-Jun 2019	Apr-Jun 2020	Apr-Jun 2021
Number of patients	144	127	150
Age (median)	60	63	63
Presentation			p=0.004
With symptoms	85 (59)*	56 (44)	95 (63)
Without symptoms	59 (41)	71 (56)	55 (37)
POC type			p=0.153
Breast radiologist	51 (35)	29 (23)	55 (37)
Breast surgeon	88 (61)	92 (72)	87 (58)
Medical Oncologist	2 (1)	4 (3)	6 (4)
Other	3 (3)	2 (2)	2 (1)
Tumour stage			p=0.881
T0	10 (7)	7 (6)	14 (9)
T1	75 (52)	73 (57)	81 (54)
T2	46 (32)	37 (29)	41 (27)
T3-T4	13 (9)	9 (7)	13 (9)
Unknown	0	1 (1)	1 (1)
Nodal stage			p=0.098
N0	87 (60)	88 (69)	104 (70)
N1	38 (26)	29 (23)	27 (18)
N2-N3	9 (7)	9 (7)	8 (5)
Unknown	10 (7)	1 (1)	11 (7)
Treatment type			p=0.957
Surgery	109 (76)	98 (77)	114 (76)
NACT [§]	35 (24)	29 (23)	36 (24)
Time to treatment (median in days)	44	37	43

*Numbers in brackets are percentages; [§]NACT: neo-adjuvant chemotherapy

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12/7/2022

5:00 PM - 6:15 PM

P3-03-02

Can artificial intelligence derived ultrasound breast density provide comparable breast cancer risk estimates to density derived from mammograms

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Can artificial intelligence derived ultrasound breast density provide comparable breast cancer risk estimates to density derived from mammograms Dustin Valdez^{1,2}, Arianna Bunnell², Thomas Wolfgruber¹, Aleen V. Altamirano³, Brandon Quon¹, Gertraud Maskarinec¹, Peter Sadowski², John A. Shepherd¹ ¹ University of Hawaii Cancer Center, Honolulu, HI ² University of Hawaii at Manoa, Honolulu, HI ³ Instituto Radiodiagnóstico, Managua, Nicaragua
Background: Breast cancer is the second leading cause of cancer-related death among women in Hawaii and the Pacific. However, while there are programs like the Breast and Cervical Cancer Early Detection Program (BCCEDP) implemented throughout the Pacific, the lack of access to mammography screening and low screening participation rates contributes to very high advanced breast cancer rates in most cases over 50%. Portable breast ultrasound is a promising screening technology for low resource areas. However, without mammography, mammographic density is not available for risk modeling to determine who should participate in screening programs or at what frequency. In this study, we ask if breast ultrasound (US) images can be used to derive an equivalent mammographic density for risk modeling. We utilized artificial intelligence to derive breast density from diagnostic ultrasound images and compared to BI-RADS mammographic density in an established breast cancer risk model¹.
Methods: We selected women with negative screening visit who either later developed cancer (positives) or did not (negatives) over a 10-year period. Temporally-matched negative mammographic and ultrasound images, cancer outcome status and cancer risk information were sourced from the Hawaii and Pacific Islands Mammography Registry. US images had to have occurred within a year of the mammogram. BI-RADS mammographic density was derived using an existing deep neural network model². Mammographic density was estimated from US images by training a deep-learning convolutional neural network model. A hold out set of images (Test set of 20% of the total) was used to compare 10-year breast cancer risk using the

Tyrer-Cuzick (TC) risk model¹ when calculated using breast density from either mammograms or US. The AUC values, confidence intervals, ROC plots and Pearson correlation were calculated and compared. Results: Over the 10-year study period, 1337 had matched mammograms and US images and 65 went on to develop breast cancer. Using the test set, the Pearson's correlation between breast density from mammography and US was 0.31 (moderate correlation). There were no covariates found to improve this association. The AUC for TC 10-year personal risk was higher when breast density from mammograms was used 0.71 (95% CI=0.57-0.86) versus US images 0.65 (95% CI=0.53-0.76). Conclusion: Overall breast cancer risk was similar when breast density was derived from either mammograms or US. The performance of our US breast density model is expected to improve further when more US training data becomes available. Breast cancer screening programs exclusively using US imaging may be able to provide equivalent risk modeling to clinics using mammography.

1. Tyrer J, Duffy SW, Cuzick J (2004). A breast cancer prediction model incorporating familial and personal risk factors. *Stat Med.* 2004 Apr 15;23(7):1111-30. doi: 10.1002/sim.1668. Erratum in: *Stat Med.* 2005 Jan 15;24(1):156. PMID: 15057881. 2. Wu, N., K. J. Geras, Y. Shen, J. Su, S. G. Kim, E. Kim, S. Wolfson, L. Moy and K. Cho (2018). Breast Density Classification with Deep Convolutional Neural Networks. 2018 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP), IEEE.

Disclosure(s):

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P3-03-03

Risk factors associated with chemotherapy-induced nausea and vomiting among breast cancer patients receiving highly emetogenic chemotherapy

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Purpose: Although risk factors related to chemotherapy-induced nausea and vomiting (CINV) have been identified by prior studies, there are only few studies evaluating risk factors associated with the contemporary antiemetic prophylaxis, including that of olanzapine/aprepitant- or NEPA- containing regimens. The present study aimed to identify the risk factors related to CINV development in Chinese breast cancer patients receiving doxorubicin and cyclophosphamide chemotherapy. Methods: Data from 304 patients who were enrolled to 3 previously reported prospective antiemetic studies were included. Multivariate logistic regression models were used to predict risk factors associated with the occurrence of CINV. Additionally, likelihood of treatment failure in relation to number of risk factors of individual patient was evaluated. Results: Multivariate analysis of the entire study group revealed that obese status (defined as body mass index ≥ 25.0 kg/m²) and the use of olanzapine/aprepitant- or NEPA- containing antiemetic regimens were associated with high likelihood, while history of motion sickness was associated with lower likelihood, of complete response (CR) and 'no nausea' in the overall phase. History of vomiting in pregnancy was also associated with lower likelihood of overall CR. Patients with increasing number of risk factors had higher likelihood of treatment failure as well as shorter time to first vomiting. Those who did not achieve CR and 'no nausea' in the first cycle were less likely to achieve these parameters in the subsequent cycle of chemotherapy. Conclusions: This present study confirmed the previously reported risk factors to be important for CINV in Chinese breast cancer patients receiving doxorubicin and cyclophosphamide. Further optimization of CINV control is required for patients with identifiable risk factors; olanzapine/aprepitant- or NEPA- containing prophylaxes are the preferred contemporary antiemetics regimens for Chinese breast cancer patients undergoing doxorubicin and cyclophosphamide chemotherapy.

Disclosure(s):

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5:00 PM - 6:15 PM

P3-03-04

Cyclin-dependent kinase 4/6 inhibitor in advanced breast cancer during the COVID pandemic period: efficacy in relation to vaccination for SARS-COV 19

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Introduction

More than 2 years after the WHO declaration of a pandemic, SARS-Cov-2 still represents a public health problem

The pandemic has increased the complexity of cancer treatments including breast cancer.

These difficulties were highlighted in adjuvant treatments but above all in metastatic disease.

Vaccination has been one of the most important public health factors that has reduced deaths, hospitalizations and the severity of symptoms related to infection.

In metastatic breast cancer hormone receptor positive and HER2/neu negative currently the first line of treatment is given by the association between cyclin 4/6 inhibitors and hormone therapy (aromatase inhibitors or fulvestrant)

A well-known and frequent side effect of this therapy is the reduction of white blood cell values and neutrophils.

The hypothesis that this study is to evaluate whether treatment with cyclin inhibitors initiated before the period of vaccinations may have influenced, due to the reduction in white blood cell values, an increased risk of infection in these patients.

Materials and methods

In our study, we selected patients who had started treatment with cyclin inhibitors before

starting the vaccination cycle (in Italy up to the fourth dose in cancer patients) and continue it without evidence of disease progression.

All patients were offered a vaccination cycle with mRNA COVID vaccines and were followed during their cancer treatments.

All patients, at least 90 days after the last dose of vaccine, have been tested for antibodies against SARS CoV-2 (trimeric spike protein) with a value expressed in binding antibodies unit (BAU) according to international standard WHO

During the observation period (starting from the first dose of vaccine administered) the patients were clinically checked and in case of suspicion of infectious pathology with symptoms suggestive of SARS-COV-19 infection, they were tested with molecular swab

Results

We evaluated 52 patients who started cyclin treatment before the vaccination course and who are currently without signs of disease recurrence

During the study period we found 14 SARS-COV19 infections (28% of patients) and one patient with two infectious episodes.

No patients needed treatment in a hospital or resuscitation setting. All patients have fully recovered from the infection and at most after 21 days have resumed the treatment still in place. Statistically, a linear regression calculation was applied to evaluate a functional relationship between variables measured on the basis of sample data.

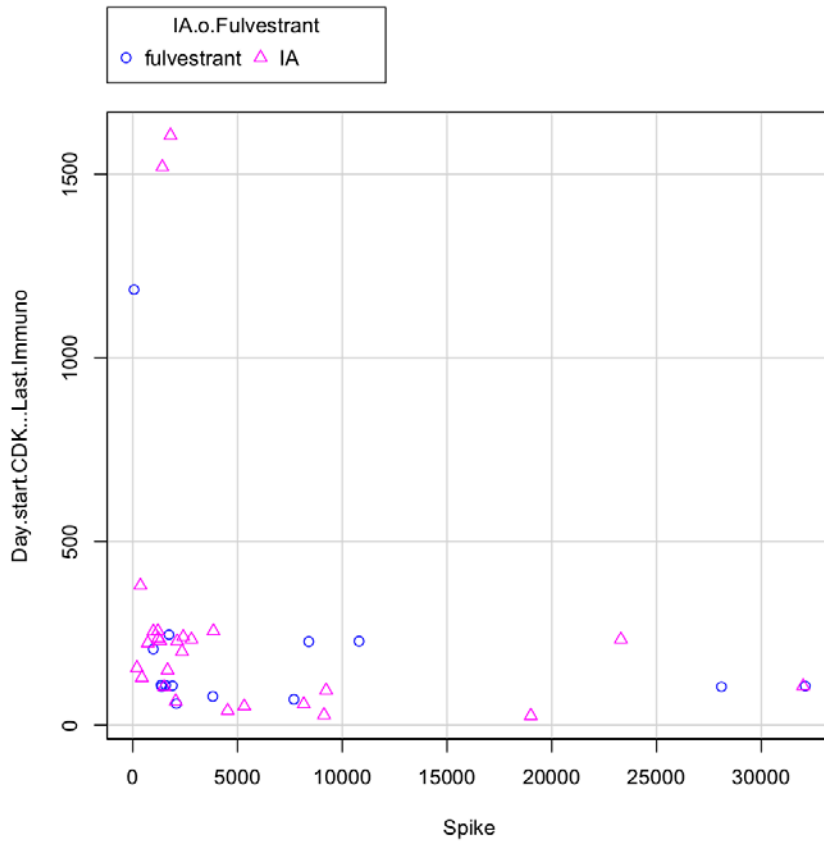
We did not find a relationship between spikes or infections compared to the start date of the vaccination cycle; instead we observed a relationship between the value of the spike and the date of last immunization (considered as an active infection or fourth dose of vaccine) with a reduction in the values the further you go away

Conclusion

The data of the study show that there is a correlation between the time elapsed between the last vaccination and the risk of getting sick. For this reason, the fourth recall represents a strong help to reduce this risk.

We did not find any ranges we could refer to regarding the dosage of trimeric spike protein. Considering the positivity rate of infections that does not exceed the general vaccinated population and the absence of serious infectious symptoms with hospitalization, treatment with cyclin inhibitors appears to be a safe treatment even in a pandemic period.

Last day immunization and spike with IA or fulvestrant



Disclosure(s):

Filippo Giovanardi, n/a: No financial relationships to disclose

Edoardo Carretto, n/a: No financial relationships to disclose

Giancarlo Bisagni, MD: No financial relationships to disclose

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5:00 PM - 6:15 PM

P3-03-05

A randomized study assessing interventions to improve comfort during screening mammography

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Background: Although screening mammography leads to an early detection of breast cancer and a reduction in breast cancer mortality, many women have apprehension about mammograms due to reported discomfort and pain [would cite the source]. A study showed that pain was the cause of non-attendance of screening mammograms in 25-46% of reported cases by women. Despite this, there is limited research on strategies to reduce discomfort and anxiety associated with mammography screening and improve patient experience and compliance with national screening recommendations. Herein, we performed a double-blind randomized clinical study to determine if the use of local analgesia and calming music can improve patient satisfaction during routine screening mammogram. Methods: This study was designed as a double-blind randomized clinical trial with a 2x2 factorial design. A total of 251 patients who presented for mammographic screening were randomized to receive: breast lidocaine gel at a dose of 1200 mg or placebo gel on both breast and experience calming music or no music. Patients with history of mastectomy, breast cancer or recent (within 24 hours) analgesic use were excluded. Pain was measured with a 5-point face pain scale. Benjamini-Hochberg false discovery rate was used for analysis. Results: Of the 251 patients who were randomized between June 2017 and October 2019, 195 self-identified as Hispanics (77%). Median age was 58.5 years old and there were no differences in between groups. 100% were female. 99.3% presented for screening with no concerning symptoms. A total of 126 patients were randomized to music vs 125 to no Music. 79 patients in music group and 51 patients in no music group were randomized to lidocaine. Regarding pain assessment, 18.96% of patients had a pain score of 4 and 5 in the music group randomized to lidocaine gel as opposed to 10.64% to placebo gel. In the non-music group, 17.65% of patients expressed pain score of 4 and 5 to lidocaine gel vs. 18.91% to placebo gel. (P value music: 0.95, P value lidocaine: 0.93 P value music and lidocaine: 1). Patients randomized to lidocaine gel to music reported their

prior mammogram to be at a pain score of 4 to 5 in 41.7% of the subjects vs 45% of patients in the no music group. (P value music: 0.45, P value lidocaine: 0.93 P value music and lidocaine: 1). Despite this, majority patients in both groups expressed no reluctance for future mammograms. Conclusion: The addition of calming music and breast lidocaine gel did not show a statistically significant difference in the level of pain perceived by patients getting screening mammography. The data appear to suggest less severe pain (pain score 4 and 5) when these strategies are combined. Further prospective trials with larger patient populations are needed to explore these interventions. Despite the perceived pain most patients were still willing to return for a mammogram the following year.

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Marcela Mazo-Canola, MD: No financial relationships to disclose

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Kenneth Kist, MD: No financial relationships to disclose

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Virginia Kaklamani, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Daiichi Sankyo: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Genentech: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Genomic Health: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Gilead Sciences: Honoraria (Ongoing); Novartis: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Pfizer: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Puma Biotechnology: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing)

12/7/2022

5:00 PM - 6:15 PM

P3-03-06

A pilot study of personal care product use and exposure to environmental chemicals among Black and Hispanic breast cancer survivors

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Objectives and rationale: Racial and ethnic minorities are disproportionately exposed to environmental chemicals that have been linked to cardiovascular disease, cognitive decline, metabolic disease, and premature mortality. Recent evidence suggests that personal care products are a source of such exposures and that these products are more frequently used among Black and Hispanic women. Minoritized populations also tend to experience worse breast cancer outcomes compared to White patients. However, few studies have examined personal care product use and environmental exposures among minority cancer survivors. The aim of the present study was to describe personal care product use and chemical exposures, including ambient and dermal sources of exposure, in a pilot study of Black and Hispanic breast cancer survivors. Methods: In November 2020 – December 2021, self-identified Black and Hispanic breast cancer survivors aged ≥ 21 years were recruited in Washington, DC and Hackensack, NJ. Eligible survivors had been diagnosed with primary Stage I-III breast cancer and had completed breast cancer treatment except endocrine therapy. Surveys collected data on demographics, breast cancer diagnosis, personal care product use, and potential covariates. Participants wore silicone wristbands for 1 week for passive sampling of environmental exposures. Extracts from the wristbands were assessed using a gas chromatograph-mass spectrometer to detect chemical exposures. Values were adjusted for wear time and wristband size to provide sample concentrations of detected chemicals. Results: Among the 25 study participants, 17 were Black and 8 were Hispanic, with a mean age of 58 years. Most survivors (58%) had been diagnosed with Stage I breast cancer. Survivors reported using perfume (52%), make-up (80%), and nail polish (68%) during the week, with common daily use of facial

creams, lotions, or moisturizers (60%) and body creams, lotions, or moisturizers (68%). Drinking bottled water every day (64%) or most days (24%); eating prepared food from a fast food restaurant at least once per week (88%); and eating food reheated in a plastic container at least once per week (71%) were also prevalent. However, the majority of survivors reported never using pesticides indoors (76%) or outdoors (79%). The wristbands detected 60 distinct chemicals. On average, 21.8 chemicals were detected per wristband and 19 chemicals were detected in more than half of the samples. Exposure to flame retardants and pesticides was ubiquitous. All participants were exposed to chemicals found in personal care products and in commercial products. Several of the most commonly detected chemicals, including benzyl salicylate (a UV light absorber and fragrance), diisobutyl phthalate (a plasticizer), and linal (a perfume), are biologically active compounds with potential genotoxic or endocrine effects. Discussion: Exposure to environmental chemicals was ubiquitous among Black and Hispanic breast cancer survivors in DC and New Jersey. Frequent use of personal care products and commercial products suggest an opportunity to reduce potentially harmful exposures. Future studies are needed to investigate the role of environmental chemicals in health outcomes among breast cancer survivors and whether environmental exposures contribute to cancer health disparities.

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Jennifer Hicks, MS: No financial relationships to disclose

Erin Speiser, PhD: No financial relationships to disclose

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5:00 PM - 6:15 PM

P3-03-07

The Breast Cancer Prevention Clinic: A Single Institution's Experience

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The Breast Cancer Prevention Clinic: A Single Institution's Experience Authors: Joe J. Stephenson MD¹, LeAnn Perkins, FNP-BC, DipACLM¹, Erinn Crowe, RN, BSN, OCN¹, Regina Franco, MSN, NP-C, DipACLM¹, Pamela Cloys, MSN, ANP-C¹, Carmen Hancock, MSN, APRN, FNP-C, AOCNP¹, Marie Smith, MS¹ ¹Prisma Health Cancer Institute, Center for Integrative Oncology & Survivorship Background: Roughly 1 in 8 women will be diagnosed with invasive breast cancer in their lifetime¹. Some women have higher risk for developing breast cancer due to numerous factors such as elevated risk modeling scores, a history of chest radiation therapy, a history of atypical cells on a breast biopsy or a pathogenic genetic mutation. Enhanced surveillance to detect cancers early and addressing modifiable lifestyle risks are helpful to mitigate risks. Methods: The Prisma Health's Breast Cancer Prevention Clinic (BCPC) approaches prevention by monitoring non-modifiable risks with regular surveillance and education on optimizing lifestyle habits to decrease modifiable risks. Established in 2017, the BCPC team now includes multiple medical oncologists and nurse practitioners, allowing the clinic to be offered any day of the week. During the visit, patients receive a personal risk assessment. Recommendations are given for surveillance imaging, risk-reducing endocrine therapy, and risk-reducing lifestyle modifications such as diet, alcohol consumption, and exercise routines. Family history is also reviewed to recommend Genetic Counseling if appropriate. In March 2022, a statement was added to patient mammograms, generating referrals for those with calculated elevated risk (a calculated lifetime risk >20% using

the Tyrer-Cuzick or International Breast Cancer Intervention Study model and/or a 5-year risk >1.7% using the National Cancer Institute Breast Cancer Risk Assessment Tool or Gail model). Results: In a 12-month period from June 1, 2021 through May 31, 2022, 56.2% of patients were referred based on family history, 26.9% for higher-risk breast pathology, 8.1% for calculated elevated risk, 4.4 % for a pathogenic genetic variant that increases breast cancer risk and 4.1% for mammographic identification risk modeling. Following the BCPC visit, referrals for patients may include imaging such as mammograms, MRIs, genetic counseling or testing, or surgical evaluations. Referrals for lifestyle modifications may include nutrition, exercise navigation, mindfulness classes, or Sexual Health Evaluations. From June 2021 through May 2022, 41.4% of patients were referred for a breast MRI, 26.6% were referred to genetic counselors for genetic testing recommendations, 11.1% were referred to nutrition or exercise services, 8.42% were referred for a Bone Density Scan (DXA), 4% were referred to a Breast Surgeon and 3.7% were referred to the Genetic Management Clinic. Additionally, 79.5% of patients were referred to the High-Risk Breast Lifetime Clinic for continued monitoring and surveillance for early detection of breast cancer, continued reinforcement of lifestyle modifications, and management of risk-reduction endocrine therapy. Conclusion: The unique structure of this model allows for enhanced surveillance through greater use of evidence-based cancer prevention, early detection methods, and increased education for lifestyle medicine practices with the overall goals of reducing breast cancer risk, earlier breast cancer detection, and increasing quality of life. Reference List 1. DeSantis C, Ma J, Gaudet, M, et al. Breast cancer statistics, 2019. CA: A Cancer Journal for Clinicians. 2019;69(6), 438-451. <https://doi.org/10.3322/caac.21583>.

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5:00 PM - 6:15 PM

P3-03-08

Depression and breast cancer recurrence among female veterans in the United States: a retrospective cohort study

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Background: The importance of mental health to improve the quality of cancer survivorship and outcomes is gaining increased attention. Major depressive disorder (MDD) has been associated with higher breast cancer (BC) incidence, BC-specific and all-cause mortality. The effect of MDD on BC recurrence remains under-studied. The Veterans Health Administration (VHA) provides a unique opportunity to examine this relationship as it mandates annual MDD screening in the primary care setting and reports national screening rates of 96%. **Objective:** To examine the relationship between pre-existing MDD and BC recurrence among a diverse cohort of women in the United States. **Methods:** We established a retrospective cohort of women (age ≥ 18 years) diagnosed with early-stage incident BC from 2010 through 2019 using the VHA's electronic medical record database. We used a two-year window to identify women with clinically diagnosed MDD prior to their BC diagnosis. Our outcome of interest was BC recurrence (local recurrence/second primary and distant recurrence). We used multivariable proportional hazards regression to examine the association between MDD and BC recurrence, accounting for competing risk of death. Our analyses were adjusted for age, race, ethnicity, marital status, priority group rating (proxy for socioeconomic status), rurality of primary residence, geographical region, cancer stage, year of BC diagnosis, and comorbidity burden. Priority group rating is a metric that incorporates patients' income, receipt of VHA assistance benefits, capacity for gainful employment, and severity of service-connected conditions. We conducted subgroup analyses by tumor subtype. **RESULTS:** Our cohort consists of 6,045 women with BC, of whom 1,750 (29.0%) had a pre-existing MDD diagnosis. The median length of follow-up from BC diagnosis was 4.5 years (IQR=4.8 years). The average age at BC diagnosis was 57 years (SD=11 years) overall and 56 years (SD=10 years) among women with

MDD. Sixty-one percent of women were white, 29% were black, 27% were married, and 28% were rural dwelling. Forty-four percent of invasive carcinomas were localized and 21% were regional. Thirty-five percent of patients had ductal carcinoma in situ. Women with MDD had a higher average Charlson Comorbidity Index score (mean=0.75, SD=1.13 vs. mean=0.58, SD=1.03) and proportion with a priority group rating between 1-4 (40% vs. 32%). The distribution of other described patient characteristics among women with MDD were similar to the overall cohort. On multivariable analysis, women with MDD had a 31% (95% CI: 1.11, 1.56) higher risk of BC recurrence compared to women without MDD. MDD was associated with a 29% (95% CI: 1.01, 1.66) and 33% (95% CI: 1.05, 1.67) higher risk of local recurrence/second primary and distant recurrence, respectively. The relationship between MDD and BC recurrence remained significant after adjusting for tumor subtype (HR=1.40, 95% CI: 1.07, 1.83). In subgroup analyses stratified by tumor subtype, MDD was associated with a higher risk of BC recurrence among women with estrogen receptor positive versus negative tumors (HR=1.65, 95% CI: 1.27, 2.14 vs. HR=0.71, 95% CI: 0.34, 1.46) and HER2/neu negative versus positive tumors (HR=1.53, 95% CI: 1.16, 2.00 vs. HR=1.24, 95% CI: 0.51, 2.96). The interaction between estrogen receptor status and MDD was statistically significant (p-interaction=0.02). CONCLUSION: Women with incident BC should be screened for MDD early in the cancer care continuum given the prevalence of MDD and association with increased risk of local recurrence/second primary and distant BC recurrence. Further research is needed to understand the interplay between these two diseases and their treatments.

Disclosure(s):

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5:00 PM - 6:15 PM

P3-03-09

Assessment of Breast Cancer Chemotherapy Dose Reduction in an Integrated Healthcare Delivery System

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Background: Most cytotoxic drugs are dosed according to body surface area (BSA), yet not all patients receive the full BSA-determined dose. Prior work suggests that dose reduction may occur more frequently in obese patients, likely due to concern about inducing toxicity at high doses. Other factors, such as race/ethnicity, have been suggested to be associated with dosing, yet the factors associated with dose reduction remain poorly understood, with little known about dosing patterns in integrated healthcare delivery systems and how such patterns have changed over time. Methods: We examined chemotherapy dosing in 452 women diagnosed with stage I-IIIa primary breast cancer at Kaiser Permanente Northern California. All study participants were a part of the Pathways Study, diagnosed between 2006-2013, and treated with the common breast cancer regimen, ACT (cyclophosphamide and doxorubicin, followed by paclitaxel). We explored the association between obesity and dose reduction, and further explored other factors in relation to dose reduction, including various sociodemographic characteristics, tumor characteristics, and comorbidities. We assessed dosing using first cycle dose proportion (< 90% expected dose) and average relative dose intensity (ARDI, a metric of dose intensity over the entire course of chemotherapy). Results: Overall, 8% of women received a dose reduction >10% in the first cycle of chemotherapy and 21.2% of patients had an ARDI < 90%. Obesity was a strong predictor of dose reduction, both in the first cycle and across all cycles. In the first cycle, 21.9% of severely obese patients (body mass index, BMI: 35+ kg/m²) were dose reduced, whereas no normal weight patients (BMI: 18.5-< 25 kg/m²) experienced a first cycle dose reduction. Across all cycles, 38.4% of severely obese women had an ARDI < 90%, as compared 12.8% of normal weight women. In logistic regression models adjusted for age, race/ethnicity, and white blood cell count, obese women had 4.1-fold higher odds of receiving a dose reduction of 10% or more over the course of chemotherapy than their normal weight counterparts (95% CI: 1.9, 8.9; p-trend: 0.006). Increasing age was positively associated with dose reduction across the course of chemotherapy, as was the presence of comorbidity. Importantly, dose reduction was less common in later calendar years. Sensitivity analyses revealed that the positive association between obesity and dosing was robust to further adjustment for these other significantly associated factors. Impact: These results offer insight on factors associated with variation in chemotherapy dosing for a common breast cancer treatment regimen. Larger studies are required to evaluate relevance of these findings to other treatment regimens. Further work will be needed to determine whether dose reductions impact breast cancer outcomes.

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5:00 PM - 6:15 PM

P3-03-10

The Impact of Type 2 Diabetes on Complications after Primary Breast Cancer Surgery: a Danish population-based cohort study

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Introduction Type 2 diabetes (T2D) is associated with obesity and other comorbidities involving multiple organ systems, which may increase the risk of postsurgical complications. Knowledge is sparse on the impact of T2D on the postsurgical outcome after breast cancer (BC) surgery in primary BC. Objectives To investigate the association of T2D and risk of complications after primary BC surgery, and according to neoadjuvant chemotherapy. Methods Our cohort included all Danish women diagnosed with early-stage operable BC during 1996-2018 registered in the Danish Breast Cancer Group clinical database. All patients had primary surgical treatment—mastectomy or breast conserving surgery. Information on prevalent T2D was collected from Danish medical and prescription registries, defining T2D via diagnostic codes or redemption of ≥ 2 prescriptions for glucose-lowering drugs. We defined postoperative complications as hospital admissions for medical or surgical complications (re-operations (excluding seromas), bleeding, infection, thrombosis, kidney or arterial cardiovascular disease) up to 30 days after primary BC surgery. We calculated the 30-day cumulative incidence function (CIF) of postoperative complications and used Cox regression to estimate hazard ratios (HR) and associated 95% confidence intervals (95% CI) overall, and stratified by the receipt of neoadjuvant chemotherapy, adjusting for potential confounders. Results Among 84,491 women with operable BC, 4,669 (5.5%) had prevalent T2D at time of BC surgery. Overall, 800 (17.1%) and 8,621 (10.8%) of BC patients with and without T2D developed postoperative complications corresponding to CIFs of 17% (95%CI: 16% - 18%) and 11% (95%CI: 10% - 11%), respectively, and a HR of 1.44 (95%CI: 1.34-1.56). 173 (3.7%) BC patients with T2D and 2,805 (3.5%) without T2D received neoadjuvant chemotherapy. Among those who did not receive neoadjuvant chemotherapy, the CIFs of postoperative complications was 17% (95% CI: 16% - 18%) and 11% (95% CI: 10% - 11%) for women with and without T2D, respectively, with a corresponding HR of 1.42 (95% CI: 1.31-1.53). For those with and without T2D who received

neoadjuvant chemotherapy, the CIFs were 24% (95% CI: 18% - 30%) and 10% (95% CI: 9% - 11%), respectively, and with a corresponding HR of 2.08 (95% CI: 1.49-2.91). Conclusion Among women with BC, prevalent T2D at the time of primary BC surgery increases the risk of postoperative complications. This excess risk is particularly pronounced among patients who undergo neoadjuvant chemotherapy.

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P3-03-11

Racial and Ethnic Disparities in Screening Mammography During COVID-19

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Purpose: Studies conducted prior to COVID-19 suggested that racial/ethnic disparities in breast cancer screening percentages have substantially reduced over time. COVID-19 has had devastating effects on racial/ethnic minorities and resulted in delays in preventive breast cancer screening. Our purpose was to determine if racial/ethnic minorities were less likely to receive recommended breast cancer screening after the resumption of preventive care during the COVID-19 pandemic. Methods: HIPAA-compliant, institutional review board exempt retrospective cohort study was performed at a multi-location academic medical center located in the Midwest. Patients included women aged 50-74 years old between June 2021 and May 2022, derived from the electronic medical records. Primary outcomes variables included receipt of screening mammogram within the last two years. Primary exposure variables included race (American Indian/Alaska Native, Asian/Native Hawaiian/Other Pacific Islander, Black or African American, White) and ethnicity (Hispanic/Latino, and Not Hispanic/Latino). Binary outcomes were analyzed using logistic regression, adjusted for potential confounders (insurance, age, preferred language, employment status, rural status). Results: 37,509 female patients without

histories of mastectomies were included (mean age 63.1). 73.8% of eligible patients received a mammogram within the last two years. By race, 74.7% of White patients, 57.6% of Black patients, 67.0% of Asian/Pacific Islander patients, and 60.1% of American Indian patients received a screening mammogram within the last two years. In our unadjusted analyses, Black (OR 0.46, 95% CI 0.41 to 0.52, $p < 0.001$), Asian (OR 0.69, 95% CI 0.60 to 0.79, $p < 0.001$), and American Indian patients (OR 0.51, 95% CI 0.39 to 0.66, $p < 0.001$) were less likely to receive recommended mammography screening. In our adjusted analyses, Black (OR 0.54, 95% CI 0.47 to 0.61, $p < 0.001$), Asian (OR 0.79, 95% CI 0.68 to 0.92, $p = 0.003$), and American Indian patients (OR 0.63, 95% CI 0.48 to 0.82, $p = 0.001$) were less likely to receive recommended mammography screening. By ethnicity, 74.1% of Non-Hispanic patients and 64.2% of Hispanic patients received a screening mammogram within the last two years. In our unadjusted analyses, Hispanic patients (OR 0.62, 95% CI 0.55 to 0.71, $p < 0.001$) were less likely to receive recommended mammography screening. In our adjusted analyses, Hispanic patients (OR 0.92, 95% CI 0.79 to 1.08, $p = 0.338$) were comparably likely to receive recommended mammography screening. Patients with non-English preferred languages, uninsured or Medicaid patients, and patients living in rural areas were less likely to receive recommended mammography screening ($p < 0.001$). Conclusions: Racial/ethnic minority patients were less likely to receive recommended cancer screening after the resumption of preventive breast cancer screening during the COVID-19 pandemic. Targeted outreach efforts are required to ensure equitable access to breast cancer screening for racial/ethnic minorities, patients with non-English preferred languages, uninsured, Medicaid, and rural patients.

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Risk of recurrence with adjuvant endocrine therapy in real world patients with hormone receptor positive/human epidermal growth factor receptor-negative early breast cancer: a US database analysis

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Background The recommended 5-10 years of adjuvant endocrine therapy (ET) as standard of care has improved outcomes in patients with HR+/HER2- early breast cancer (EBC); however, risk of recurrence persists. The monarchE study demonstrated improvement in invasive disease-free survival (iDFS) with abemaciclib in node-positive, high-risk EBC, the majority of which were stage III (Johnston SRD, et al. J Clin Oncol. 2021;38:3987); however, monarchE's relatively short follow-up time to date only allowed for observation of early recurrences—longer follow-up is needed to evaluate late recurrences. Risk of recurrence is a concern for patients

with all stages of EBC (Pan H, et al. N Engl J Med. 2017;377:1836). We assessed the risk of recurrence in a real-world setting among patients with stage II-III HR+/HER2- EBC after initiation of adjuvant ET. **Methods** This was a retrospective analysis of ConcertAI's deidentified electronic medical records data set among patients treated from January 1, 1995, to April 30, 2021. The cohort included stage II-III patients with HR+/HER2- EBC who underwent surgery and initiated adjuvant ET (if IIIB or IIIC, confirmation was required on residual tumor status). Patients were from academic and community oncology clinics across the US. Data were missing from the database for some variables; thus, percentages may not add up to 100%. iDFS was assessed to determine the risk of disease recurrence, death, or second primary tumor and was defined as the time interval between start of ET and first iDFS event. Kaplan-Meier methods were used to estimate cumulative probabilities of experiencing an iDFS event at 5 and 10 years from the start of ET. **Results** A total of 3133 patients (98.8% female) with stage II-III HR+/HER2- EBC were included in the analysis. The median follow-up time was 68.1 months. The median age was 59 years; 22.2% of female patients were pre/perimenopausal and 44.7% were postmenopausal; 80.9% of all patients had stage II disease, while 19.1% had stage III disease. In total, 42.1% and 3.7% of those with stage II and III disease had no nodal involvement, respectively. Overall, 51.2% of patients did not receive radiotherapy, and 59.5% of patients did not receive (neo)adjuvant chemotherapy. In the total sample, the 5- and 10-year risk of an iDFS event was 26.1% and 45.0%, respectively. In patients with stage II disease, the 5- and 10-year risks were 22.7% and 40.5%, respectively, and 40.4% and 62.9% among stage III. **Conclusions** These real-world data demonstrate that the risk of recurrence with adjuvant ET, particularly in those with stage II EBC, is higher than reported in many randomized controlled trials. Importantly, our data show that, in the real-world setting, the stage II population represents a significant proportion of patients (nearly 4 times more than stage III). These findings confirm and underscore the clear unmet need in this population and highlight the need for improved treatment options in this broader EBC population. The NATALEE study will investigate ribociclib + ET in a broad population of patients including stage II and stage III HR+/HER2- EBC with high-risk features, regardless of nodal status.

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5:00 PM - 6:15 PM

P3-03-13

Long-term heart failure risk of trastuzumab with or without anthracyclines in early stage breast cancer: A SEER-Medicare Database Analysis

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Background: Cardiotoxicity associated with use of trastuzumab (T) in breast cancer has been assessed in multiple studies with short-term follow up. However, long-term risk of clinical heart failure (CHF) with the use of T, either with or without anthracyclines (A), is poorly understood. Since the approval of T for use in early-stage breast cancer (ESBC) in 2006, long-term follow up data is now available in the SEER-Medicare database.

Methods: We performed a retrospective cohort study in patients (pts) with ESBC identified in the SEER-Medicare database, diagnosed between 2005-2016, excluding pts with in-situ or metastatic disease at time of diagnosis or a history of CHF prior to diagnosis. Primary exposure variables were identified using HCPCS codes and included receipt of T or A. The reference baseline population used for univariate logistic regression of the primary exposure variables was pts with ESBC who received neither T nor A. For multivariate analyses, to avoid collinearity in the final model, the exposure variables were categorized as either having or not having the exposure (i.e. with or without T, with or without A). The primary outcome variable was CHF, identified using codes 428.0-9, 402.11, 402.91 (ICD9) and I50.0-9, I110 (ICD10). Covariates used in multivariate logistic regression (MLR) included hypertension (HTN), valve disease, hyperthyroidism, diabetes (DM), emphysema, coronary artery disease (CAD), left sided radiation, age, and race. MLR models were constructed using a stepwise-up approach and confirmed using the stepwise-down method with a cutoff of $p < 0.05$ for inclusion in the final model.

Results: A total of 244,129 pts were identified with a median follow up of 6.7 years (7.7 years in the T cohort). Median age was 68. Other demographics are listed in Table 1. Of these, 10,603 were HER2-positive (HER2+) pts who all received T and all of whom also received some form of chemotherapy. Of the HER2+ pts, 19.1% (2,026) also received A in addition to T as part of

their treatment regimen. Pts who received T had significantly higher baseline rates of HTN, valve disease, hyperthyroidism, DM, emphysema, and CAD as compared to pts who did not receive T. Compared to pts who received T without A, pts who received T with A had significantly higher baseline rates of HTN, valve disease, hyperthyroidism, emphysema, and CAD with no difference in baseline rate of DM. Risk of CHF with exposure variables are summarized in Table 2. The overall rate of CHF for the entire 244,129 population was 21.3% with a rate of 20.8% in pts who did not receive any T or A (the baseline population). The rate of CHF in pts who received T without A was 19.1% (OR 0.90, 95% CI 0.85-0.95), and 29.0% for those who received T with A (OR 1.55, 95% CI 1.41-1.71). Associations of covariates of interest with risk of CHF as well as MLR models are summarized in Table 3. After adjusting for all baseline cardiac comorbidities as well as other covariates, receipt of T was associated with a reduced risk of CHF (OR 0.74, 95% CI 0.70-0.79, $p < 0.001$), and receipt of A remained associated with an increased risk of CHF (OR 1.19, 95% CI 1.15-1.24, $p < 0.001$).

Conclusions: With long-term follow up, the addition of A to T significantly increased the risk of CHF over T without A (from 19.1% to 29.0%) in pts with ESBC. Additionally, pts who received T without A had a similar risk of CHF compared to the baseline population who received neither T nor A. After adjusting for potential confounders in the MLR model, T was associated with a slightly decreased overall risk of CHF, while A remained associated with an increased risk of CHF. Possible explanations for these findings include potential increased cardiac monitoring in the T population which may have led to optimization of cardiac comorbidities, which were higher in the T population at baseline. Taken together, these data indicate concern with use of T plus A in ESBC regarding the long-term development of clinical CHF; especially when non-A regimens with similar efficacy are available.

Table 1: Demographics

Demographic	Yes Trastuzumab (N=10,605)	No Trastuzumab (N=227,319)	P Value
Age, median	67	68	<0.001
Race			
Black	1,198 (11.3%)	23,744 (10.2%)	
White	8,670 (81.8%)	194,994 (85.5%)	
Other	703 (6.6%)	13,727 (5.9%)	
Unknown	32 (0.3%)	1,061 (0.5%)	<0.001
T Stage			
T1	4,428 (43.0%)	140,959 (62.0%)	
T2	3,975 (38.6%)	63,638 (28.0%)	
T3	937 (9.1%)	13,787 (6.1%)	
T4	947 (9.2%)	8,535 (3.9%)	<0.001
Nodes			
N0	5,431 (51.6%)	166,575 (71.9%)	
N1	3,273 (31.1%)	46,004 (19.9%)	
N2	1,122 (10.7%)	12,575 (5.4%)	
N3	700 (6.7%)	6,427 (2.8%)	<0.001
Grade			
1	381 (3.8%)	53,530 (24.3%)	
2	3,381 (33.8%)	101,723 (46.3%)	
3	6,240 (62.4%)	64,636 (29.4%)	<0.001
Hormone Receptor Status			
ER+/PR+	4,468 (43.6%)	160,046 (71.8%)	
ER+/PR-	1,894 (18.5%)	28,132 (12.6%)	
ER-/PR+	152 (1.9%)	1,519 (0.9%)	
ER-/PR-	3,706 (36.1%)	32,770 (14.7%)	<0.001
Chemotherapy			
Yes, anthracycline	2,026 (19.1%)	14,397 (6.2%)	
Yes, non-anthracycline	8,577 (80.9%)	28,446 (12.2%)	
No	0 (0%)	190,683 (81.7%)	<0.001
Radiation (+ Laterality)			
None	5,024 (47.6%)	107,700 (46.4%)	
Left	2,536 (23.9%)	58,264 (25.0%)	
Right	2,398 (22.6%)	56,171 (24.1%)	0.011 (for overall radiation)
Hypertension	8,811 (83.1%)	179,770 (77.0%)	<0.001
Valve Disease	5,948 (56.1%)	70,512 (30.2%)	<0.001
Hyperthyroidism	907 (8.6%)	17,553 (7.5%)	<0.001
Diabetes	4,607 (43.5%)	96,496 (41.3%)	<0.001
Emphysema	2,881 (27.1%)	59,619 (25.5%)	<0.001
Coronary Artery Disease	3,732 (35.2%)	77,993 (33.4%)	<0.001

Table 2: Risk of Heart Failure with Primary Exposure Variables

Systemic Therapy	Rate of CHF	Odds Ratio	95% CI
No Trastuzumab or Anthracycline (baseline)	45,663/219,129 (20.8%)	-	-
Trastuzumab + Non-Anthracycline Chemo	1,638/8,577 (19.1%)	0.90	0.85-0.95
Trastuzumab + Anthracycline Chemo	587/2,026 (29.0%)	1.55	1.41-1.71

Table 3: Univariate and Multivariate Analyses

Comorbidity		Rate of CRF (%)	p value	Univariate Analysis		Multivariate Analysis	
				Odds Ratio	95% CI	Odds Ratio	95% CI
Trastuzumab	Without	49,807/233,526 (21.3%)	0.398	0.98	0.93-1.03	0.74	0.70-0.79
	With	2,225/10,603 (21.0%)					
Anthracycline Chemo	Without	47,301/227,706 (20.8%)	<0.001	1.54	1.49-1.60	1.19	1.15-1.24
	With	4,731/16,423 (28.8%)					
Hypertension	Without	1,551/55,548 (2.8%)	<0.001	12.73	12.09-13.40	3.30	3.12-3.49
	With	50,481/188,581 (26.8%)					
Valve Disease	Without	18,691/167,669 (11.2%)	<0.001	6.16	6.04-6.29	2.80	2.73-2.86
	With	33,341/76,460 (43.6%)					
Hyperthyroidism	Without	45,456/225,669 (20.1%)	<0.001	2.19	2.13-2.26	1.12	1.08-1.16
	With	6,576/18,460 (35.6%)					
Diabetes	Without	18,547/143,026 (13.0%)	<0.001	3.32	3.26-3.39	1.66	1.62-1.70
	With	33,485/101,103 (33.1%)					
Emphysema	Without	24,883/181,629 (13.7%)	<0.001	4.84	4.74-4.94	2.51	2.46-2.57
	With	27,149/62,500 (43.4%)					
CAD	Without	15,054/162,404 (9.3%)	<0.001	8.09	7.92-8.27	3.29	3.21-3.37
	With	36,978/81,725 (45.3%)					
Left Radiation	Without	41,176/183,329 (22.5%)	<0.001	0.75	0.73-0.77	0.83	0.81-0.86
	With	10,856/60,800 (17.9%)					
Race	White/Other	45,411/218,094 (20.8%)	<0.001	1.33	1.29-1.37	1.37	1.32-1.42
	Black	6,457/24,942 (25.9%)					
Median Age (68)	Below Median	14,541/113,115 (12.9%)	<0.001	2.72	2.66-2.78	1.61	1.57-1.65
	Median or above	37,491/131,014 (28.6%)					

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Comparing risk of breast cancer and cardiovascular disease and uptake of chemoprevention and statins among racially/ethnically diverse women with atypical hyperplasia or lobular carcinoma in situ

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Background: Chemoprevention with selective estrogen receptor modulators (SERMs) and aromatase inhibitors (AIs) has been shown in randomized controlled trials to decrease breast cancer incidence by 50-65% among women at high risk for breast cancer. However, chemoprevention uptake remains low among high-risk women. Women with atypical hyperplasia (AH) or lobular carcinoma in situ (LCIS) derive the greatest benefit from SERMs and AIs for breast cancer risk reduction. A potential barrier to chemoprevention uptake is competing comorbidities, including atherosclerotic cardiovascular disease (ASCVD). We calculated risk of breast cancer and ASCVD among women with AH or LCIS and assessed uptake of chemoprevention and statins among women who met high-risk criteria for both breast cancer and ASCVD. Methods: We conducted a retrospective cohort study among women, age 40-74 years, with AH or LCIS diagnosed in 2007-2015 at Columbia University Irving Medical Center (CUIMC) in New York City. Eligible women had sufficient data in the electronic health record (EHR) to calculate 5 and 10-year invasive breast cancer risk according to the Breast

Cancer Surveillance Consortium (BCSC) risk calculator, including age, race/ethnicity, first-degree family history of breast cancer, breast biopsy results, and mammographic density. We calculated 10-year ASCVD risk using the 2013 American College of Cardiology (ACC)/American Heart Association (AHA) ASCVD risk calculator using additional EHR data, including systolic blood pressure, total and HDL cholesterol, history of diabetes, treatment for hypertension, and current smoking status. High-risk criteria to determine eligibility for SERMs/AIs and statins was defined as a 5-year invasive breast cancer risk \geq 1.67% and 10-year ASCVD risk \geq 7.5%, respectively. We compared mean 10-year risk of breast cancer vs. ASCVD using a paired t-test and uptake of SERMs/AIs vs. statins among women at high risk for breast cancer and ASCVD, respectively, using McNemar's test. Results: Among 298 evaluable women, mean age was 58.2 years (standard deviation [SD], 8.34), with 33% non-Hispanic White, 41% Hispanic, 9% non-Hispanic Black, 6% Asian, and 11% other/unknown race/ethnicity. About 98% of women met high-risk criteria for breast cancer and 30% were high risk for ASCVD. Mean 10-year risk of breast cancer was higher than mean 10-year risk of ASCVD (9.14% vs. 6.69%, $p < 0.001$). Among women who met high-risk criteria for both breast cancer and ASCVD, uptake of statins was higher compared to SERMs/AIs (58% vs. 21%, $p < 0.001$). Comparing non-Hispanic Whites vs. racial/ethnic minorities, mean 10-year breast cancer risk was higher (12.12% vs. 7.71%, $p < 0.001$), but there were no statistically significant differences in ASCVD risk or uptake of chemoprevention or statins. Conclusions: Among women with AH or LCIS, mean absolute risk of breast cancer was higher compared to risk of ASCVD, however, uptake of statins was higher compared to chemoprevention with SERMs or AIs. To address under-utilization of chemoprevention among high-risk women, use of SERMs or AIs should be placed in the context of medications used for other chronic diseases, such as statins for ASCVD.

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5:00 PM - 6:15 PM

P3-03-15

Physical Activity and Risk of Death in Breast Cancer Survivors: A Prospective Study

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BACKGROUND. Strong evidence exists supporting the protective effect of physical activity on the risk of developing breast cancer; however, its impact on survival after breast cancer diagnosis remains controversial with limited research in long-term survivors. The aim of the current study was to evaluate the association of physical activity and risk of all-cause mortality in long-term breast cancer survivors.

METHODS. We conducted a prospective cohort of 315 post-menopausal breast cancer survivors who were at least 2 years post their initial diagnosis (median 6 years of survivorship). They initially were diagnosed with early stage (AJCC TNM Stages 0-II) breast cancer between January 1996-December 2012. Baseline interviews were conducted between August 2013 and March 2015, and participants were followed until date of death or study's end (April 2022). Subjects were queried on physical activity and fatigue using validated questionnaires, Godin Leisure Physical Activity Scale (GLPAS) and Fatigue Symptom Inventory (FSI). Physical activity was defined in 3 levels (active, moderately active, insufficiently active). Cox proportional hazards regression model was used to estimate the association of physical activity with risk of all-cause mortality, adjusted for age at baseline, breast cancer stage, Charlson comorbidity index (CCI), years since cancer diagnosis, fatigue, race/ethnicity, lifetime history of insomnia and depression, and adjuvant cancer treatments (endocrine, chemotherapy and radiation).

RESULTS. Of the 315 women, mean age at interview was 71 years (range: 57-86). The cohort included 30% women of color, mainly African American/Black and Asian/Pacific Islander women. Over a maximum follow-up of 8.7 years (median:7.8, IQR:7.3-8.3) after their baseline interview, 45 subjects (14.3%) died due to all causes. The mortality rates were: 12.9 per 1000 person years (PY) for active; 13.4 per 1000 PY for moderately active; and 32.9 per 1000 PY for insufficiently active. In multivariable analysis, compared to insufficiently active women, those who were active or moderately active had a markedly 60% decreased risk of death (active: HR=0.42, 95% CI: 0.21-0.85; moderately active: HR=0.40, 95% CI:0.17-0.95).

CONCLUSION: We found that even moderate physical activity was associated with a significantly decreased risk of all-cause death in long-term breast cancer survivors.

Survivorship care plans should consider incorporating physical activity because even moderate activity is vital for extending survival as well as health-related quality of life.

	N Deaths	Rates per 1000 PY (95% CI)	Adjusted HR (95% CI)
Total	45	18.9 (14.1-25.3)	
Godin Physical Activity			
Active (>24 units)	14	12.9 (7.6-21.8)	0.42 (0.21-0.85)
Moderately Active (14-23 units)	8	13.4 (6.7-26.8)	0.40 (0.17-0.95)
Insufficiently Active (< 14 units)	23	32.9 (21.9-49.5)	1.00 (ref)

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A methodology for using real-world data from electronic health records to assess chemotherapy administration in women with breast cancer

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Introduction Chemotherapy administration in real-world cancer care can differ extensively from clinical trials. It is important to understand real-world practice to identify dose reductions, delays, regimen changes and early discontinuations that impact cancer outcomes. Such variables require knowledge of intended regimens, which may not be well-documented in structured data in electronic health records (EHRs). We examined EHR data from the Kaiser Permanente Northern California (KPNC) site of the Optimal Breast Cancer Chemotherapy Dosing (OBCD) study to develop a process to identify each patient's intended regimen. Methods In this study of women diagnosed and treated with primary stage I-IIIa breast cancer at KPNC from 2006-2019, and ages 18+y at diagnosis, we analyzed treatment patterns using structured EHR data on the drugs, dosages, and dates at which they were administered (from which intervals and total length can be derived). Chemotherapy agents were identified using the NCI's CANMED database augmented with other sources. We used these data to categorize patients into the 22 drug combinations described in the National Cancer Care Network (NCCN) guidelines for breast cancer treatment. Within these 22 drug combinations, women were then subcategorized into 45 distinct chemotherapy administration schedules, defined as NCCN guideline regimens (NGRs). For this step, algorithms were developed that categorized patients into NGRs if they received the exact regimen described in the guidelines. For the second step, we conducted a manual review of the EHR data for patients who were unable to be categorized. This enabled us to gradually loosen the criteria (in terms of cycle intervals or number of cycles) so patients whose chemotherapy administration aligned closely with NGRs were categorized into each of the 45 NGRs. Clear patterns emerged of regimens that were administered to multiple patients, despite being outside of the NCCN guidelines, which we have defined as non-standard NGRs. For example, in the drug combination TC (cyclophosphamide and docetaxel) the NGR was TC every 21 days for 4 cycles. We found approximately 1 in 10

patients received 6 cycles , which we defined as a non-NGR. For the remaining uncategorized patients, medical chart abstraction was undertaken as a third step, at which point patients were categorized into either existing regimens or new non-NGRs if their intended regimen had not been previously described in the guidelines. Results Among 31,418 women with breast cancer, 12,427 (39.6%) received chemotherapy. We determined the intended chemotherapy regimens for 6,559 (52.8%) receiving the 45 NGRs using EHR data. We further expanded the algorithms through a manual review of the EHR data, which enabled us to categorize 2,977 (24.0%) additional women into their intended regimens. Abstracted medical notes were reviewed for the remaining patients for whom we had not been able to identify the intended regimen. Across both the manual review and abstraction processes, we were able to identify additional non-standard NGR regimens. In total, 9,536 (76.7%) of women were categorized into their intended regimen through the algorithm/manual review process, while 2891 (23.3%) of women underwent medical chart abstraction to identify the intended regimen. Conclusion Here, we describe the challenges and approaches to operationalize complex, real-world data to identify intended chemotherapy regimens at a granularity and scale not seen previously. We are adapting this method at a second OBCD study site, Kaiser Permanente Washington, where all women have undergone medical chart abstraction. We hope this methodology leads to increased feasibility and efficiency of use of large-scale clinical data, in turn improving cancer care delivery, patient outcome evaluation, and other real-world questions.

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The Impact of Cardiovascular Disease Risk on Cancer Progression among Female Breast Cancer Survivors: A Longitudinal Study within The Boss Cohort

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Background Among breast cancer (BC) survivors, cardiovascular disease (CVD) is one of the most common comorbidities contributing to mortality. Data on to what extent CVD risk impacts disease progression and second cancers in younger women is limited. We conducted a prospective cohort study to examine whether CVD risk is associated with disease recurrence or new primary cancer among female BC survivors enrolled in a cohort of women with a family history of BC. Methods The study included 301 females with a first primary diagnosis of BC in the Breast and Ovarian Surveillance Service (BOSS) Cohort, after excluding those who had a history of recurrence or second primary cancer prior to enrollment (N=125), a diagnosis of ductal carcinoma in situ (DCIS) (N=66), and with missing CVD risk factors (N=3). A risk score based on 7 CVD risk factors (age 65 or older, diabetes, hypertension, high cholesterol, body mass index (BMI), smoking status, and physical activity) was assessed at baseline and updated 4 and 8 years after enrollment. Each risk factor was given a score (0, 1, or 2) and was summed and categorized into low (score=0 or 1), intermediate (score=2 or 3), and high (score >3) risk. The primary outcome was either BC progression or all second primary cancers. Analyses limited to BC progression and second BC only were also conducted. Outcomes were ascertained through active follow-up and confirmed by pathology records. Kaplan-Meier graphs and two different Cox regression models were used to compare risk groups: model 1 adjusted

for participants' age, race, BMI, time from diagnosis, education, tumor stage, and estrogen receptor (ER) status; model 2 included further adjustment of cancer treatments (chemotherapy, hormone therapy, radiation), statin use, baby aspirin use, and specifically cardiotoxic treatments. For subgroup analyses, a more parsimonious model was used including age, race, BMI, education, cancer treatments, and cardiotoxic treatment. Results Participants' mean age of BC diagnosis was 47.4 years and the median follow-up time was 11.5 years. The incidence rate of recurrence or any second cancer was 21 cases per 1000 person-years. At baseline, there were 168, 130, and 84 survivors in the low, intermediate, and high CVD risk groups respectively, and their use of statins increased from 12.7%, 34.5% to 52.7%. In the multivariable model, BC survivors with an intermediate CVD risk score had a 2.23 times greater risk of recurrence or second primary cancer as compared to those with a low CVD risk score (95% CI=1.20- 4.17). After further adjusting for cancer and CVD treatment in model 2, the HR was attenuated but still significant to 2.01 (95% CI = 1.20- 4.17). Interestingly, the association was attenuated and non-significant in the high-risk group (model 2: HR=1.37, 95% CI = 0.54-3.45). The positive association between intermediate CVD risk score and recurrence or second cancer was also observed among subgroups of BC survivors including those who were postmenopausal (HR = 2.23, 95% CI = 1.01-4.93), with ER-positive BC (HR=2.07, 95% CI=1.08-3.99), regional disease (HR = 2.74, 95% CI = 1.06-7.04), diagnosed 5 years or greater (HR = 4.85, 95% CI = 1.14-20.66). There was a significant interaction between intermediated CVD risk and diagnosis time of 5 years (P interaction = 0.033). Restricting the outcome to disease progression and second BC alone led to similar results. The HR comparing the intermediate risk group and low risk group was 2.65 (95% CI = 1.27-5.55) in model 1 and decreased to 2.28 (95% CI = 1.06-4.89) in model 2. Conclusion There was a significant association between CVD risk and subsequent cancer progression in female breast cancer survivors, particularly among long-term BC survivors. The non-significant results among the women with high CVD risk scores may reflect the fact that a greater proportion of these women compared to women in the intermediate group reported taking cardiac treatments that can favorably impact cancer progression.

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P3-03-18

M1 registration: Signaling patients who develop metachronous metastases after primary breast cancer

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Background At the moment, over 180,000 breast cancer survivors are living in the Netherlands and survival after a breast cancer diagnosis and treatment is still increasing. Therefore, the number of survivors is rising, and these patients are at risk of metachronous metastases. Data at a national level on the development of metachronous metastases are limited, as this is not registered in the Netherlands Cancer Registry on a regular basis. Due to the vast amount of survivors, it is not feasible to actively monitor all patients to signal and register metachronous metastases. Applying machine learning may be an option to overcome this issue. The aim of our study is to develop a M1 detection algorithm based on hospital data to signal patients who developed metachronous metastases after their primary breast cancer treatment. **Methods** The Netherlands Cancer Registry (NCR) collects data on all individuals newly diagnosed with cancer in one of the 76 hospitals in the Netherlands since 1989. Dutch Hospital Data (DHD) collects and processes data from hospitals, including data on diagnosis and treatment. DHD data from 2019-2020 were linked to the NCR using a probabilistic matching method. We matched on date of birth, gender, diagnosis, postal code, hospital and patient ID. Column values that matched were weighted inversely proportional to the respective column's probability distribution, where a match on a rare column value (e.g. postal codes with a relatively small population) increased the probability that the match was correct. Scores for each column were combined and patients with high matching scores were included in the algorithm development, validation and deployment. Actively signaled and manually registered data on metastases were available for subgroups of breast cancer patients included in previous studies ('the golden standard'). First, 80% of these data was used to train the model, 20% was used to validate the model. Second, a pilot study was performed in which patients files were checked for 928 patients, sampled with variance in prediction probability, to evaluate a diverse range of cases. **Results** We included 4,395 patients. Variables that were included to predict metastases were

i.e. specific medication for metastatic disease (palbociclib), counselling for metastatic breast cancer, Carcinoembryonic Antigen test, a confirmed diagnosis of metastases, and number of patient visits. The first validation step (including 20% of known data) showed that the model had a precision of 0.91 to predict metachronous metastases, 0.93 to predict free of metastases. The pilot study confirmed that a higher prediction probability of >0.8 correlated with a higher chance that a patient has metachronous metastases. However, false positive predictions did occur. Conclusion We developed a M1 detection algorithm to signal patients with metachronous metastases after breast cancer treatment on a national level. With this algorithm we are one step closer to identify all patients with metachronous metastases and to reach a complete registration of all breast cancer metastases reusing existing data sources. After review of patients with a high prediction probability, the model will be re-trained using these data and updated data from DHD.

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P3-03-19

Real-world data of clinical characteristics, risk factors and outcomes of Chilean triple-negative breast cancer patients

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Background: triple-negative breast cancer (TNBC) is associated with hereditary and environmental risk factors plus an overall worse prognosis compared to other Breast Cancer (BC) subtypes. While TNBC risk factors, prevalence, clinical characteristics and prognosis may vary throughout different populations, limited data on Latin American patients forces clinical decisions to be based predominantly on data coming from non-Hispanic women. To obtain local epidemiological information, regarding risk factors and clinical outcomes, we analysed the largest Chilean BC registry.

Methods: we conducted a retrospective population-cohort study involving females with any stage TNBC, treated at a community hospital (mid-low income) and at an academic private hospital (high income), between the years 2010 and 2021. Risk factors, reason for consultation, clinical and pathological characteristics and prognosis were separately analysed for both TNBC

and non-TNBC subgroups. Univariate and multivariate analyses were performed to identify prognostic factors for survival on TNBC patients.

Results: From 5,806 patients, 647 (11.2%) were identified as TNBC. Compared to non-TNBC patients, women were younger (median age 55.2 vs. 57.2, $p=0.0001$), with 15.8% of TNBC patients having been diagnosed before the age of 40 compared to 9.6% in non-TNBC ($p=0.0001$). TNBC had a significantly lower screen-detected cancer rate (14.5% vs. 31.6% $p=0.0001$) and worse stage at diagnosis. No differences were seen between patients seen at a community hospital and private centre, for both TNBC rate and stage. Other risk factors such as parity, age at first gestation, menarche, hormone therapy replacement and obesity showed no significant differences between TNBC and no-TNBC patients (table 1).

With a median follow up of 57 months, 5-year overall survival (OS) and BC specific death were significantly shorter for TNBC compared to non-TNBC (76.4% vs 88.1% and 78.9% vs 91.2%, respectively; $p=0.0001$) (table 2). In the multivariate analysis, TN subtype (HR=2.3, $p=0.0001$), stage (HR=2.05 for stage II vs stage I, HR=7.04 for stage III vs. stage I, $p=0.0001$), lower income (HR= 1.64, $p=0.0001$), and non-screened detected BC (HR=1.32, $p=0.03$) were all associated with worse overall survival (table 3).

Conclusion: This is the first study focusing on TNBC characteristics in Chilean BC patients and to our knowledge, the largest performed in a Latin American population. We identified a lower proportion of TNBC patients when compared with data reported from other LA groups and worldwide, a very low screen detected cancer rate and as expected significantly lower TNBC survival rate compared to non-TNBC women. While TNBC patients were younger compared to the non-TNBC group, this age difference was marginal compared to other reported studies. Community hospital patients (with mid-low income) were associated with lower survival rates for both all-cause mortality and BC specific survival, regardless of a similar stage distribution at diagnosis. Reflecting an underlying interaction between social and biological factors that needs to be addressed.

Table 1. Patient characteristics: Triple-negative versus non-triple negative breast cancer

Variables	TNBC: 647 (11.2%)	Non-TNBC: 5,159 (88.8%)	p valu
Age at diagnosis in years Median (range)	55.2 (20 - 98)	57.2 (18 - 101)	0.0001
Cancer Institution			0.20
- Public	10.7%	89.3%	
- Private	11.8%	88.2%	
Reason for consultation			0.0001
- Mammography	14.8%	31.6%	
- Symptoms/signs	85.2%	68.4%	
BMI, median (range)	27,6 (16,8 - 44,4)	27,8 (18,0 - 54,4)	0.52
Obese	32.0%	33.1%	0.68
Hormonal BC risk factors			
Nulliparity	13.3%	13.2%	0.93
Nulliparity in postmenopausal patients	9.2%	10.1%	0.62
Age first birth ≥35	6.8%	6.9%	0.99
Number of Children, median (range)	2 (1-8)	2 (1-12)	0.90
Breast-feeding in months (range)	16 (0-180)	12 (0-244)	0.23
Menarche < 12	2.5%	7.2%	0.12
Menopause Status			0.0001
- Premenopausal	33.5%	26.6%	
- Postmenopausal	66.5%	73.4%	
Menopause ≥ 55	7.2%	8.2%	0.58
Hormone replacement therapy	26.2%	25.7%	0.87
HRT duration in years (median)	3.5	5	0.77
Cancer family history	61.5%	58.5%	0.13
- First grade	36.7%	37.9%	0.66
Breast or ovarian cancer FH	31.7%	31.0%	0.71
First grade	14.4%	15.0%	0.72
Comorbidities at diagnosis			
Hypertension	21.6%	21.7%	0.94
Diabetes	12.4%	13.1%	0.66
Hypothyroidism	11.6%	13.3%	0.49
Other cancer (not breast cancer)	4.2%	4.9%	0.49
Medication at diagnosis			
Metformin	10.9%	13.4%	0.16
Statins	9.2%	9.9%	0.66
Aspirin	7.8%	6.2%	0.27
Stage at diagnosis			0.0001
I	16.0%	33.0%	
II	42.0%	38.2%	
III	31.9%	21.4%	
IV	10.1%	7.4%	

BMI: Body mass index; FH: Family history * Difference is statistically significant.

Table 2. Survival comparison in triple-negative versus non-triple negative breast cancer

Variables	TNBC	Non-TNBC	p value
Median follow-up (months)	57	57	
Any invasive recurrence	26.1%	16.2%	0.0001*
Distant recurrence	21.4%	12.2%	0.0001*
Brain Metastasis	5.8%	2.9%	0.003
5-y IDFS (CI 95%)	68.5% (64.3-72.4)	84.8% (83.7-85.9)	0.0001*
5-y DDFS (CI 95%)	72.5% (68.3-76.2)	87.9% (86.8-88.8)	0.0001*
5-y BCSS (CI 95%)	78.9% (75.3-82.0)	91.2% (90.3-92.0)	0.0001*
5-y OS (CI 95%)			
Non-metastatic	76.4% (72.7-79.7)	88.1% (87.1-89.0)	0.0001*
Stage IV	4.6% (3.3-0.9)	30.5% (25.1-36.0)	0.0001*
Stage IV median time	18 months	33 months	0.0001*
Median time from diagnosis to distant recurrence	22 months	46 months	0.0001*
Median time from metastasis to death	8 months	16 months	0.0001*
Median time from brain metastasis to death	4 months	6 months	0.03*

* Difference is statistically significant.

Table 3. Cox Regression Multivariate analysis

VARIABLES	IDFS		DDFS		BCSS		OS	
	HR	p	HR	p	HR	p	HR	p
Age	0.99	0.10	0.99	0.10	1.005	0.11	1.02	0.0001*
Reason for consultation		0.001*		0.001*		0.02*		0.03*
Screening	1		1		1		1	
Symptoms	1.58		1.79		1.46		1.32	
Type of Hospital		-		-		0.0001*		0.0001*
Private	-		-		1		1	
Public	-		-		1.53		1.64	
Stage								
I	1		1		1		1	-
II	1.78	0.001*	3.72	0.0001*	3.13	0.0001*	2.05	0.0001*
III	5.98	0.0001*	15.2	0.0001*	14.54	0.0001*	7.04	0.0001*
IV			-		80.80	0.0001*	31.1	0.0001*
Subtype		0.0001*				0.0001*		0.0001*
Non-TN	1		1		1		1	
Triple Negative	2.06		2.17	0.0001*	2.97		2.30	

* Difference is statistically significant.

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Breast cancer stage, molecular subtype and survival in patients with obesity: a Brazilian cohort study.

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Background Breast cancer (BC) continues to be highly prevalent and lethal among women worldwide. Obesity is an established risk factor for several types of cancer, including BC, particularly in postmenopausal women. Obesity may also be a prognostic factor for BC in all ages, as it increases the risk of surgery complication, decreases the response to chemotherapy, and increases mortality. This study aimed to evaluate if obesity was related to poor prognosis of patients with BC in Brazil. Methods In this retrospective, single center, cohort study, an electronic database from Pérola Byington Hospital (in São Paulo, SP, Brazil) was used to select patients with BC followed between January 2011 and June 2021. All included women had a confirmed diagnosis of BC and were divided in four groups according to BMI categories, defined by weight (kg)/height² (m): < 18.5 kg/m²: underweight; 18.5 to < 25 kg/m²: healthy weight; 25 to < 30 kg/m²: overweight; ≥30 kg/m²: obese. This study was approved by the local Institutional Review Board. Outcomes The overall survival (OS) was the primary outcome, evaluated by the comparison of the incidence of death from BC among groups. Progression-free disease survival (PFS) was also measured. Statistic methods The descriptive analysis was expressed as continuous variables in summary measures (mean, median, standard deviation, and quartiles), while categorical variables were expressed in frequencies and percentages. The Kaplan-Meier method was used for survival graphs, the Log-rank method to evaluate the difference between the survival curves, and Cox regression to calculate the hazard ratio (HR) and OR for death. The significance level adopted in the tests was 0.05, two-tailed hypotheses considered, and the confidence intervals (CI) constructed are 95%. R version 4.1.1 software was used to carry out all analyses. Results A total of 10,117 patients were screened, 7,424 were included, and 6,992 were considered for the survival analysis. The mean age was 55.12 ±12.47 years at diagnosis and the mean BMI was 27.97 ±5.55 kg/m². Patients with obesity corresponded to 30.81% of the study population, and 64.82% of them were ≥ 50 years old (postmenopausal), p < 0.001. For each BMI group, most patients were postmenopausal, p < 0.001; without significant difference among groups, p=0.2133. Considering staging by breast (n=6,872), 42.97% of the underweight group were stage III; 41.90% of the healthy weight, 42.79% of overweight, and 39.38% of obese groups were stage II, p < 0.001 (within-group), and p=0.0944 among groups. Molecular subtype did not differ neither within the

group ($p=0.068$) nor among groups, $p=0.1155$. A total of 6,992 patients were included in the survival analyses, corresponding to 7,090 breasts. During the 10 years-follow up, 265 patients (3.79 %) died from BC. Figure 2 shows the Kaplan–Meier estimates of OS according to BMI, $p=0.12$. There was no difference in OS according to menopausal status. According to the multivariate Cox-regression analysis results, none of the variables evaluated significantly impacted the OS of patients with BC. BMI did not significantly impact the results. The variables that significantly impacted the chances of pCR were HER2+ and triple-negative compared with luminal A, staging zero compared with I, recurrence, adjuvant therapy, age, and time between diagnosis and surgery. Conclusion In conclusion, obesity did not impact the survival or progression of BC in this retrospective analyses. This study, despite not demonstrating significance in its primary objective, brings important epidemiological data from the Brazilian population with BC not previously published, with high prevalence of overweight and obesity among Brazilian women with BC and highlights the importance of further studies, especially prospective, addressing obesity and BC.

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P3-03-21

Biological and Cultural Drivers of Early-Onset Breast Cancer: a mixed-method study

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Background: The incidence of early-onset breast cancer (BC) in adults < 40 years old has increased dramatically in the US over recent decades. The increase in incidence means that identifying higher risk individuals through family-history based guidelines will miss many young adults. As no population-based screening is recommended for adults under 40, so how they detect their BC remains unclear. Using data from a nested case-control study in the Breast Cancer Family Registry, we found that the steroid metabolome may improve risk assessment. If replicated in larger studies, it will be important to know more about the clinical contexts in which this biomarker screening could be implemented from both the provider and patient perspectives. One way to fill these gaps is to identify biocultural drivers of risk that deepen our etiologic understanding and inform risk assessment. We use quantitative and qualitative (mixed) methods to integrate “emics”—the on the ground perspective—from young adults with BC into metabolomic studies. Methods: For the provider perspective, we administered a survey to Obstetricians/gynecologists (OBGYNs) about their knowledge of American College of Obstetrics and Gynecology (ACOG) breast cancer screening guidelines for women under 40 and determined the proportion of correct responses. For the patient perspective, we examined qualitative data from the Young Survival Coalition (YSC). The YSC hosts an online forum where young adults with breast cancer “tell their story” in posts. We reviewed text from posts published between March 2009 and December 2019 and coded text (n=750 posts) according to themes: “first signs and symptoms,” “steps to diagnosis,” “staging type,” and “patient-provider feelings.” Then, we used natural language processing and machine learning with the support vector machine algorithm to build classification models and detect the themes in all posts (n=571,602). We repeated this process for sub-themes. Results: ACOG guidelines recommend that women at “average risk” of breast cancer are counseled about breast self-awareness, and 75% of OBGYN respondents answered this survey question correctly. Our qualitative, “emic” data suggest that the vast majority of young adults find their BC through self-awareness and

first seek care from OBGYNs. They first noticed signs (n=3,266) of breast changes through self-detection of lumps (56.5%), self-detected breast and health changes (25.0%), and through a provider (17.2%). The first steps to diagnosis (n=31,640) mainly started with clinic visits (66.5%), others with surgery (23.3%). Stage at diagnoses (n=71,879) were Stage 4 (7.3%), followed by Stage 0 (7.2%), Stage 2-3 (5.5%), and Stage 1 (4.8%), while others mentioned being diagnosed with any invasive cancer (7.3%). Out of 24,648 posts, 70.3% were not satisfied with their providers and felt ignored, their treatment delayed, lacked trust, and felt their providers were not informed. One person said, "My doctor has not had a patient as young as me get diagnosed with cancer and has not suggested ANYONE." Conclusions: In addition to counseling about breast self-awareness as a means of detection, the OBGYN setting may be a place to implement biomarker-based screening for early-onset BC. These results are derived from our mixed-methods approach, designed to identify biocultural drivers of cancer prevention by incorporating "omics" and "emics". In the era of "omics," when molecular markers are incorporated into cancer risk reduction and early detection, "emics" are equally important to identify what is feasible in "real-world" settings.

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P3-03-22

Overweight and obesity trends over 5 years in early stage and metastatic breast cancer patients

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Background: Obesity is associated with 25-33% of all breast cancer (BC) cases, and BC survivors with obesity have a 35% higher risk of BC-related death and 41% higher risk of all-cause mortality. We hypothesized that the prevalence of overweight (body mass index [BMI] 25-29.9 kg/m²) and obesity (BMI \geq 30) after a diagnosis of early stage or metastatic BC increases, and baseline characteristics may increase risk of weight gain.

Methods: We conducted a retrospective chart review of 222 patients with Stage 0-IV BC who newly presented to Johns Hopkins from 2015-2018. Patients were part of the BC Program Quality Improvement Project Database, had 1 chest CT scan within 6 months of initial visit, and at least 1 subsequent CT. Data extracted from the medical record included: demographics, menopausal status, diagnosis date, cancer characteristics/treatment, recurrence/vital status, family history of BC, and tobacco/alcohol use. All BMI measured on patients were collected. Baseline BMI was defined as the closest measurement to BC diagnosis between 1 year prior and 1 month after diagnosis. We estimated time to overweight/obesity from diagnosis using the Kaplan Meier method and compared between subgroups with the log rank test. Patients who were overweight/obese at diagnosis were included in the analysis with an event time of zero.

Results: Among 222 patients, 110 patients (50%) had newly diagnosed early-stage BC, 98 (44%) had de-novo or recurrent metastatic BC, and 14 (6.3%) had locally recurrent BC. Most patients were women (98%) and non-Hispanic (93%). Patients identified as White (62%), Black (23%), and Asian (8%). Among 34% with alcohol use, 5% reported \geq 8 drinks/week. There were current (6%) and former smokers (34%). Family history of BC was present in 10%. Among those with early-stage primary BC, most were postmenopausal (61%) and received chemotherapy (61%). Hormone receptor (HR)-positive, HER2-positive and triple negative subtypes were 70%, 24% and 19%, respectively. For those with metastatic BC, most were postmenopausal (62%). Hormone receptor (HR)-positive, HER2-positive and triple negative subtypes were 71%, 12% and 24%. At diagnosis, 73% of the whole cohort had BMI \geq 25 kg/m², with the whole cohort and subgroups having mean BMI \geq 25 kg/m². The incidence of elevated BMI increased in all groups and overall, over 5 years (Table 1). Weight gain was significantly associated with premenopausal status ($p=0.04$). Stage at diagnosis, smoking/alcohol use,

receipt of chemotherapy/radiation/endocrine therapy, and subtype were not associated with weight gain.

Conclusion: Patients with early stage and metastatic BC have elevated BMI at diagnosis, and this risk increases over 5 years, especially for those who are premenopausal. Further investigation of the implications of these changes is needed. Additionally, while BMI is accessible, it may underestimate body fat in older people and others who have lost muscle, does not identify fat distribution (a major factor in metabolic health risk), and may not be equally valid across gender, race and ethnicities and age groups. We will assess body composition by CT scan and report correlations with BMI and cancer-related outcomes.

Prevalence of BMI \geq 25 kg/m² in patients with breast cancer at diagnosis and by 1-, 2-, and 5-years after

	N	At Diagnosis [95% CI]	2y [95% CI]	5y [95% CI]	P
Entire Cohort	222	71 [65, 77]	82 [75, 86]	85 [77, 90]	N/A
Stage					
Early stage primary	110	75 [66, 82]	85 [76, 90]	85 [76, 90]	0.34
Metastatic	98	79 [42, 92]	79 [42, 92]	100 [NA,NA]	
Locally recurrent	14	65 [54, 74]	79 [67, 86]	86 [67, 94]	
Menopausal status					
Pre	43	60 [43, 73]	76 [58, 86]	79 [61, 89]	0.04
Post	76	83 [72, 90]	88 [78, 94]	88 [78, 94]	

Prevalence of BMI \geq 25 kg/m² increased over 5 years post-diagnosis. Premenopausal status was more associated with BMI \geq 25 kg/m² versus postmenopausal status.

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P3-03-23

Breast Cancer and Subsequent Risk of Type 2 Diabetes Mellitus: A systematic review and Meta-Analysis

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Introduction Due to improvements in breast cancer (BC) diagnostics and treatment, the population of BC survivors is growing. BC treatments may have adverse effects that lead to an increased risk of developing type 2 diabetes mellitus (T2D). It is therefore important to investigate the risk of T2D in patients with BC in general and according to type of adjuvant BC treatment. **Objectives** To conduct a systematic review and meta-analysis investigating the association between early BC and the risk of subsequent T2D diagnosis. A secondary aim was to examine this association according to type of adjuvant BC treatment—chemotherapy and endocrine therapy (ET). **Methods** We searched PubMed and Embase using variations of the search terms breast cancer (population), ET, tamoxifen, aromatase inhibitors (AIs) and chemotherapy (exposures), and diabetes mellitus (outcome). Two authors screened papers for eligibility by title and abstract using Covidence and reviewed full texts of eligible papers. Guided by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) checklist, study data were extracted. Using random-effects models, we calculated relative risks (RRs) and associated 95% confidence intervals (CIs) for the association between BC, adjuvant BC treatment (ET overall, tamoxifen, and AIs), and subsequent T2D. We used funnel plots to assess publication bias in the analyses. **Results** Among 16 eligible studies, 11 reported on T2D risk after BC, chemotherapy, or ET; five studies investigated more than one association. Compared with patients without BC, those with BC had elevated risk of T2D overall (RR=1.27, 95%CI=1.15-1.41), particularly those who received any ET (RR=1.23, 95% CI=1.16-1.32). Among BC patients only, risk of T2D was higher for those who received tamoxifen compared with those who did not receive tamoxifen (RR=1.19, 95% CI=1.13-1.25). Due to few studies, analyses investigating T2D risk after treatment with AIs and chemotherapy were inconclusive. **Conclusion** Our findings support an association between BC and subsequently elevated risk of T2D, particularly after tamoxifen use. Further research is needed to determine the impact of ET overall, AIs and chemotherapy on the incidence of T2D in patients with early BC. **Funding** This

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The WISDOM Study: Early Ascertainment of Breast Cancer Diagnoses by Utilizing Self-Reported Questionnaires and Data Warehouse Electronic Health Records

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BACKGROUND WISDOM (Women Informed to Screen Depending on Measures of risk) is a pragmatic trial comparing the safety, efficacy, cost, and patient acceptability of personalized versus annual breast cancer screening in women ages 40-74 years with no personal history of breast cancer. Cancer registry reporting is considered the gold standard for ascertaining cancer diagnosis data; however, the time lag between diagnosis and reporting (1-2 years or more) by the California Cancer Registry (CCR) presents challenges. The WISDOM study must quickly ascertain and report accurate cancer diagnoses to the Data Safety Monitoring Board; delays could lead to preventable harm, unnecessary costs, and unwarranted early trial termination. To ascertain cancer diagnoses in a timely manner, we used multiple data collection methods and compared self-reported with Electronic Health Records (EHR) information, and in some cases verified with chart review. Specifically, we conducted a procedural study with WISDOM participants who sought care at a University of California (UC) health system by extracting their data from the University of California Data Warehouse (UCDW) to 1) verify self-reported breast cancer diagnoses in WISDOM; 2) ensure that all on-study breast cancer diagnoses have been captured within the WISDOM study cohort; and 3) assess the accuracy and reliability of self-reported data. The UCDW provides harmonized EHR data from the six University of California (UC) health systems and constitutes ~120 billion data points from 7.8 million patient records.

METHODS We provided the UCDW with a list of WISDOM participants who indicated they had sought care from a UC health system. Participants with recorded breast cancer diagnostic code (ICD-10CM C50.) were matched with the WISDOM self-reported cancer dataset to uncover participants who had no recorded breast cancer diagnosis in the study system. For those individuals with no recorded self-report diagnosis, coordinators conducted manual chart review to determine whether the participants had been diagnosed with breast cancer.

RESULTS This cohort included 11,314 enrolled WISDOM participants who self-reported care at a UC and had at least one diagnostic or procedural breast care code. Among these participants, 160 had a ICD-10-CM C50 breast cancer diagnostic code of which 132 breast cancer cases were confirmed: 111 were already self-reported through WISDOM and 21 additional confirmed breast cancer cases were identified through the UCDW. As a standard process, only WISDOM self-reported cancer cases that were confirmed by chart review are entered into the study database. The percentage of confirmed UCDW-identified cases that were not also self-reported was greater for recent diagnoses (16% overall and 6% for period prior to June 2020). Among the 11,314 participants in our cohort, the CCR identified 61 pre-June 2020 cancer diagnoses. Of these 61 diagnoses, 92% (56) were identified by the UCDW procedural process. If the UCDW had been used as the single source for cancer diagnosis, 21 participants without cancer and 7 participants with unclear status (unlocated or inaccessible records) would have been classified as cancer cases.

DISCUSSION/CONCLUSION Self-reported data provides quick ascertainment with relative accuracy compared to cancer registry. Cancer ascertainment can be further improved by combining self-reported data with EHR data from a health system data warehouse registry, particularly for self-reported questionnaire issues such as timing and lack of response. Accuracy of self-reported cancer diagnosis from annually distributed questionnaires improves over time. Identifying cancer diagnosis discordance between data sources can inform processes to improve self-reported study accuracy.

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P3-03-25

An Automated Risk Stratification System for Breast Cancer Screening using Thermalytix

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Background: As opposed to conventional age-based population-level breast screening strategies, risk-stratified breast screening programs are emerging as a new approach to balanced population screening methodology where the screening frequency and choice of modality (mammography/tomosynthesis or magnetic resonance imaging) is determined based on accurate personalized estimation of an individual's risk score. A woman identified with low risk can now be screened less frequently, avoiding repeated mammography screening where radiation risk outweighs the benefits in that particular individual. The standard questionnaire based risk stratification is found to be less reliable and imaging based risk stratification mechanisms are being explored in recent years. In this study, we evaluate the performance of a new computer-aided image analysis technique called Thermalytix that automatically generates a personalized risk score using a combination of imaging and questionnaire information for risk stratification of women.

Methodology: Thermalytix is an artificial intelligence system that uses thermal imaging and questionnaire data for predicting the risk of breast cancer. Thermalytix analyzes spatio-thermal signatures and vascular patterns in the breast region along with patients' complaints and age to generate a score called B-Score (or BHARATI Score) which ranges from 1 to 5. B-Score of 1 indicates low risk of malignancy and a B-Score of 5 indicates the highest risk of malignancy. To evaluate the effectiveness of risk stratification using B-Scores, we performed retrospective analysis of thermal and participants' data acquired from two registered clinical studies. One study (CTRI/2017/10/0 10 115) is a multi-site study conducted in Bangalore, India, and the other study (NCT04688086) is a single site study conducted in Delhi, India. Both these study sites are geographically distant with 2000 KM apart from each other and comprise a diversified population from India.

Results: In total, 717 eligible women were considered in this study with age varying from 18 years to 80 years. Reports from standard of care procedures involving mammography,

ultrasound and biopsy (as needed), were collectively considered by a radiologist to determine the ground truth for malignancy. Out of 717 women, 85 women were thus concluded as malignant. When used in a blinded fashion, Thermalytix graded 275 women as B-Score 1 (lowest risk), 225 women as B-Score 2, 44 women as B-Score 3, 137 women as B-Score 4 and 36 women as B-Score 5 (highest risk). The fraction of malignancies in the cohorts corresponding to B-Score categories from 1 to 5 were found to be progressively higher (0.36%, 1.33%, 29.55%, 33.58% and 61.11%, respectively) - showing the correctness of the proposed personalized risk scoring methodology.

Conclusion: Thermalytix test, a low-cost, radiation-free, contactless and privacy aware test was used as a technique to determine the breast cancer risk of a woman.. The results obtained in the study show that a high B-score of 5 indicates a high risk for malignancy with 61.11% chance of breast cancer. Likewise the lowest B-Score of 1 indicates low risk for malignancy with just 0.36% percentage of women in the cohort found with malignancy. These results combined with other experiential benefits of Thermalytix test makes it a promising risk stratification mechanism enabling differential frequency of screening while balancing the cost and risk versus benefit. Large scale studies, however, need to be conducted to see the ground benefits of the proposed approach in a screening program implementation.

Distribution of study population in different risk cohorts

Risk Stratification	No. of Women in the Cohort (n=717)	No. of malignant cases (n=85)	Malignancy Rate
B-Score 1 (Lowest Risk)	275	1	0.36%
B-Score 2	225	3	1.33%
B-Score 3	44	13	29.55%
B-Score 4	137	46	33.58%
B-Score 5 (Highest Risk)	36	22	61.11%

Higher risk correlates with higher malignancy rate

Disclosure(s):

Siva Teja Kakileti, n/a: Niramai Health Analytix Pvt Ltd: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Salary (Ongoing)

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12/7/2022

5:00 PM - 6:15 PM

P3-03-26

Osteopenia and osteoporosis in women with breast cancer in Taiwan: single center retrospective data

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Purpose:

Osteopenia and osteoporosis are commonly encountered in elder women. One third of women older than fifty years suffer a fracture second to osteoporosis around the world. Standard treatments for breast cancer such as chemotherapy or hormonal therapy may increase the risk of both osteopenia and osteoporosis. Premenopausal women treated with standard adjuvant chemotherapy frequently develop ovarian failure, or early menopause, which is associated with accelerated bone loss.

Trabecular bone score (TBS), an index extracted by DXA that provides an indirect measurement of bone axial microarchitecture. In addition to the BMD, TBS are warranted to improve the prediction of fracture risk at the individual level.

However, due to regulations of National Health Insurance in Taiwan, data are limited on the incidence of osteopenia and osteoporosis in women with breast cancer in Taiwan. In this study, we investigated the proportion of osteopenia and osteoporosis in women with breast cancer in Taiwan.

Materials and Methods:

There were enrolled 201 female who diagnosed with breast cancer between May 2019 and December 2020 in this retrospective study. Patients with bone metastasis (n=11) and double cancer (n=3) were excluded. All patients received dual energy X-ray absorptiometry (DXA) at least once, including bone mineral density (BMD), T-score (spine and total hip) and trabecular bone score (TBS) data.

The data were retrospectively analyzed baseline age, BMD, breast cancer type, aromatase inhibitors (AIs) usage status by Kruskal-Wallis test.

Results:

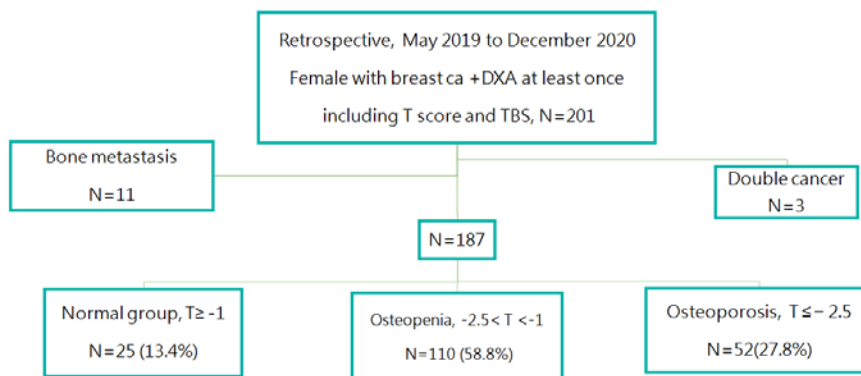
Based on the lowest T-score from measurements at the spine or total hip, 58.8% (n=110) of osteopenia ($-2.5 \leq T < -1$) and 27.8% (n=52) of osteoporosis ($T < -2.5$) were identified in women with breast cancer (figure 1). Statistics significance was noted in patients' age and BMI between three groups. There was no difference in bone mineral density according to breast cancer subtype. (table 1)

Patients who ever use aromatase inhibitors (n=90) had lower BMD ($T = -2.14$) and trabecular bone score (TBS=1.3) than non-AI group (n=97, $T = -1.84$, TBS=1.34). (figure 2) (table 2)

Conclusions:

According to Taiwan's NHI sampling data from 1999 to 2001, the averaged prevalence of osteoporosis in those aged ≥ 50 years was 11.35% for women. Breast cancer survivors are at higher risk for osteopenia and osteoporosis compared to cancer-free women in Taiwan. Aromatase inhibitors (AIs) group had lower BMD and TBS ($p < 0.05$). In our study, forty percent of TNBC patients diagnosed osteoporosis, which is compatible with increased bone loss due to chemotherapy-induced ovarian failure. Therefore, clinicians should be aware not only of AI-associated bone loss but also of patients who ever accepted long-term chemotherapy. A normal range for TBS values in postmenopausal women has been proposed: a TBS of ≥ 1.350 is considered normal; a TBS between 1.20 and 1.35 is considered consistent with partially degraded microarchitecture, and a TBS of ≤ 1.200 defines degraded microarchitecture. In our study, mean TBS in women with breast cancer ($n=187$) is 1.32. Further research is needed to determine the validity of cut-points for guiding treatment decisions.

figure 1

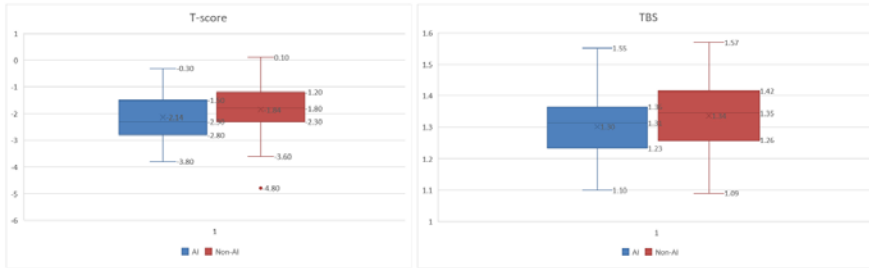


Inclusion/exclusion criteria and flow chart

table 1

	Normal group (n=25)	Osteopenia group (-2.5 ≤ T < -1), n= 110	Osteoporosis group (T ≤ -2.5), n=52	p value
Age	52 (46.5-53.5)	55 (46.75-61)	60 (54.25-66.75)	0.002**
BMI (n=172)	24.30 (21.76-26.77)	24.52 (21.91-26.9)	22.37 (21.03-25.99)	0.046*
Luminal type	22 (13.01%)	100 (59.17%)	47 (27.81%)	0.451
Her2-enriched type	1 (12.50%)	6 (75.00%)	1 (12.50%)	0.935
TNBC	2 (20.00%)	4 (40.00%)	4 (40.00%)	0.479

figure 2



	AI, N=90	Non- AI, N=97	p-value
Mean T-score	-2.14	-1.84	0.016*
Mean TBS	1.3	1.34	0.019*

Aromatase inhibitors group had lower BMD and Trabecular bone score

Disclosure(s):

Chia-Hua Liu, n/a: No financial relationships to disclose

Chih-Chiang Hung, n/a: No financial relationships to disclose

I-Chen Tsai, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

P3-03-27

Assessment of the proliferative activity of breast tissue after the administration of combined oral hormonal contraceptive, associated or not with estriol

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The molecular mechanisms related to the breast cancer development are poorly understood, particularly those associated with estrogen. Evidence is mounting that developmental differences may influence the risk of cancer. However, understanding breast development, morphology and the biochemical factors that influence them is pertinent to study pre-malignant and malignant conditions that affect the breasts.

Objective: To evaluate the proliferative activity of normal breast epithelium, through the c-myc expression, after the administration of combined oral hormonal contraceptive, associated or not with estriol.

Retrospective double-blind study, in which the effect of combined oral contraceptives on the normal breast epithelium in women with fibroadenoma was evaluated. We analyzed 33 women in a cohort of 70 selected (37 excluded). The control group (1) received a compound containing levonorgestrel 0.15mg (LNG) and ethinylestradiol 0.03mg (EE), associated with 2mg of placebo (PLC) manufactured in the same capsule ingested daily for 21 days with an interval of 7 days, during four cycles. The study group (2) received a compound containing levonorgestrel 0.15 mg (LNG) and ethinylestradiol 0.03 mg (EE), associated with estriol 2 mg (E3) manufactured in the same capsule ingested daily for 21 days with an interval of 7 days, up to four cycles, when was proceeded the lumpectomy plus normal breast tissue sample. The UNIFESP-EPM Department of Pathology received the samples collected and fixed in 10% buffered formalin. We used an automation device to perform the Immunohistochemistry reactions, using c-myc antibodies, added DAB developer (diaminobenzidine) that provides a bright brown color that provides good contrast. We used conventional optical microscopy to read TMA slides. We considered positive the nuclei stained with dark brown in contrast to the blue negative to the c-myc reactions. We evaluated the epithelial areas at least five acinar units were present in the sample at 40X magnification. In the statistical analysis, the initial stages of consolidation as well as the analysis were performed in Software R (2020) and Rstudio (version 4.1), using the packages Tidyverse (2016), Psycho, SummaryTools, Janitor and DataExplorer. After verifying the assumptions of normality, independence and linearity, Student's T test was performed for independent samples. An alpha of 0.05 was chosen for rejection of the null hypothesis, that is, a confidence interval of the test results of 95%. An effect size measure of the difference

between the groups was also performed, called Cohen's D; it ranges from -1 to 1, and the closer to 0, the smaller the effect size of the difference between the groups. Regarding the control group (30.30%) and the case group (69.70%). The table 2 presents the results for group 1 (COC + Placebo), while table 3 presents the results for group 2 (COC + Estriol). The T test was performed to verify a possible significant difference in the levels of cell proliferation in patients with or without Estriol. The normality was verified by the Shapiro-Wilk test, with data following a normal distribution ($W = 0.901$ and 0.96 , p value > 0.3). The equitable variance was verified by the Levine test, which verified the equitable variance in both groups ($F(1) = 0.24$, p value $= 0.62$).

A mean positive nucleus of 14 (SD = 10.65) was observed in the group of patients with contraceptive plus placebo and a mean of positive nuclei of 20.81 (SD = 9.88) in the group of patients with contraceptive plus Estriol. The ratio of positive nuclei to total was higher in the estriol group than in the control group. However, it was not possible to verify a significant difference in the two groups ($T(14.57) = 1.3$, p value $= 0.215$, d Cohen $= 0.53$). Cohen's d pointed to a moderate difference effect (table 4).

Number of positive, negative and total normal epithelial cell nuclei in immunohistochemical investigation of c-myc antigens in Group 1 (COC + Placebo) (N = 10)

Table 2. Number of positive, negative and total normal epithelial cell nuclei in immunohistochemical investigation of c-myc antigens in Group 1 (COC + Placebo) (N = 10)

Patient	Positive nuclei	Negative Nuclei	Total	Percentage (%)
VSN	12	102	114	10.53
PCJ	5	54	59	8.47
MCN	5	65	70	7.14
RAC	NA	NA	NA	NA
MPSS	21	81	102	20.59
ACS	NA	NA	NA	NA
EAP	34	208	242	14.05
IVSS	15	85	100	15.00
VCAJ	6	75	81	7.41
IS	NA	NA	NA	NA
(SD)	14 (10.65)	95.1 (51.79)	109.7 (61.43)	

COC – Combined Oral Contraceptive. NA = only cytoplasm. SD = Standard Deviation.

Table 2

Number of positive, negative and total normal epithelial cell nuclei in immunohistochemical investigation of c-myc antigens in Group 2 (COC + Estriol) (N = 23)

Table 3. Number of positive, negative and total normal epithelial cell nuclei in immunohistochemical investigation of c-myc antigens in Group 2 (COC + Estriol) (N = 23)

Patient	Positive nuclei	Negative Nuclei	Total	Percentage (%)
SRA	26	108	134	19.40
RMN	13	75	88	14.77
JMPS	18	189	207	8.70
CAS	NA	NA	NA	NA
RNS	23	118	141	16.31
RALS	27	66	93	29.03
FLR	NA	NA	NA	NA
JBS	NA	NA	NA	NA
PPS	25	79	104	24.04
MMC	24	84	108	22.22
DT	NA	NA	NA	NA
SMS	42	254	296	14.19
SLOC	12	104	116	10.34
RPP	NA	NA	NA	NA
NRG	NA	NA	NA	NA
SSS	10	75	85	11.76
HSZ	27	141	168	16.07
RGLN	7	116	123	5.69
MAL	12	75	87	13.79
ACCM	10	112	122	8.20
RMM	36	182	218	16.51
ROR	21	196	217	9.68
LSA	NA	NA	NA	NA
Média (DP)	20.81 (9.88)	123.38 (54.80)	144.19 (60.90)	

NA = only cytoplasm. SD = Standard Deviation.

Table 3

Inferential results of the ratio of positive normal epithelial cell nuclei as a function of the control and case groups

Table 4. Inferential results of the ratio of positive normal epithelial cell nuclei as a function of the control and case groups

Marker	COC		COC + Estriol		Significance		Relevance
	Average	SD	Average	SD	T test	P value	D Cohen
C-myc	0.119	0.049	0.150	0.063	1.297	0.215	0.534

SD = Standard Deviation

Table 4

Disclosure(s):

Osmar Pellegrini, n/a, Jr.: No financial relationships to disclose

Afonso Nazário, Dr Afonso Nazário: No financial relationships to disclose

Angela Flavia L. Waitzberg, n/a, N/A: No financial relationships to disclose

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5:00 PM - 6:15 PM

P3-03-28

Clinicopathological Risk Factors of Brain Metastasis in Breast Cancer Patients: A Systematic Review and Meta-analysis

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BACKGROUND: Breast cancer brain metastasis (BCBM) has an incidence rate of 5.1% among Breast Cancer (BC) patients. In BCBM, cancerous cells come from a primary tumor that implant and grow in the brain leading to potentially lethal neurologic symptoms and signs. With more clinical options and therapeutics strategies becoming available, a multi-disciplinary approach for treatment is needed in order to best meet BCBM patients' needs, however, systematic guidelines for the screening of high-risk asymptomatic patients are still lacking and the BCBM diagnoses are performed only after symptoms manifestation. Therefore, understanding the clinical and pathologic drivers of BCBM aids in improving medical interventions by guiding future research directions. This study aims to determine the clinicopathological risk factors of brain metastasis (BM) among BC patients. **METHODS:** Retrospective cohort studies on the clinicopathological characteristics of BM versus non-BM (NBM) patients were retrieved through reputable search databases. Review Manager version 5.4.1 was used for statistical analyses. In the presence of heterogeneities, a pragmatic approach was undertaken to employ both random-effects (RE) and fixed-effect (FE) meta-analyses. The statistical significance of the pooled effect estimates was examined by the Z-test. Interstudy variations and heterogeneities were estimated using Cochran's Q-statistic with $P < 0.05$ indicating a statistically significant heterogeneity. The risk of bias and the quality of studies were assessed at a study level using ROBINS-I tool. **RESULTS:** A total of four (4) retrospective cohort studies were included in the analyses. Random-effects meta-analyses with $i^2 < 50\%$ ($P > 0.05$) had shown significant association ($P < 0.05$) on the increased incidences of BCBM development for HER2+ expression [OR: 2.43, 95% CI: 1.88 – 3.12, $P < 0.00001$] and for pre-menopausal status [OR: 1.77, 95% CI: 1.13 – 2.76, $P = 0.01$]. Fixed-effect meta-analyses had shown significant association ($P < 0.05$) on the decreased incidence of BCBM development for TNBC disease [OR: 0.66; 95% CI: 0.47 – 0.92; $P = 0.02$]. The risk of bias was low to moderate in the majority of studies. **CONCLUSION:** HER2 positivity and pre-menopausal status are risk factors for increased BCBM development while the absence of regional lymph node metastases and ILC findings are less likely to progress to BCBM. Higher T and N categories, higher histological grade, ER negativity, and PR negativity may be associated with higher risks of BCBM while lower T categories, HER2 negativity, and TNBC may likely be associated to less BCBM development. More powerful relevant and upcoming randomized clinical trials with larger sample sizes among BCBM patients versus non-BM patients must be made exploring certainty on the clinicopathological factors contributing to BM among BC patients. **Keyword/s:** risk factors, breast cancer, brain metastasis

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5:00 PM - 6:15 PM

P3-03-29

SMARTphone-Based Cardiovascular Risk Reduction in Breast Cancer Patients [SMART-BREAST]: A Randomized Controlled Trial

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Introduction Breast cancer survivors are at greater risk for cardiovascular-related mortality compared to women without breast cancer. Accordingly, attention to reducing the risk of cardiovascular disease must be a priority in the long-term management of these patients. **Objective** To assess the efficacy of a smartphone-based model of care for exercise promotion, cardiovascular risk reduction and psychological wellbeing in women undergoing treatment for breast cancer. **Methods** Female patients with breast cancer across four tertiary Australian hospitals were screened for inclusion in this randomized controlled trial. Patients were randomized to standard care (SC), with or without an adjunctive smartphone application 'BreastMate' (SP) at time of diagnosis. The primary endpoint was change in exercise capacity, measured by the change in six-minute walk test (6MWT) distance at 12-months when compared to baseline, between groups. Secondary endpoints included changes in cardiovascular risk factors, psychological wellbeing, and major adverse cardiovascular events (MACE). **Results** Of the 103 patients recruited, complete follow-up data was available in 80 (77.7%) patients (age 60±12 years, SP=41, SC=39). At 12-months follow-up, the SP group had a statistically and clinically significant improvement in 6MWT distance (Median Δ46 (IQR 28 to 63) metres vs. Δ8 (-10 to 35) metres; p< 0.001). Compared to SC, patients in the SP group had a greater reduction in systolic blood pressure (Δ-5.1 (-10 to 0) vs 0 (-10 to 7) mmHg; p=0.03) and waist circumference (Δ-1 (-4 to 0) vs 0 (-1.5 to 1) centimetres; p=0.003) as well as a greater improvement in vitality as measured by the sf-36 questionnaire (48.1 ± 18.4 to 63.3±19.2 vs 48.3 ± 24.2 to 59.6±18.8; p=0.04). There was no significant difference in

cholesterol levels, diabetes control, smoking cessation or incidence of MACE between groups (p-value for all=NS). Conclusion In patients with breast cancer, a smartphone-based cardiovascular risk reduction program, as an adjunct to standard care, improved exercise capacity, systolic blood pressure, waist circumference and patient-reported vitality at 12-months. This innovative model of care could be implemented to improve the cardiovascular risk profile of breast cancer survivors. Australia and New Zealand Clinical Trials Registry (ANZCTR12620000007932).

Disclosure(s):

Alexandra C. Murphy, MBBS, BMedSci: No financial relationships to disclose

Omar Farouque, MBBS, PhD: No financial relationships to disclose

Anoop N. Koshy, MBBS, PhD: No financial relationships to disclose

Belinda Yeo, MBBS, MD: No financial relationships to disclose

Ron Dick, MBBS: No financial relationships to disclose

Voltaire Nadurata, MBBS: No financial relationships to disclose

Laura Roccisano, RN: No financial relationships to disclose

Christopher Reid, PhD: No financial relationships to disclose

Matias Yudi, MBBS, PhD: No financial relationships to disclose

12/7/2022

5:00 PM - 6:15 PM

P3-04-01

The role of routine post-operative mammogram after breast conserving surgery

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Introduction:

The use of routine post-operative mammogram (RPM) in search of residual calcifications after breast conserving surgery (BCS) remains controversial due to a paucity of data and conflicting results. In our institution it is common practice is to send all patients who presented with malignant calcifications and underwent BCS with negative surgical margins for RPM before radiotherapy. Patients are also sent for post-operative mammogram if they had malignant calcifications and positive surgical margins, to look for residual calcifications and use localization to ensure their removal in the re-excision.

Methods:

We reviewed the records of 182 patients in our institution referred for RPM between January 7, 2018, and July 14, 2021. Continuous variables were described using medians and interquartile range (IQR). Categorical variables were described as frequencies and percentages. Logistic regression was used to examine factors associated with residual calcifications.

Results:

Median patient age was 59 (48-67) and 39 (21.4%) patients received neoadjuvant systemic treatment. Eighty-five (46.7%) patients had pure DCIS and 66 (36.3%) had mixed IDC with DCIS. On surgical pathology 14 (7.7%) patients had involved surgical margins and an additional 28 (15.3%) had margins less than 2 mm to pure DCIS. Tumor characteristics and RPM results are presented in table 1. Of the 19 (10.4%) patients with suspicious residual calcifications on RPM, 17 (89%) underwent biopsy of the calcifications and the other 2 (11%) patients were referred directly for re-excision. Seven (36.8%) of the patients with suspicious residual calcifications had DCIS. No patients had residual invasive disease. The pathology results of patients with residual calcifications on RPM are presented table 2. Of the 7 patients with residual DCIS, 4 underwent re-lumpectomy, 2 underwent completion mastectomy and 1 patient was lost to follow-up. Additional DCIS was found in all the re-excisions. Two patients with residual DCIS had surgical margins under 2mm from pure DCIS while 5 patients (2.7% of all patients) had no indication for postoperative imaging or re-excision and the residual disease was identified solely based on the mammographic findings. Close or involved surgical margins

were not significantly associated with residual calcifications on post-operative mammogram. Age under 50 was the only factor significantly associated with residual calcifications (OR 3.2 95% CI 1.1-9.7) and residual DCIS (OR=11 95% CI 1.13-109).

Conclusion:

In our cohort RPM revealed a small percentage of cases of residual DCIS that would have otherwise gone untreated. Larger studies are required to better identify factors associated with residual disease on RPM and to identify its impact on local recurrences.

Tumor histology	DCIS	IDC	ILC	MIXED DCIS+IDC	ypTis	ypT0
	85 (46.7%)	15 (8.2%)	5 (2.7%)	66 (36.3%)	4 (2.2%)	7 (3.8%)
Multifocal	No	Yes				
	124 (68.1%)	58 (31.9%)				
Margins	Uninvolved	Involved	Pure DCIS<2mm			
	140 (76.9%)	14 (7.7%)	28 (15.4%)			
Suspicious calcifications on RPM	No	Yes				
	163 (89.6%)	19 (10.4%)				

DCIS- ductal carcinoma in situ, IDC-invasive ductal carcinoma, ILC-invasive lobular carcinoma, ypTis-residual DCIS only post-neoadjuvant, ypT0-no residual invasive or in situ disease, RPM-routine postoperative mammogram

Table 1: Tumor characteristics and RPM results

RPM suspicious calcification pathology	Number (%)
DCIS	7 (37%)
Atypical hyperplasia	4 (21%)
Fat necrosis	3 (16%)
Papillary lesion	2 (11%)
LCIS	1 (5%)
Fibrocystic changes	1 (5%)
Giant cell reaction	1 (5%)

RPM-routine post-operative mammogram, DCIS- ductal carcinoma in situ, LCIS-lobular carcinoma in situ

Table 2: Pathological results of patients with residual suspicious calcifications on RPM

Disclosure(s):

Opher Globus, n/a: Eli Lilly: Consulting Fees (e.g., advisory boards) (Terminated, June 20, 2022), Honoraria (Terminated, June 20, 2022); Gilead: Consulting Fees (e.g., advisory boards) (Terminated, May 17, 2022); Merck: Honoraria (Terminated, July 12, 2022); Pfizer: Honoraria (Terminated, March 15, 2022); Roche: Honoraria (Ongoing)

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5:00 PM - 6:15 PM

P3-04-02

Population level access to diagnostic mammography and ultrasound guided breast biopsy in Nigeria: a geospatial analysis

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Introduction: Breast cancer is the most common cause of cancer-related mortality among women in Nigeria. Physical proximity to a diagnostic center is an important component of access, which has direct implication on the cost and timeliness of diagnosis and treatment. Beyond diagnostic mammography, ultrasound (US)-guided biopsy is an essential tool in the diagnostic pathway for suspicious lesions of the breast and is recommended by the Whole Health Organization Breast Health Global Initiative for LMICs. Unfortunately, there is a dearth of data on the population level access to mammography and US-guided breast biopsy in Nigeria and little is known about the geospatial inequities in access that targeted programming or investment could potentially address. This study undertook a comprehensive evaluation of breast imaging and diagnostic services in Nigeria and using a previously validated geographic information system (GIS) model, evaluated geospatial access to diagnostic mammography and US-guided breast biopsy in Nigeria. Methods: A comprehensive list of public and private facilities offering diagnostic mammography and/or US-guided breast biopsy was compiled using publicly available facility data from the Nigerian Ministry of Health, a survey administered to members of the Breast Imaging Society of Nigeria (BISON) as well as key stakeholder interviews from each of the countries six geopolitical zones. A novel survey was delivered to BISON members to identify additional / new facilities not captured by the latest Nigerian Ministry of Health data. Facility location, administration (public vs. private) and duration of service delivery were elicited from respondents and paired with the Ministry of Health facility dataset. Data on provider training and volume were also captured in the survey. All facilities were geolocated using Google Earth™ (Google, Mountain View, CA). A previously described cost-distance model, that uses open-source population density data to 100m2 (GeoData Institute) and road network data (OpenStreetMap) was used to estimate population level travel time to the nearest diagnostic center. Any portion of a route that included travel over terrain without roads was assigned a walking speed of 5 kmh-1. Geospatial access was calculated for mammography and US-guided biopsy separately and as well as by geopolitical zone. This study was approved by the research ethics board at Obafemi Awolowo University. Results: In addition to publicly available data from the Ministry of Health, facility and practice data was obtained from 63 Nigerian Radiologists from across the country. In total, 124 centers were identified that offer diagnostic mammography, of which 78 (63%) are privately administered. Nine of the countries 36 states did not have a center offering this service. Across the country,

33 centers offer US-guided breast biopsy, of which the majority (72.7%) are public. At a population level, 83.1% of the population has access within 120 minutes of continuous one-way travel to a center with diagnostic mammogram or US. At 240 minutes of continuous one-way travel, which corresponds to a full day of travel round-trip, 80.8% of the population has access to US-guided breast biopsy. However, there are differences in access between geopolitical zones. Just 68.7% of the population in the North East geopolitical zone has access to US-guided biopsy within a day's travel (i.e. 240 minutes one-way). The remaining five geopolitical zones have population level access to this service of $\geq 80\%$. Conclusions: This is the first comprehensive evaluation of breast cancer imaging and diagnostic services in Nigeria. Our results, demonstrate that the majority of the population in Nigeria has reasonable geospatial access to basic breast cancer imaging services. However, there are inequalities in access between states and geopolitical zones in the north and south of the country, which may have an impact on timely diagnosis and care.

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P3-04-03

Safety, tolerability, and efficacy of the novel intravenous manganese-based contrast agent SN132D in patients with breast cancer: initial results of a Phase I, First-In-Human clinical trial SPAGOPIX-01

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Introduction: SN132D is a manganese (Mn) -containing, polymeric nanomaterial developed as an intravenous contrast agent for tumor selective MRI. It was designed for optimal physiological targeting and preferential accumulation in malignant lesions by means of the Enhanced Permeability and Retention (EPR) effect. Combined non-clinical data have demonstrated proof of concept (PoC) in various in vivo cancer models and a safety profile in line with FIH administration of SN132D in the SPAGOPIX-01 clinical study. Methods: SPAGOPIX-01 is a Phase I, FIH, open-label, non-randomized and non-placebo-controlled study in participants with diagnosed breast cancer. MRI was performed prior to and at 2 h and 4 h after the end of the SN132D infusion. SN132D safety and tolerability were the primary objectives. MRI enhancing properties of SN132D in primary tumor, liver, and pancreas as well as pharmacokinetics of SN132D were secondary objectives. Results: So far, 12 female breast cancer patients of planned up to 20 have been enrolled between September 2019 and December 2021. Of these,

six patients received SN132D at 10 $\mu\text{mol Mn/kg}$ (cohort 1) and six patients at 20 $\mu\text{mol Mn/kg}$ (cohort 2). In cohort 1 (10 $\mu\text{mol Mn/kg}$), SN132D was well-tolerated. No clinically significant findings were observed for clinical laboratory tests, vital signs, 12-lead electrocardiogram (ECG), or physical examination. No serious adverse events (SAEs) were registered; nine mild AEs were reported for four subjects. The most reported AEs in patients administered 10 $\mu\text{mol Mn/kg}$ SN132D were injection site reactions (2 AEs) and flushing (2 AEs). In cohort 2, SN132D was also well-tolerated. No clinically significant findings were observed for vital signs, ECG, or physical examination. No SAEs were registered; 12 AEs were reported for six patients. The most common AE was transiently elevated transaminase levels, with single reports from four patients. The second and third most common AEs were moderate vomiting (reported twice from a single patient) and mild flushing. Remaining AEs were single events reported by single patients. None of the AEs required treatment and all resolved without any intervention. Pharmacokinetics of SN132D was assessed at up to 24 h post dose. In cohort 1, SN132D, based on Mn plasma concentrations, had a mean C_{max} of $0.915 \pm 0.187 \mu\text{g/mL}$, a mean initial half-life of $7.17 \pm 1.02 \text{ min}$, a mean AUC_{inf} of $0.890 \pm 0.20 \text{ h} \cdot \mu\text{g/mL}$ and a mean plasma clearance of $0.646 \pm 0.157 \text{ L/h/kg}$. In cohort 2, SN132D had a mean C_{max} of $2.0 \pm 0.341 \mu\text{g/mL}$, a mean initial half-life of $7.0 \pm 1.60 \text{ min}$, a mean AUC_{inf} of $2.04 \pm 0.28 \text{ h} \cdot \mu\text{g/mL}$ and a mean plasma clearance of $0.548 \pm 0.068 \text{ L/h/kg}$. MR image analysis in cohort 1 revealed that although contrast was insufficient for the generation of clinically relevant tumor images at the 10 $\mu\text{mol Mn/kg}$ dose level, there was still a measurable enhancement. In cohort 2, MR images were analyzed for five subjects and clinically relevant contrast increase in the primary tumor without signal increase in the background was observed in all patients. In addition, all MRI images, including both dose cohorts, showed contrast increase in both liver and pancreas at post-dose imaging timepoints. Conclusions: Initial clinical data generated to date demonstrate an acceptable safety profile and PoC for SN132D in the breast cancer patients. Physiological targeting with functional nanoparticles appears suitable for tumor MRI imaging. Our data are in agreement with preclinical data in rodent tumor models. The data are supporting the continuation of the SPAGOPIX-01 clinical trial and we will further explore SN132D in a cohort of pancreatic cancer patients with liver involvement.

Disclosure(s):

Fredrik Wärnberg, MD, PhD: PreludDX: Institutional grants to Uppsala Academic Hospital (Terminated, December 31, 2018); Spago Nanomedical AB: Coordinating Investigator (Ongoing)

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P3-04-04

Correlation of Mammographic Microcalcifications with Final Surgical Pathology after Neoadjuvant Chemotherapy for Breast Cancer

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Introduction: Benefits of neoadjuvant chemotherapy (NAC) in breast cancer include de-escalating surgical management, treating occult systemic metastases and the assessment of in-vivo tumor response. Guidelines for post-NAC imaging to assess response lack specificity on appropriateness and utility of individual imaging modalities for surgical planning. Mammographic microcalcifications are a confounder that are not well studied. We examined the correlation between the mammographic extent of microcalcifications present post-NAC, corresponding MRI lesions, and definitive surgical pathology.

Methods: In this retrospective cohort study, patients with calcifications on pre-NAC mammograms were collected from a database of consecutive breast cancer patients receiving NAC at an academic center between January 1st 2014 – December 31st 2019. The primary objective was to determine how the maximum diameter of post-NAC calcifications correlates with final surgical pathology, stratified by tumor receptor subtype. The secondary objectives were to assess correlation of the maximum diameter on final pathology with the maximum diameter of (1) post-NAC mammographic mass (if present) and (2) post-NAC MRI, mass (ME) and non-mass enhancement (NME). Parameters on final surgical pathology included the diameters of invasive disease, ductal carcinoma in-situ (DCIS) and the tumor bed (TB). Pearson's correlation coefficient was used to evaluate statistical significance and considered strong if $R^2 \geq 70\%$, moderate if $R^2 = 25-70\%$ and weak if $R^2 \leq 25\%$.

Results: 343 patients received NAC, of which 157 were excluded for lack of calcifications (n=147), lack of imaging reports (n=8) or inflammatory breast cancer (n=2). 186 patients met the inclusion criteria with a mean age of 49.9 years. 34 (18.3%) patients had triple negative breast cancers (TNBCs).

Mammographic calcifications correlated poorly with residual invasive disease ($R^2 = 10.8\%$), overestimating by 57%. TNBCs demonstrated the strongest correlation between

microcalcifications and invasive disease (R²=83%), but calcifications overestimated pathology by 41%. Mammographic calcifications correlated moderately with the TB (R²= 50.3%) and poorly with DCIS (R² = 3.4%). By subtype, both correlations were strong in TNBCs (R² = 76.3% and 77.9% respectively). Similarly, focal mass on mammography correlated poorly with pathology except in TNBCs, which correlated moderately with all three pathology parameters (Table 1). In patients with calcifications on mammography, MRI ME and NME correlated weakly with invasive disease, except in TNBCs, where correlation was moderate in ME (R² = 37.7%) and NME (R² = 28.4%).

Conclusion: In breast cancer patients with microcalcifications, current post-NAC imaging modalities appear to overestimate the extent of residual disease. Surgical excision of all residual microcalcifications may maximize oncologic safety but may also represent over-treatment. Ongoing feasibility trials on surgical omission rely on post-NAC imaging to determine trial candidacy. Our data suggests that potentially eligible patients are excluded on the basis of post-NAC imaging overestimating the extent of residual disease. Further studies are needed to determine the most accurate imaging correlate of residual disease after NAC to plan better surgeries, identify candidates for surgical omission and establish optimal post-NAC imaging guidelines. Current imaging modalities appear most accurate for TNBCs and may be more reliable at identifying exceptional responders for surgical omission in this subtype.

Table 1. Summary of Correlation Analyses in Overall and Triple Negative Breast Cancer (TNBC) cohorts.

	Overall Average % Difference*	Overall Correlation (R ²)	Average % Difference in TNBC	Correlation (R ²) in TNBC
Post-NAC Calcifications				
Invasive Disease	-57.0%	10.8%	-41.5%	83.0%
Tumor Bed	-20.2%	50.1%	-11.7%	76.3%
In-situ Disease	-46.4%	3.4%	-18.1%	77.9%
Post-NAC Mammographic Mass				
Invasive Disease	-0.2%	4.5%	34.5%	16.5%
Tumor Bed	54.0%	19.2%	54.7%	39.1%
In-situ Disease	40.0%	13.6%	40.2%	14.5%
Post-NAC MRI Mass Enhancement				
Invasive Disease	7.7%	12.6%	-46.1%	37.7%
Tumor Bed	79.6%	3.4%	14.5%	25.6%
In-situ Disease	37.3%	17.9%	4.7%	11.3%
Post-NAC MRI Non-Mass Enhancement				
Invasive Disease	-44.4%	9.6%	-44.0%	28.4%
Tumor Bed	16.5%	18.3%	19.5%	37.6%
In-situ Disease	-23.7%	0.0%	-24.7%	11.1%

* Average % difference in maximal diameter calculated as (pathology – radiology)/radiology

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P3-04-05

Artificial Intelligence Detects, Classifies, and Describes Lesions in Clinical Breast Ultrasound Images

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Purpose Many low-middle income countries (LMIC) suffer from chronic shortages of resources that inhibit the implementation of effective breast cancer screening programs. Advanced breast cancer rates in the U.S. Affiliated Pacific Islands substantially exceed that of the United States. We propose the use of portable breast ultrasound coupled with artificial intelligence (AI) algorithms to assist non-radiologist field personnel in real-time field lesion detection, classification, and biopsy, as well as determination of breast density for risk assessment. In this study, we examine the ability of an AI algorithm to detect and describe breast cancer lesions in clinically-acquired breast ultrasound images in 40,000 women participating in a Hawaii screening program. Materials and Methods The Hawaii and Pacific Islands Mammography Registry (HIPIMR) collects breast health questionnaires and breast imaging (mammography, ultrasound, and MRI) from participating centers in Hawaii and the Pacific and links this information to the Hawaii Tumor Registry for cancer findings. From the women with either screening or diagnostic B-mode breast ultrasound exams, we selected 3 negative cases (no cancer) for every positive case matched by age, excluding Doppler and elastography images. The blinded images were read by the study radiologist to delineate all lesions and describe in terms of the BI-RADS lexicon. These images were split by woman into training (70%), validation and hyperparameter selection (20%) and testing (20%) subsets. An AI model was fine-tuned for lesion and BI-RADS category classification from a Detectron2 framework [1] pre-trained on the COCO Instance Segmentation Dataset [2]. Model performance was evaluated by computation of precision and sensitivity percentages, as well as Area under the Receiver Operator Curve (AUROC). Detections were considered positive if they overlapped a ground truth lesion delineation by at least 50% (Intersection over Union = 0.5), and a maximum of 4 detections were generated for each image. Timing experiments were run on a GPU-enabled (Nvidia Tesla V100) machine on unbatched images. Results Over the 10-year observation period, we identified 5,214 women with US images meeting our criterion. Of these, 111 were diagnosed with malignant breast cancer and 333 were selected as non-cases for a total of 444

women. These 444 women had a total of 4,623 ultrasound images with 2,028 benign and 1,431 malignant lesions identified by the study radiologist. For cancerous lesions, the AI algorithm had 8% precision at a sensitivity of 90% on the testing set. For benign lesions, a sensitivity of 90% resulted in 5% precision on the testing set. The AUROC for bounding box detections of cancerous lesions was 0.90. The AUROC for bounding box detections of benign lesions was 0.87. The model made predictions at a rate of 25 frames/second time (38.7 milliseconds per image). Conclusion Detection, segmentation, and cancer classification of breast lesions are possible in clinically-acquired ultrasound images using AI. Based on our timing experiments, the model is capable of detecting and classifying lesions in real-time during ultrasound capture. Model performance is expected to improve as more data becomes available for training. Future work would involve further fine-tuning of the model on portable breast ultrasound images and increasing model evaluation speed in order to assess utility in low-resource populations [1] Wu Y, Kirillov A, Massa F, Lo W-Y, Girshick R. Detectron2. <https://github.com/facebookresearch/detectron2>. [2] Lin T-Y, Maire M, Belongie S, et al. Microsoft COCO: Common Objects in Context. Computer Vision – ECCV 2014. Springer International Publishing; 2014:740-755.

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P3-04-06

Artificial intelligence-based triaging of breast cancer screening mammograms and radiologist workload reduction: a systematic review and meta-analysis

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Introduction: Deep learning (DL) has shown promising results for mammographic breast cancer diagnosis. However, the impact of artificial intelligence (AI) in the screening process have not yet been fully addressed in terms of workload reduction, which has potential to decrease healthcare disparities. Radiologists are tasked with overwhelming volumes of screening mammograms, particularly in medically underserved areas. Therefore, when applied to workflow improvement, AI might be a tool to reduce healthcare disparities. The purpose of this systematic review and meta-analysis was to assess if AI-based triaging of breast cancer screening mammograms could reduce the radiologist's workload with non-inferior sensitivity. Methods: PubMed, EMBASE, Cochrane Central and Web of Science databases were systematically searched for studies that evaluated AI algorithms on computer-aided triage of breast cancer screening mammograms. We extracted data from homogenous studies and performed a proportion meta-analysis with random-effects model to verify the radiologist's workload reduction and the software's sensitivity. Results: A total of 14 studies were systematically selected. Three studies using the same commercially available DL algorithm were included in the meta-analysis, with 156852 examinations evaluated at the threshold of 8. The radiologist's workload decreased by 68.3% (95%CI 0.655-0.711, $I^2 = 98.76%$, $p < 0.001$), with a sensitivity of 93.1% (95%CI 0.882-0.979, $I^2 = 83.86%$, $p = 0.002$). Conclusion: Our findings suggest that DL computer-aided triage of breast cancer screening mammograms significantly reduces the radiologist's workload with high sensitivity. Although AI's implementation remains complex and heterogeneous, it is a promising tool to optimize healthcare resources with a potential large impact in low resource settings that struggle with workforce shortage.

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P3-04-07

Safety and artifact testing of a nitinol breast biopsy clip in an ultra-high resolution magnetic resonance imaging (MRI) environment

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Background: The lack of safety clearance of several metallic breast implants in 7T(Tesla) poses a significant hurdle to standard clinical breast cancer care and research from reaping the benefits of ultra-high resolution MR imaging. A breast biopsy clip (Ultracor Twirl, Becton, Dickinson and Company, Vernon Hills, IL) composed of nitinol, was tested for safety and artifact susceptibility clearance in a 7T MRI scanner, using standardized procedures. This clearance is significant in henceforth allowing patients with this implant to be scanned in now FDA approved ultra-high-field MRI scanners of 7T or less for clinical and research purposes. Methods: Tests for magnetic susceptibility (torque and translational attraction), MRI-related heating, and artifacts were conducted as per standardized protocols. The torque and translational attraction tests evaluated the effects of magnetic force by the MRI to cause the clip to move and twist respectively. The heating test was conducted with customized MR parameters of short TR (repetition time) and maximum echo-train length, designed to induce temperature change. The artifact test using T1 weighted spin and gradient echo imaging sequences, evaluated potential localized signal loss that may result in misrepresentation of the

imaged area. This may occur due to the presence of the metallic clip in the MR environment. Results: The torque and translational attraction tests respectively indicated that the MR environment did not induce any movement in the clip in eight orientations, with a deflection angle of 0 degrees. Results of the heating test indicated no significant temperature change of the clip. A temperature change of less than 0.45C° was observed in the phantom gel in both the absence and presence of the clip, which is well within the safety threshold (< 1°C). Results of the artifact test indicated a very small artifact, with the largest artifact cross-sectional area appearing on gradient echo images. Conclusion: These cumulative results indicate that the Ultracor Twirl breast biopsy clip is safe for imaging patients at 7T.

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P3-04-08

Comparison Of Cone Beam Breast CT And Breast MRI In Preoperative Assessment Of Primary Breast Cancer Tumor Size

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Comparison Of Cone Beam Breast CT And Breast MRI In Preoperative Assessment Of Primary Breast Cancer Tumor Size Yinan Ji * 1, Geyi Liao * 1, Ningbing Luo², Yi Jiang¹, Xiaoming Liao¹, Wei Tang¹, Huawei Yang¹. 1Department of Breast Surgery, 2Department of Radiology, Guangxi Medical University Tumor Hospital, Nanning, China Correspondence to: Dr. Huawei Yang, Department of Breast Surgery, Guangxi Medical University Cancer Hospital, 71 Hedi Road, Nanning, Guangxi Zhuang Autonomous Region 530021, P.R. China Email: Lordyhw@163.com * Contributed equally Background: Breast cancer is the malignant tumor with the highest incidence among women in China, seriously endangering women's health. After breast cancer is diagnosed, surgery is one of the primary treatments. Assessing the extent of breast cancer is vitally important to formulate the best surgical option, obtain clear margins while minimizing the volume of removed tissue, and improve the treatment outcome and patient's quality of life. Currently, breast surgery relies heavily on Breast MRI (bMRI) for preoperative assessment. However, bMRI may overestimate the tumor sizes. bMRI is contraindicated in patients with claustrophobia, metal implants, and allergy to gadolinium contrast medium. In addition, bMRI is generally expensive and time-consuming. Some patients find bMRI less favorable for cost and time concerns. Cone Beam Breast CT (CBBCT) is a new modality using Cone Beam CT technology and iodinated contrast media for true 3D high-resolution imaging of the breast. Our previous studies have proved the feasibility of CBBCT in the preoperative assessment of breast cancer. A large-scale study has been done to further examine the clinical significance of CBBCT in pre-operative assessment compared with bMRI. Methods: 273 female primary breast cancer patients were included in this study. The maximal diameters of the tumors were measured in CBBCT and bMRI images by an experienced radiologist. The differences between the image-measured size and surgical pathology size (gold standard) were calculated as Δ DCT and Δ DMR. Δ D > 5mm was considered an overestimation and Δ D < -5mm was considered an underestimation. The absolute values of Δ DCT and Δ DMR were also calculated as Δ DCT_abs and Δ DMR_abs. A Student t-test was

used to compare the statistical differences between Δ DCT_abs and Δ DMR_abs. Among Δ DCT_abs and Δ DMR_abs, a 5mm cut-off value was used to determine the concordance between image and pathology. The concordance rates of CBBCT-Pathology and bMRI-Pathology were tested with the χ^2 method. Factors that may affect the accuracy of tumor size measurement were analyzed. Results: Overall there were no statistically significant differences between Δ DCT_abs and Δ DMR_abs. (0.58 ± 0.68 cm vs. 0.65 ± 0.68 cm; $t=1.653$, $P=0.100$). Using 5mm as the cut-off value of concordance, there was no significant difference in the CBBCT-Pathology and bMRI-Pathology concordance rates (64.8% vs. 60.1%, $\chi^2 = 1.320$, $P=0.251$). The overestimation rate of CBBCT was significantly lower than that of bMRI (11.4% vs. 19.4%, $\chi^2=6.810$, $P=0.009$). But there was no significant difference in the underestimation rates (23.8% vs. 20.5%, $\chi^2=0.860$, $P=0.354$). Δ DCT_abs is significantly smaller than Δ DMR_abs among the invasive ductal carcinoma group ($P=0.017$), the premenopausal group ($P=0.004$), and the small tumor size (≤ 2 cm) group ($P=0.003$). Δ DCT_abs and Δ DMR_abs have no significant differences among the lymph node metastasis group, multi-lesion group, and enhancement type group ($P > 0.05$). Conclusions: CBBCT is concordant with surgical pathology in breast tumor size measurement and provides more accurate tumor size estimation compared with bMRI. CBBCT can be used as a valuable modality for pre-operative assessment.

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3-dimensional intraoperative analysis of screen-detected breast cancers reduce re-excision rates

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Introduction:

Breast conserving therapy, has generally been accepted as treatment of choice for early invasive breast cancer.

However adequate local control depends on obtaining negative margins and receipt of radiation. In 20-30 % of patients with breast conserving surgery a second re-excision procedure is due to tumor-positive margins at histopathology. Margins re-excision rate are variable across the countries.

Mean re-excision rate of 17.2% across units in UK. Intraoperative specimen radiography, used to evaluate partial mastectomy specimens ensure that the lesion is adequately removed.

Objective:

to determine whether 3D-intraoperative imaging better predicts margin status and reduces the re-excision rate than conventional 2D imaging.

Methods:

Retrospective study comparing two cohorts of patients

360 screen-detected breast cancer (2D cohort). April 2015 to March 2018

300 screen-detected breast cancer (3D cohort) April 2018 to March 2021

Royal Cornwall Hospital (RCHT) introduced a 3D intraoperative system for all cases in April 2018

Prior to the introduction of 3D intraoperative imaging at RCHT the re-excision rate was stable at approximately 15%.

All patient had undergone preoperative digital mammogram and ultrasound.

All patients had core biopsy diagnosis

All malignancies were localised with ROLL (Radio-guided occult lesion localization) techniques.

All wide local excision were performed by 5 fully trained oncoplastic breast surgeons (similar distribution within the two cohort)

Specimen radiograph was performed intraoperatively using:

2D x-ray device (Faxitron system; Trident Hologic, Marlborough, MA) or

3D tomosynthesis (Mozart system; Kubtec Medical imaging, Stratford, CT).

For both methods of assessment, specimen was placed in the device and auto exposed without any compression of tissue.

All specimens were marked with orienting sutures and clips according to local protocol.

All specimens were painted in theatre by the operating surgeon.

All specimens were examined by the same pathologists.

No change in margin protocol for 12 years (already compliant to ABS guidelines)

- A clear margin for invasive cancer was defined as tumour found within 1mm of margin. For ductal carcinoma in situ (DCIS), a margin was classified as positive if ink on tumour, was classified as close ink is found in under 2 mm from tumour and as negative if more or equal to 2 mm, in accordance with NICE guidelines. (22)

Statistical Analysis:

- The study compares patient demographics, histology, and re-excision rates between 2D and 3D
- Descriptive and comparative statistics are be calculated for all collected data

TABLE 1:

3D/2D RR 0.59 (P:0.01), CI 0,3369-09068, Z -2.3473, P 0.0189

Conclusions:

The use of intraoperative 3D specimen X-ray reduced the relative risk of re-excision rate by

41% (P=0.01) without any negative impact on other parameters.

Table 1: Results

	2D Cohort		3D Cohort	
Screening patients	336		300	
Re-excision rate	51	15.17%	27	9.00%
Wle average weight	27.87 gm		28.64 gm	
Cavity shaves average weight	3.00 gm		3.00 gm	
DCIS only	85	5.29%	80	26.33%
Invasive only	176	52.38%	157	52.33%
Invasive + DCIS	75	22.32%	63	21.00%

3D intraoperative imaging versus 2D intraoperative imaging

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The TILs-US score adding vascularity assessment based on ultrasonography for predicting tumor-infiltrating lymphocytes in human epidermal growth factor receptor 2-positive and triple-negative breast cancer

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Background: Tumor-infiltrating lymphocytes (TILs) are a useful prognostic factor and predictive biomarker of neoadjuvant chemotherapy treatment response for breast cancer, especially in

human epidermal growth factor receptor type 2 (HER2)-positive breast cancer and triple-negative breast cancer (TNBC). However, due to heterogeneity of TIL expression and distribution in the tissues, accurately predicting TIL expression, especially using limited core-needle biopsy specimens, is difficult. Therefore, an accurate and simple preoperative evaluation method is needed. We have reported that the TILs-ultrasonography (US) score determined by characteristic US findings has a predictive performance for lymphocyte-predominant breast cancer (LPBC). This study aimed to investigate whether the TILs-US score with added vascularity assessment has a better predictive performance for LPBC.

Methods: This multicenter, retrospective study investigated the validation and scoring of the LPBC characteristic imaging findings and applied it for LPBC and non-LPBC prediction. A total of 100 patients with HER2-positive breast cancer (n = 59) and TNBC (n = 41) treated by curative surgery between January 2014 and December 2021 were evaluated. Stromal lymphocytes in surgical pathological specimens were evaluated; the cutoff value for predicting LPBC was defined as $\geq 50\%$ stromal TILs. Preoperative US was examined for TIL indicators. The US images with characteristic TILs were scored for LPBC prediction. Univariate and multivariate logistic regression analyses were employed for each potential predictor variable of LPBC.

Results: A total of 40 patients with $\geq 50\%$ stromal TILs were defined as having LPBC. The examined characteristic US findings for predicting LPBC, shape (more lobulated), internal echo level (weaker), posterior echoes (stronger), and vascularity assessment (hypervascularity), were significantly associated with LPBC and used to assign the scoring for predicting LPBC. As previously reported, the TILs-US score ranged from 0–7 points based on three ultrasonic tissue characteristics: shape (round, oval, and polygonal or irregular, 0 points; lobulated, 1 point; and small lobulated, 2 points), internal echo level (high or equal, 0 points; low, 1 point; and extremely low, 2 points), and posterior echoes (shadowing or attenuating, 0 points; no change, 1 point; accentuated, 2 points; and extremely accentuated, 3 points). We further added vascularity assessment (avascular or hypovascular, 0 point; moderately vascular, 1 point; and hypervascular, 2 points) to this scoring system. Based on the receiver operating characteristics (ROC) curves (AUC [Area Under the Curve] 0.77), the score cutoff for predicting LPBC was 4 points for TILs-US score (sensitivity, 0.83; specificity, 0.55; and accuracy, 0.66). Multivariate logistic regression analysis revealed that cT ($< T_2$), estrogen receptor (ER) negativity, and a TILs-US score of ≥ 4 points were significant LPBC predictors (odds ratio [OR] 3.60; $p = 0.028$; OR 8.68; $p = 0.020$; OR 5.99; $p = 0.005$). Conversely, based on the ROC curves (AUC 0.78), the score cutoff for predicting LPBC was 5 points after adding vascularity assessment (sensitivity, 0.93; specificity, 0.57; and accuracy, 0.71). Multivariate logistic regression analysis revealed that cT ($< T_2$), ER negativity, and a TILs-US score adding vascularity assessment of ≥ 5 points were significant LPBC predictors (OR 5.12; $p = 0.010$; OR 10.3; $p = 0.019$; OR 20.1; $p < 0.001$).

Conclusions: Including the vascularity assessment to the TILs-US score, which can be noninvasively obtained using US, is a more accurate preoperative predictor of LPBC. Vascularity assessment may be an auxiliary factor in predicting LPBC.

Univariate and multivariate logistic analysis of significant clinicopathological factors predicting lymphocyte-predominant breast cancer.

Characteristic	Univariate logistic regression analysis			Multivariate logistic regression analysis			
	OR	95%CI	P	OR	95%CI	P	
Clinical T	<T2 vs. T2	1.24	0.54 – 2.84	0.614	5.12	1.48 – 17.8	0.010
Clinical N	Positive vs. Negative	2.47	0.65 – 9.39	0.184	2.14	0.44 – 10.4	0.349
Nuclear Grade	3 vs. 1-2	2.41	0.95 – 6.07	0.063	1.10	0.33 – 3.60	0.880
Ki67	≥20 vs. <20	8.76	1.08 – 70.8	0.042	1.79	0.14 – 22.5	0.652
ER	Negative vs. Positive	1.90	0.84 – 4.31	0.122	10.3	1.46 – 72.5	0.019
HER-2	Positive vs. Negative	1.08	0.47 – 2.48	0.865	5.87	0.90 – 38.5	0.065
TILs+US score adding vascularity assessment	≥5 vs. <5	16.1	4.47 – 58.2	< 0.001	20.1	3.98 – 101.3	< 0.001

Univariate and multivariate logistic analysis of significant clinicopathological factors predicting lymphocyte-predominant breast cancer.

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P3-04-11

Longitudinal Changes of Contralateral Breast Mammographic Artificial Intelligence Algorithms Score in Ductal Carcinoma In Situ patient with Tamoxifen

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Background Mammographic Artificial intelligence (AI) algorithms (Lunit insight MMG) draws attention as a diagnostic support tool for breast cancer detection. Lunit insight MMG provides a location suspected of breast cancer with a heatmap and a score reflecting the probability of the presence of suspicious areas. We investigated whether the Lunit insight MMG score is relevant for predicting the response to adjuvant tamoxifen. Methods Patients diagnosed with DCIS and underwent treatment at Seoul National University Hospital in 2010 were retrospectively enrolled. Clinical characteristics, tamoxifen use, survival data, and mammography images were extracted from the electronic medical records, and Lunit insight MMG scores were calculated retrospectively. We classified two groups according to tamoxifen treatment and compared the score change of contralateral breast from baseline to 5 years after surgery for DCIS. Change categories of Lunit insight MMG score included maintaining high risk, maintaining low risk,

increasing from low risk to high risk, and decreasing from high risk to low risk. Results Of 100 patients, 50 (50%) had undergone tamoxifen treatment (group 1) and 50 (50%) had not (group 2). The median age of the patients was 48.4 years for group 1 and 51.5 years for group 2 (p=0.172). The median follow-up duration was 8.7 years for the whole cohort. Using Lunit insight MMG score, more patients in group 1 decreased in contralateral breast cancer (CBC) risk compared with group 2 (6.0% vs. 2.0%; P=.008). No patients in group 1 had an increase in CBC risk while 9 patients increased in group 2 (0% vs. 18.0%; P =.008). There was no ipsilateral breast cancer recurrence for the whole cohort, and two patients experienced contralateral invasive breast cancer in group 2. In two patients with CBC, the Lunit insight MMG score increased five years after surgery, one year and three years before the CBC diagnosis. Conclusions Longitudinal Changes of Mammographic AI algorithms Score may be a predictive surrogate marker for response to tamoxifen therapy in hormone receptor-positive DCIS.

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Intraoperative valuation of the resection margin with the usage of digital two-point sectorography (Faxitron BioVision)

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Background. Surgical method is fundamental in complex and combined approach of the treatment of the early breast cancer. It is a common fact, that purity of the resection margin is the main indicator of oncological safety of the breast-conserving surgery (BCS). The presence of tumor cells in examined margin is one of the predictors of the development of local recurrence after BCS with breast cancer. Currently the necessity of searching for adequate and quick method of intraoperative valuation of the state of the resection margin is kept. Intraoperative valuation of the resection margin state with the usage of digital two-point sectorography (Faxitron BioVision) appeared as the alternative of urgent histological test, providing the optimum size of the information about adequacy of the carried out surgical treatment. Objective – to evaluate diagnostic features of the digital two-point sectorography Faxitron BioVision in the intraoperative valuation of the resection margin status after the

conducted surgical treatment in comparison with planned histologic study. Materials and methods. 368 conducted conservative surgeries were analyzed, patients were divided in two groups depending on carrying out of non-adjuvant chemotherapy (NAC). The first group of patients included 236 patients, who didn't received NAC before operative treatment stage; second group included 132 patients, who received NAC. Subset analysis of detection rate of the positive resection margin was carried out with the usage of the intraoperative valuation of the resection margin on the X-ray apparatus Faxitron BioVision or without carrying out this method. After each BCS conducted when planned histologic study resection margin were tested for the presence of the tumor cells and the frequency of carrying out of reoperations when positive margin were found. Results. From 368 tested anatomic medications after BCS positive resection margin (R1) is found in 25 cases, which is 6,8 %. From 236 patients of the first group after BCS R1 is found in 20 cases, which is 8,5 %; from 132 conducted operations in the second group in 5 (3,8%) cases – the presence of R1 is found. Reoperations were conducted in 13 cases, when repeated pathomorphological study tumor cells found in 3 cases in the subgroup, which didn't receive intraoperative valuation on the X-ray apparatus Faxitron BioVision. Conclusion. Assessing the results of our study we can make a conclusion about the positive experience of conducting of BCS and intraoperative evaluation of conservative surgery and intraoperative valuation with the usage of the digital two-point sectorography (Faxitron BioVision) and low frequency of positive margin (3,8%) in comparison with refusal from carrying out of this method (8,5%).

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P3-04-13

Patient experience with automated SoftVue 3D whole breast tomographic ultrasound

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Authors: Mary Yamashita, MD; Rachel Brem, MD; Lauren Baker, Ph.D; MD; Taylor Mahoney, PhD; Patrick Walker, PharmD, MPH; Rachel Treat, MA; Linda Hovanessian Larsen, MD. Title: Patient experience with automated SoftVue 3D whole breast tomographic ultrasound. Purpose: SoftVue (SV) is an automated, 3D whole breast ultrasound tomographic imaging device which is FDA PMA approved as adjunct to mammography for women with dense breasts. Screening with handheld US is labor intensive and with ABUS is associated with significant patient

discomfort. A benefit of SV is that image acquisition is not operator dependent and does not require compression. Because acceptance by patients is crucial to implementation of US screening, we evaluated patients' experience with SV, specifically, asymptomatic women with BI-RADS c or d density undergoing FFDM. Materials and Methods: As part of a prospective, 10-site study, 7,439 asymptomatic women with BI-RADS density category c or d were screened on the same day with FFDM and SV. Each patient's experience was assessed for perceived pain, discomfort and anxiety, discretion and modesty, overall satisfaction, and whether they would recommend it to others. The responses were measured on a Likert scale with 5 choices from strongly agree to strongly disagree, then studied by Chi-Squared analysis. Results: The mean age was 53.9 ± 9.7 yo, mostly white women (87.7%). The median BMI was 24.4. Majority had no personal history of breast cancer (97.2%), but 24.8% had a previous biopsy and almost half (46.3%) had a family history of breast cancer. Almost all patients (99.6%) completed the survey. SV was perceived as significantly more comfortable than FFDM (83.7% vs 52.2%, $p < 0.001$), was painless (94.9% vs 53.1%, $p < 0.001$), and was associated with less anxiety during the procedure (95.1% vs 79.9, $p < 0.001$). Lastly, 99.3% felt the experience was private and discreet, and 95% would recommend the SV exam to other women. Conclusion: Pain, fear, anxiety, and modesty concerns are some of the barriers preventing widespread implementation of screening breast US. This data suggests that SV, an FDA PMA approved adjunctive screening exam for women with dense breast tissue, is painless, offers a private and discreet scan that limits anxiety, and is well accepted by patients. Clinical relevance statement: SV is a novel automated US tomographic screening technology that is comfortable, well-accepted, FDA PMA approved, and will likely result in improved implementation of screening breast ultrasound in women with dense breasts.

Disclosure(s):

Mary Yamashita, MD: Delphinus Medical Technologies: Consulting Fees (e.g., advisory boards) (Ongoing)

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P3-05-02

Trends in clinical treatment of early stage ER+PR- breast cancer in the National Cancer Database

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Background Estrogen receptor positive (ER+) progesterone receptor negative (PR-) tumors are a distinct subset of breast cancers that are not well characterized. It is critical to better understand the biology of ER+PR- tumors and tailor therapy accordingly for this unique subgroup. The objective of this study is to compare the ER+PR- subgroup of breast cancer as compared to the double positive ER+PR+ group in a large, well-characterized database to determine if the tumors that are PR- are associated with higher rates of genomic testing and chemotherapy receipt. Methods We identified patients diagnosed with ER+Her2-, Stage 1-3 invasive breast cancer from 2010-2015 in the National Cancer Database. We excluded patients who received neoadjuvant therapy. Demographics and clinical characteristics for the ER+PR+ and ER+PR- groups were obtained. Differences between groups were assessed using the chi-square test. Multivariable logistic regression analysis was performed on both the node negative and node positive patients in order to identify factors independently associated with having a genomic test and receiving chemotherapy in the ER+PR+ and ER+PR- cohorts. Results Of the 363,945 eligible patients, 327,357 (89.9%) patients had ER+PR+ breast cancer and 36,588 (10.1%) had ER+PR- breast cancer. A trend towards larger tumor size in the ER+PR- population as compared to the ER+PR+ population was noted with 23.1% vs 17.3% of tumors 2-5cm and 2.2% vs 1.2% of tumors > 5cm, respectively. Higher grade was also seen in the ER+PR- group as compared to the ER+PR+ group with 27.1% versus 11.7% grade 3 tumors. In both the node negative and node positive populations, genomic testing was less likely to be sent on a PR- breast cancer than a PR+ breast cancer. When genomic testing was sent, there were more high risk Oncotype Recurrence scores (RS > 30) in the PR- group than the PR+ group. For node negative breast cancer high risk Oncotype recurrence scores were found in 32.4% of the ER+PR- population versus 5.6% in the ER+PR+ population. In the node positive cohort high risk Oncotype Recurrence scores were seen in 27.8% of the ER+PR- population as compared to 5.0% in the ER+PR+ population. Patients with discordant ER+PR- breast cancer were more likely to receive chemotherapy than their ER+PR+ counterparts in both the node negative cohort (32.2% vs 12.7%) and the node positive cohort (73.2% vs 64.5%). Conclusion There have been limited studies to date specifically focused on the ER+PR- subgroup. Patients with ER+PR- breast cancer have a higher grade, larger size, higher risk genomic testing, and

are more likely to receive chemotherapy than their ER+PR+ counterparts. Discordance in hormone receptor status contributes to a more aggressive type of breast cancer that may impact clinical and treatment decisions.

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P3-05-03

Long-term survival and intra-tumor heterogeneity of progesterone receptor expression in estrogen receptor-positive/progesterone receptor-positive premenopausal women with breast cancer

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Background: Women with estrogen receptor (ER)-positive disease have a long-term risk of distant recurrence. The poor survival of premenopausal women diagnosed with breast cancer combined with the otherwise long life expectancy makes it especially important to identify tumor characteristics associated with long-term survival. Intra-tumor heterogeneity, having cancer cells of varying characteristics across the tumor, may promote therapeutic resistance and metastatic capacity. We have previously shown that high intra-tumor heterogeneity of ER increases the risk of fatal breast cancer. To our knowledge, the relation between intra-tumor heterogeneity of progesterone receptor (PR) expression and long-term survival is not known. We aimed to study the association between intra-tumor heterogeneity of PR and long-term survival of premenopausal women in the Stockholm tamoxifen trial (STO-5), with 20-years complete follow-up.

Methods: This study was a secondary analysis of 504 ER-positive/PR-positive premenopausal women from the STO-5 trial (1990-1997). 451 women had human epidermal growth factor receptor 2 (HER2)-negative tumors. Patients were randomized to receive either 2 years of endocrine treatment (tamoxifen and/or goserelin) or no endocrine treatment. Lymph node-positive patients (n=251) also received standard chemotherapy (CMF). Immunohistochemical analysis, including estimating the proportion of tumor cells for each PR intensity level (0, 1+, 2+, or 3+), was completed in 2020. Intra-tumor heterogeneity of PR was calculated using Rao's quadratic entropy and then categorized into low and high intra-tumor heterogeneity groups, using a predefined cutoff at the second tertile. Complete long-term (20 year) follow-up was obtained from high-quality Swedish registries. Long-term distant recurrence-free interval (DRFI) was assessed using univariate Kaplan-Meier analysis and multivariable Cox proportional hazard modeling, adjusting for patient and tumor characteristics.

Results: A statistically significant difference in 20-year DRFI was seen between patients with high and low intra-tumor heterogeneity of PR in the univariate Kaplan-Meier analysis (log-rank $P < 0.01$). Survival proportions for DRFI at 20 years were 60.2% (95% CI, 53.2%-68.1%) and 73.3% (95% CI, 68.6%-78.3%) for patients with high and low PR intra-tumor heterogeneity, respectively. Analysis in patients with HER2-negative tumors yielded similar results.

In the multivariable analysis, women with high intra-tumor heterogeneity of PR had a significantly increased long-term risk of distant recurrence, compared to women with low intra-tumor heterogeneity, hazard ratio (HR)=1.49 (95% CI, 1.08-2.06). The same pattern was seen in HER2-negative women, HR=1.50 (95% CI, 1.06-2.12), see Table.

Conclusions: This study suggests an increased long-term risk of distant recurrences in ER-positive/PR-positive premenopausal women with high intra-tumor heterogeneity of PR as compared to women with low intra-tumor heterogeneity of PR, independent of HER2 status. Ongoing analyses include using deep learning for image analysis of breast cancer tumors to examine intra-tumor heterogeneity at higher resolution and for various tumor characteristics. Better understanding of tumor characteristics associated with long-term risk in premenopausal women is needed, given the poor prognosis and early onset of the disease.

Long-term risk of distant recurrence by PR intra-tumor heterogeneity and HER2 status

ER-positive/PR-positive premenopausal breast cancer patients	PR intra-tumor heterogeneity	No. patients	No. events	Crude model	Full model
				HR (95% CI)	HR (95% CI)
All patients (n=504)	High	172	67	1.53 (1.11-2.11)	1.49 (1.08-2.06)
	Low	332	87	1.00 (Ref)	1.00 (Ref)
HER2-negative patients (n=451)	High	150	58	1.55 (1.10-2.18)	1.50 (1.06-2.12)
	Low	301	77	1.00 (Ref)	1.00 (Ref)

Multivariable Cox proportional hazard regression modeling of 20-year distant recurrence-free interval (DRFI) by high and low PR intra-tumor heterogeneity. ER-positive/PR-positive and ER-positive/PR-positive/HER2-negative premenopausal women were analyzed separately. The crude model was adjusted for age, randomization year, lymph node status, and endocrine treatment. The full model was adjusted for age, randomization year, lymph node status, endocrine treatment, tumor size, Ki-67 status, and HER2 status.

Disclosure(s):

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P3-05-04

Absence of Lobular Carcinoma In Situ, a Poor Prognostic Marker in Invasive Lobular Carcinoma

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Background: Lobular carcinoma in situ (LCIS) is known to be a risk factor for the development of invasive lobular carcinoma (ILC). Recent genetic analysis indicates that LCIS is a facultative precursor of ILC. It was reported that ~50% of ILC co-occur with LCIS, however it is unclear whether patients with this co-occurrence behave similarly to patients with pure ILC.

Methods: We retrospectively searched for patients treated at MD Anderson Cancer Center with a diagnosis of stage I-III ILC in our prospectively collected electronic database. Patients were divided into 2 groups: those with ILC with co-occurring ipsilateral LCIS (ILC/LCIS) and those with pure ILC without a histologically detected co-occurring ipsilateral in situ lesion (ILC alone). We obtained data on demographics, tumor size (T), lymph nodes (N) involvement, estrogen (ER), progesterone (PR) receptor status, HER2 expression, Ki67, treatment received, distant

recurrence and survival status. The Kaplan-Meier product-limit method was used to compare distant recurrence-free survival (DRFS) and overall survival (OS) between the two groups. Multivariate analysis using Cox regression was used to assess association between co-variables and recurrence/survival.

Results: We identified 4,217 patients with stage I-III ILC treated at MDACC between 1966 and 2021. 45% of cases (n = 1,881) had co-existing LCIS . 90% of ILCs were classical and 96% of LCIS were classical. Overall, the median age was 56 years, 95% of cases were ER+, 80% PR+, 5% HER2+. 40% of cases were T1, 60% N0 and 70% of tumors with available Ki67 data had low Ki67 (< 20%). Around 65% underwent mastectomy, 20% received neoadjuvant chemotherapy, and 35% received adjuvant chemotherapy. Statistically and numerically, ILC alone tended to have more T4 and N3 disease (P < 0.001), more ER/PR negative disease (P = 0.0002), more HER2+ disease (P = 0.010), higher Ki67 (P = 0.005), more non-classical ILC subtype (P = 0.04) and more exposure to neoadjuvant chemotherapy (P = 0.0002) than the ILC/LCIS group. The median follow-up time was 6.5 years. Patients with ILC co-existing with LCIS had better DRFS (28.0 vs 14.3 years, Hazard ratio (HR) 0.53, 95% confidence interval (CI) 0.47 – 0.59, P < 0.0001) and better OS (18.9 vs 13.7 years, HR 0.62, 95% CI 0.56 – 0.69; P < 0.0001). Multivariate (MV) analysis showed the absence of LCIS to be a poor prognostic factor along with a higher T and higher N for distant recurrence and overall survival (Table 1).

Conclusion: The findings of this study suggests that the co-existence of LCIS with ILC is a good prognostic factor and that further studies are warranted to understand this phenomenon.

Table 1. Multivariate Analysis between Clinico-Pathological Variables and Distant Recurrence-free Survival/Overall Survival

	DRFS		OS	
	MV-HR	95% CI	MV-HR	95% CI
Absence of LCIS	2.361	1.810 – 3.104	1.605	1.260 – 2.051
T2	2.493	1.753 – 3.591	1.404	1.027 – 1.923
T3	2.447	1.618 – 3.725	1.492	1.018 – 2.181
T4	5.269	3.399 – 8.212	3.189	2.126 – 4.763
N1	5.579	4.061 – 7.725	2.343	1.763 – 3.110
N2	5.850	3.081 – 10.39	3.421	1.832 – 5.937
N3	10.02	6.758 – 14.86	3.181	2.148 – 4.650

Disclosure(s):

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P3-05-05

Racial disparities among patients with breast cancer receiving neoadjuvant chemotherapy therapy and impact on pathologic response: An urban, single-institution experience

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Background: Neoadjuvant systemic therapy (NAT) is typically administered to patients diagnosed with non-metastatic invasive breast cancer (IBC) with high-risk features. The goal of NAT in this setting is a pathologic complete response (pCR), meaning no residual invasive disease observed on final review of surgical pathology . It is broadly accepted that pCR may be used as a surrogate marker of predicted long term benefit of treatment and overall survival. Prior studies have demonstrated that the time interval between a diagnosis and initiating NAT may impact the overall outcome for patients.

In this study we sought to determine if there were any differences between African American (AA) patients and other races with respect to time-to-treatment (TTT) in initiating NAT. In addition, we explored the relationship between TTT and pCR rates and the factors influencing this relationship.

Methods: This is a single-institution retrospective study, all patients diagnosed with non-

metastatic IBC who were treated with NAT and completed definitive surgery between 2015-2021 were included. Demographic and clinicopathologic details were abstracted from the electronic medical record. Data was analyzed in aggregate; subgroup analysis was completed according to race and histopathologic subtype of breast cancer.

Results: A total of 392 female patients were included in this study: 59.2% White, 35.7% AA, 5.1% were of other races. The average age at the time of diagnosis was 54.1 ± 13.4 years old for the total population, and 54.0 ± 13.0 years old for AA patients.

Mean TTT was 33.4 (SD = 18.7) days for all patients, 37.0 (SD = 21.3) days for AA patients and 31.3 (SD = 16.9) days for White patients. A significant difference was identified in AA patients versus the total population (p=0.017), and particularly AA versus White patients (p=0.005).

A pCR was achieved in 40.7% of AA patients and 34.7% in the total population (p=0.050). Multivariate analysis of the factors impacting the pCR rate showed that TTT, age, tumor grade and histologic subtype independently influenced the pCR rate. However, race was not an independent factor. Among the studied factors influencing pCR rate only TTT is modifiable (Table 1).

Conclusion: The results of our study show that although AA patients achieve pCR at higher rates than the general population, they do experience delays in TTT which is an independent factor influencing pCR rates. Other factors inherently play a role in achieving a pCR, however, race is not one of them. pCR rates among AA patients may be further improved by reducing TTT and maximizing the potential benefit of neoadjuvant systemic therapy.

Table 1: Association between TTT, race, pCR.

	% Black patients	Mean TTT for total population (days/SD)	Mean TTT for Black patients (days/SD)	pCR (%)	TTT for pCR (days/SD)	
Total population	35.7	33.4 (18.7)	37.0 (21.3)*	34.7*	30.0 (16.2)*	
Subgroup Analyses	HR+	32.1	34.8 (18.6)	41.1 (19.6)*	16.0	31.0 (15.3)
	HER2+	31.4	31.7 (22.0)	29.2 (6.5)	70.6	32.7 (25.6)
	HRHER2+	39.5	34.5 (22.0)	37.4 (31.0)	45.3	28.6 (8.8)
	TNC	40.9	30.6 (12.5)	34.2 (15.6)*	37.6	28.5 (11.3)

Table 1 depicts the demographic distribution related to the mean time-to-treatment (TTT), total population and percentage of Black patients. Data was analyzed as an aggregate and subgroup analyses were conducted according to histologic subtypes. Multivariate analyses were used to explore the association between TTT and pathologic complete response (pCR). HR+=Estrogen/progesterone receptor positive; HER2+= human epidermal growth factor receptor 2 (HER2) present by IHC 3+ score or FISH ≥2 ratio; TNC=triple negative cancer. *Indicates a statistically significant finding (i.e.: p<0.05).

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P3-05-06

Prognostic impact of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis-related liver fibrosis on postoperative long-term outcomes of breast cancer

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Background: Obesity, the modern 'epidemic', has shared correlation with fatty liver disease and breast cancer. However, previous studies on the relation between fatty liver and breast cancer have shown conflicting results on the impact of fatty liver on the survival and recurrence of breast cancer patients. And there was no attempt to find out the effect of liver fibrosis, which is the consequence of fatty liver disease, on female breast cancer patients. So we attempted to

investigate the prognostic value of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis(NASH)-related liver fibrosis in patients with breast cancer undergoing surgery, using noninvasive tools like liver-to-spleen attenuation(L/S) ratio and Fibrosis-4(FIB-4) score, respectively. Methods: A total of 933 patients diagnosed with primary invasive breast cancer and receiving surgery at the university-affiliated referral center between April 2006 and December 2019 were included. After excluding patients who had significant alcohol consumption and hepatitis viral infection,838 patients were divided into two groups according to the L/S ratio of 1 measured by the preoperative low-dose computed tomography: 91 patients(10.9%) with a L/S ratio< 1 vs 747 patients(89.1%) with a L/S ratio≥1. They were also divided into two groups based on the FIB-4 score of 2.67: 804 patients (95.9%) with a FIB-4 score< 2.67 vs 34 patients (4.1%) with a FIB-4 score≥2.67. The Cox proportional hazards model was used to calculate the hazard ratio (HR) and the 95% confidence interval (CI). Results: Patients with NAFLD were older, had higher BMI, and had a higher proportion of mastectomy and hyper-transaminasemia. They showed worse overall, disease-free, and regional recurrence-free survivals compared to those without NAFLD (p=0.008, 0.043, and 0.017, respectively), but no significant differences in local recurrence-free, systemic recurrence-free, and contralateral breast cancer-free survivals. The survival outcome of breast cancer did not show any relationship with NASH-related liver fibrosis (overall survival; p=0.061, disease-free survival; p=0.557). NAFLD was a significant risk factor for mortality in multivariable analysis (HR, 2.077; 95% CI, 1.052–4.102; p=0.035). After stratifying for subtypes of breast cancer, the L/S ratio remained a significant predictor of overall, disease-free, local recurrence-free, and regional recurrence-free survivals in only the hormone receptor-positive/HER2–negative subtype (p=0.007, 0.005, 0.009, and < 0.001, respectively). Conclusion: NAFLD is significantly associated with decreased overall survival, disease-free survival and increased regional recurrence in patients with breast cancer especially the hormone receptor-positive/HER2–negative subtype. NASH-related fibrosis was not associated with survival. Therefore, NAFLD should be assessed in the preoperative setting for predicting long-term prognoses of breast cancer patients

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Primary neuroendocrine carcinoma of the breast: A case series by WHO classification in 2019

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Introduction Neuroendocrine tumours (NET) are thought to arise from cells throughout the diffuse endocrine system and can occur almost everywhere in the body. Most NETs arise from the gastrointestinal tract, lung, thymus, and pancreas. Primary neuroendocrine carcinoma (NEC) of the breast is a rare and under-recognized subtype, accounting for less than 1% of breast carcinomas. Only a few small studies and case reports have been reported and there are no clear diagnostic criteria and established treatment options. World Health Organization (WHO) classification of tumor series' fifth edition was published in 2019 and adopted 'Neuroendocrine neoplasm (NEN)' as a term encompassing all tumour classes with predominant neuroendocrine differentiation. NENs of the breast are classified into invasive ductal carcinoma (IDC) with neuroendocrine differentiation (NED), NET, and NEC of small cell or large cell types. Thus we aim to report pathologic reviews and treatment outcomes of patients with NENs of the breast at a single center. **Methods** We retrospectively screened the medical record of 34,370 patients diagnosed with breast cancer from 2007 to 2022 by Corporate Data Warehouse (CDW) and revealed there were 22 patients diagnosed with primary breast NEN. The pathologist reviewed the pathology slides and reclassified the diagnosis according to the WHO classification of tumor series' fifth edition. Clinical characteristics, treatment modalities, and therapeutic outcomes were reviewed retrospectively. **Results** We reviewed pathology slides of 22 patients with histologically proven diagnoses of primary breast NEN from 2007 to 2022. We found only 8 patients meet the criteria of primary breast NEC (large cell 2, small cell 6), 3 patients with NET, and 3 patients with IDC with NED. We excluded 8 patients who did not fulfill the criteria of NEN. The median age of NEN was 48.5 years (range, 31-70) and 6 patients (42.9%) were postmenopausal women. The median follow-up duration was 25.3 months (Interquartile range(IQR), 15.0-54.7). All patients underwent surgery, 3 patients underwent a mastectomy and 11 patients underwent breast-conserving surgery (BCS) with a curative aim. Five patients had lymph node metastasis. There was no expression of the human epidermal growth factor receptor 2 (HER2) in all 14 cases. Hormone receptor expression was shown in 4 of NECs (50%) and all NETs or IDC with NED patients. Patients with primary breast NEC had a median recurrence-free period (RFP) of 14.6 months (95% confidence interval (CI), 11.0-18.2) and median overall survival (OS) of 52.1 months (95% CI, 0.0-120.0). Patients with NET or IDC with NED had an overall favorable outcome, none of the patients died and only one patient with IDC with NED experienced disease progression. The median PFS and OS were not reached in NET or IDC with NED subgroups. **Conclusion** NETs are rare tumours with a wide range of clinical presentations according to the site of involvement. Primary breast NENs are extremely rare and there are no specific guidelines for treatment. NENs are often underdiagnosed, as neuroendocrine markers are not routinely tested in breast cancer. In this retrospective single-center study, the incidence of primary breast NENs was 0.04% (14 of 34,370 patients) and primary breast NEC was associated with poor prognosis compared with breast NET or IDC with NED. Identifying innovative treatment strategies is needed to overcome poor outcomes of primary breast NEC.

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P3-05-08

Prevalence and prognosis of ER-loss in advanced invasive lobular carcinoma

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Introduction: Estrogen receptor (ER) loss occurs in about 20% of recurrent breast cancers (BC) and is associated with unresponsiveness to endocrine therapy (ET) and poor prognosis. Prior studies evaluating ER-loss included predominately patients with invasive ductal carcinoma (IDC), and therefore the impact of ER-loss in invasive lobular carcinoma (ILC) is unknown. In this retrospective analysis, using real-world data, we aimed to determine the prevalence and clinical significance of ER-loss in ILC. **Methods:** Advanced BC were molecularly profiled at Caris Life Sciences (Phoenix, AZ) with NextGen Sequencing of DNA (592-gene panel or whole-exome sequencing), RNA (whole transcriptome sequencing, WTS) and immunohistochemistry (IHC) of select markers. A large real-world evidence (RWE) database combining Caris' molecular data with clinical information obtained from insurance claims data (CODEai) was interrogated and overall survival (OS) was calculated from time of tissue collection to last patient contact. A tumor was considered to have ER-loss if therapies approved only for ER-positive BC were prescribed prior to obtaining a negative ER IHC result. OS was compared using Kaplan-Meier estimates for defined patient cohorts; significance was determined as p values < 0.05. For molecular analyses, Fisher-Exact or Chi-Square tests were used to determine p values. Correction for multiple comparisons was performed using Benjamini-Hochberg to calculate q values. **Results:** The RWE database included 24,824 patients with advanced BC. At the time of tissue collection for molecular profiling, 6,786 advanced BC patients had been previously treated with ET (with or without mTOR or CDK4/6 inhibitors), of whom 1,338 had data available on histologic classification and ER IHC. The final analytical cohort included 263 patients with ILC and 1,075 with IDC. ER-loss was identified in 11.4% of ILC (n=30/263) and 19.6% (n=210/1075) of IDC (p=0.0017). In ILC, ER-loss was associated with significantly worse OS (HR: 1.75, 95%CI: 1.10-2.79, p=0.016) compared with no ER-loss. In the cohort of patients with ER-loss, patients with ILC had significantly worse OS compared with IDC (HR=2.03, 95% CI: 1.267-3.251, p=0.003). Further, when 1,016 tumors with ER-loss (regardless of histology) were stratified by the median OS (mOS=11mo), positive PD-L1 expression (34% vs. 22%, p=0.04, q=0.22), HER2 IHC positivity (16% vs. 7.8%, p=0.003, q=0.08) and HER2 amplification (16% vs. 4.7%, p=0.0006, q=0.04) were enriched in patients with longer mOS; while amplification of TEFB (0.38% vs. 2.6%, p=0.047, q=0.23) and MYB (0.38% vs. 2.6%, p=0.047, q=0.23) were enriched in patients with shorter mOS. WTS identified 197 differentially expressed genes, the majority of which were enriched in patients with longer mOS (q< 0.05). **Conclusions:** In this large real-world dataset, ER-loss likely occurred in 11.4% of ILC and was associated with worse OS compared to both patients with IDC and ER-loss and ILC without ER-loss. Our analysis had several limitations; notably, our definition of ER-loss was based on prior treatment, we could not distinguish between de novo or recurrent metastatic disease and time of tissue collection was not standardized during the course of treatment. Thus, additional studies are needed to confirm these findings. However, this study does suggest that ER-loss occurs in a subset of patients with ILC and has poor prognostic implications.

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LAG3+ Tumor Infiltrating Lymphocytes Predict Outcome in Treatment Naïve Triple Negative Breast Carcinoma

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Significance: Triple negative breast carcinoma (TNBC), characterized by lack of estrogen (ER) and progesterone receptors (PR) and absence of Her2/neu (Her2) receptor amplification, typically follows an aggressive course that includes high relapse rates, rapid progression, and poor outcome. Advances in treatment have been limited by molecular heterogeneity within TNBCs and lack of effective molecular targets. Although a subset of TNBC associated with tumor infiltrating lymphocytes (TILs) is more immunogenic than other breast cancers, response to immunotherapy has been variable and reported in only 10-40% of cases. Identification of prognostic immune biomarkers will identify novel therapeutic targets and facilitate appropriate patient selection for therapy. Aim: To analyze the immune gene expression profile in TNBC and identify a prognostic marker. Methods: Targeted mRNA sequencing was performed on formalin fixed paraffin embedded whole sections from 30 treatment naïve TNBC with TILs (15 cases with a favorable outcome (recurrence free overall survival (OS) ≥ 5 yrs) and 15 with unfavorable outcome (never disease free or dead of disease in < 5 yrs) using the HTG Edge Seq Assay (HTG Molecular Diagnostics, Inc. Tucson AZ) to analyze the differential expression of 1392 immune related genes in their Precision Immuno-Oncology Panel. The top 40 up- and down-regulated DE genes with adjusted p-value of < 0.001 were then validated against the TNBC mRNA profiles in The Cancer Genome Atlas (TCGA) database. LAG3 was one of four genes that showed significant differential expression in both data sets. We used immunohistochemistry (IHC) (Rabbit monoclonal AntiLAG3 antibody, Abcam plc.) to analyze LAG3 expression in whole sections from 57 consecutive TNBCs where tumor excision had been the first line treatment. All patients were female, age 29-89 years (median 55 yrs). The

infiltrating ductal carcinomas varied from 0.6 to 9.0 cm (median 2.6 cm). All tumors were ER-, PR-, Her2- with a median Ki67 of 42%. 26 patients had metastatic carcinoma in 1-17 lymph nodes (median 2). Two patients had metastatic disease at presentation. Disease free survival (DFS) varied from 0 to 114.8 months (median 81.4 mos.), and overall survival (OS) varied from 7.6 to 114.8 months (median 81.5 mos.). LAG3 expression was categorized as negative (0), low (1+) and high (2+). The student t-test was used to correlate LAG3 expression with DFS and OS. Results: Differential expression analysis from our data set yielded 222 statistically significant differentially expressed genes. Validation against the TCGA TNBC data set revealed 4 common genes, one of which is LAG3. Only TILS showed LAG3 expression by IHC: 10 cases no expression, 17 low expression and 29 high expression. Median DFS and OS in TNBC with no LAG3 expression was 32.3 and 55.2 months, in TNBC with low expression 83.3 and 81.1 and those with high expression was 82 and 82.1 month. Median DFS and OS in LAG3 negative cases was significantly different from those in LAG3 positive cases ($p=0.038$, $p=0.013$) and between LAG3 0 and LAG3 2+ positive cases ($p=0.002$, $p=0.0018$). No difference in either median DFS or OS was seen when LAG3 1+ and LAG3 2+ cases were compared. Conclusions: 1. LAG3 is a prognostic marker for TNBCs. 2. LAG3 is expressed only on TILS and shows heterogenous expression. 3. TNBC with no LAG3 expression had a median survival of 32 months, suggesting they might benefit from more aggressive therapy than TNBC that express LAG3. 4. Confirmation of these results requires a larger TNBC cohort.

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P3-05-10

Disease features, genomic profiles and outcomes of younger vs. older Chinese hormone receptor positive (HR+), HER2 negative (HER2-) metastatic breast cancer (MBC) patients

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Background: Breast cancer in younger women has been characterized as a more aggressive disease with relatively poor outcomes compared to breast cancer in older women. This pattern has been attributed to a variety of clinicopathologic characteristics including the enrichment of aggressive HER2+ and TNBC subtypes in younger patients. However, similar to older breast cancer patients, the majority of young breast cancer patients are HR+/HER2-. Here we have evaluated the clinicopathologic characteristics and genomic profiles of real-world HR+/HER2-MBC patients to examine the determinants of outcome for younger vs. older patients in this subtype. Patients and Methods: This study included 65 Chinese patients presenting with HR+/HER2- MBC at the Peking University Cancer Hospital. Blood samples were collected upon metastatic disease diagnosis before treatment and profiled with the targeted 152-gene PredicineCARE™ sequencing panel. Fourteen patients were < 40 years, 19 were 40-50 years, and 32 were > 50 years at the time of primary cancer diagnosis. Kaplan-Meier survival analysis was performed to analyze outcomes including overall survival (OS), disease free survival (DFS) and progression free survival (PFS) in association with clinicopathologic and genomic variables. OS was also evaluated in association with age in separate multivariate models using Cox proportional hazards regression. Results: Significant variation across age groups was observed for several clinicopathological features, including molecular subtype classification ($p = 0.045$),

de novo Stage IV disease ($p = 0.011$), type of adjuvant endocrine therapy ($p = 5.56E-06$), resistance to adjuvant endocrine therapy ($p = 0.015$) and receipt of adjuvant chemotherapy ($p = 0.042$). Luminal B status was most frequent in patients < 40 years (92.31%), whereas de novo Stage IV disease was more prevalent in patients > 50 years (37.5%). Aromatase inhibitors (AIs) were administered as adjuvant endocrine therapy (ET) to 73.68% of women > 50 years vs. 16.67% and 0% of women aged 40-50 years and < 40 years, respectively. Resistance to adjuvant ET was observed in 23.08% of patients < 40 years but was not observed in the other age groups. Adjuvant chemotherapy was received by a higher proportion of patients in the 40-50 year age group (94.44%) compared to patients < 40 years (69.23%) and patients > 50 years (60%). No differences in somatic gene alteration frequencies were observed across age groups, menopausal status, germline mutation status or tumor grade. However, a higher frequency of FGFR1 alterations was observed in patients classified as Luminal B vs. A ($p = 0.048$). Comparison of profiles across women who received adjuvant ET revealed a higher prevalence of FGFR1 ($p = 0.012$), ATM ($p = 0.047$) and CCND2 ($p = 0.04$) alterations in patients treated with AIs vs. SERMS. In addition, a higher frequency of APC alterations was observed in patients with high ($\geq 20\%$) vs. low ($< 20\%$) Ki67 index ($p = 0.035$). At the univariate level OS was significantly associated with age ($p = 0.039$). OS was shortest in patients > 50 years, intermediate in patients < 40 years, and longest in patients 40-50 years. Across all patients, shorter OS was also associated with de novo Stage IV disease ($p = 0.0001$), Luminal B subtype ($p = 0.008$), adjuvant ET with AIs vs SERMS ($p = 0.028$) and the presence of an FGFR1 ($p = 0.028$) or CCND2 ($p = 0.033$) alteration. In multivariate analyses, OS remained significantly longer for patients aged 40-50 years after adjustment for de novo Stage IV disease, Luminal B subtype and FGFR1 status (all $p < 0.05$). Conclusions: In this group of real-world HR+/HER2- MBC breast cancer patients, younger age was not associated with worse outcomes. While current guidelines recommend treatment decisions based on tumor biology rather than age, young HR+ breast cancer patients are more likely to receive chemotherapy. Our findings support the development of biomarker-driven treatment strategies for these patients.

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Breast cancer characteristics in premenopausal women by contraception method

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INTRODUCTION: Our knowledge regarding the levonorgestrel intra-uterine device (LNG-IUD) and breast cancer (BC) risk is limited. As the LNG-IUD is a widely used contraception method, we here explored receptor expression in BC, in women < 56 years, by having a LNG-IUD at diagnosis. We aim to validate the findings of a previous cohort treated in the University Hospitals Leuven, where we observed proportionally more progesterone receptor (PR), lower human epidermal growth factor receptor 2 (HER2) expression and more ER+PR+HER2- subtypes in LNG-IUD users compared to non-LNG-IUD users. **MATERIALS AND METHODS:** We conducted a retrospective observational monocentric study from 2015 until 2020. We included patients < 56 years consulting the University Hospitals Leuven for primary invasive BC, who were treated with primary breast surgery or neoadjuvant therapy. We compared patient and tumor characteristics, especially receptor subtypes in LNG-IUD users at diagnosis with non- LNG-IUD users. Group comparisons with regards to receptor subtypes were performed by the Chi-square test, all tests were evaluated at a two-sided 5% significance level. **RESULTS:** Of the 1347 patients with BC included in this study, 272 had a LNG-IUD at diagnosis. The LNG-IUD users were more likely ER (85.29% vs 77.77%, p=0.006) and PR positive (80.88% vs 70.95%, p< 0.001) compared to the control group. Additionally, we observed more ER+PR+HER2- (68.75% vs 58.62%, p=0.002) and fewer ER-PR- HER2- (10.29% vs 15.66%, p=0.025) subtypes when comparing with the control group. **CONCLUSION:** This internal validation study confirmed invasive BC, diagnosed in women under age 56, to be more likely PR+ and ER+PR+HER2- if they used a LNG- IUD at BC diagnosis when compared to non-LNG-IUD users.

Disclosure(s):

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5:00 PM - 6:15 PM

P3-05-12

A matched cohort study of the prognosis of early breast cancer in patients with Li-Fraumeni syndrome

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Background: Patients with germline TP53 pathogenic variants (Li-Fraumeni syndrome - LFS) have an increased risk of breast cancer, which is the most common type of cancer in premenopausal women with LFS. These women are also at risk of other second malignancies, including radiotherapy-induced malignancies. On the other hand, little is known about the prognosis of breast cancer in patients with LFS or if the disease behavior differs from non-hereditary BC. The objective of this study was to characterize the phenotype and prognosis of early BC in patients with LFS compared to a matched cohort of patients without germline pathogenic variants (PV) related to BC.

Methods: This retrospective study evaluated patients with early BC treated in an academic cancer center from Dec 1999 to Mar 2022. The LFS cohort included consecutive patients with BC who harbored a PV or likely PV of TP53. The matched control cohort (2:1) included patients with BC with no germline PV in a panel test. Primary endpoint was disease-free survival (DFS).

Since LFS is associated with an increased risk of new primary malignancies, only locoregional and distant BC recurrence were considered as events in the DFS analysis. Secondary endpoints included response to systemic therapy, sites of recurrence, and breast cancer-related deaths.

Results:

Forty-six patients with LFS were evaluated; the control cohort included 91 matched patients. In the LFS cohort, 14 different PV or likely PV were identified, with TP53 p.R337H being the most common (n=32). Median age was 40 years in both groups. In the LFS cohort, 35% of the pts had HER2-positive BC compared to 21% in the control cohort. Primary tumors greater than 5 cm were observed in 15% of pts in the LFS cohort and 25% of pts in the control cohort. Positive lymph nodes were observed in 11% and 14%, respectively.

Among 15 pts with LFS who received neoadjuvant chemotherapy, all (100%) had a response, with 5 (33%) complete responses. Thirty-five patients in the control group received neoadjuvant chemotherapy: 83% responded, with 11 (31%) presenting a complete response.

With a median follow-up of 43 months, 5-year DFS rates were 82.6% (95% CI 65.1 – 91.9%) in the LFS cohort and 91.5% (95% CI 79.1 – 96.6%) in the control cohort (P=0.427). Rates and sites of recurrence, new primary BC, and deaths are detailed in the table.

Conclusions:

In addition to a higher risk of new primary breast cancer, LFS patients with early breast cancer had numerically higher rates of locoregional and distant recurrence in comparison with a matched cohort. Nevertheless, further studies are required to understand if these differences are due to tumor behavior particularities or to differences in therapeutic management.

Recurrence and death events

Characteristic	No of Patients (%)	
	TP53 mutated (N = 46)	TP53 Wild-type (N = 91)
Recurrence	6 (13%)	7 (7.7%)
Local only	1 (2.2%)	1 (1.1%)
Distant only	4 (8.7%)	6 (6.6%)
Both (local and distant)	1 (2.2%)	0 (0%)
New primary breast cancer	6 (13%)	1 (1.1%)
Death	5 (10.9%)	4 (4.4%)
Breast cancer-related death	2 (4.6%)	1 (1.1%)

**Fisher exact test.

Disclosure(s):

Vanessa Petry, MD: AstraZeneca: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Financial support for educational programs and symposia (Ongoing); Daichii Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Financial support for educational programs and symposia. (Ongoing); GSG: Contracted Research (Ongoing); Libbs: Financial support for educational programs and symposia (Ongoing); MSD: Contracted Research (Ongoing); Novartis: Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Financial support for educational programs

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5:00 PM - 6:15 PM

P3-05-13

INFLUENCE OF METABOLIC SYNDROME ON OVERALL SURVIVAL (OS), DISEASE FREE SURVIVAL (DFS) AND INVASIVE FREE SURVIVAL (IFV) IN A COHORT OF PATIENTS TREATED FOR BREAST CANCER IN BRAZIL

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Introduction: Metabolic syndrome can be defined as a set of conditions - central obesity (waist circumference), elevated blood pressure, reduced HDL cholesterol, increased triglycerides and glucose intolerance - which is known to be associated with a higher risk in the development of cardiovascular disease and type 2 diabetes. It affects approximately 30% of the population of women over 50 years of age. In view of the risk factors described above, it is important to seek, in addition to the screening recommended by the Ministry of Health (a mammogram every two years in women aged 50 to 69 years), ways to reduce the risk of breast cancer with regard to behavioral factors. Practicing the maintenance of adequate weight and physical activities can contribute to the reduction of this pathology. Therefore, even in the pathophysiology of breast

cancer, its relationship with the metabolic syndrome is seen, which is often the cause - and even consequence - women treated for breast cancer seem to have an additional risk of metabolic syndrome, resulting from excess adiposity. and effect of treatments.

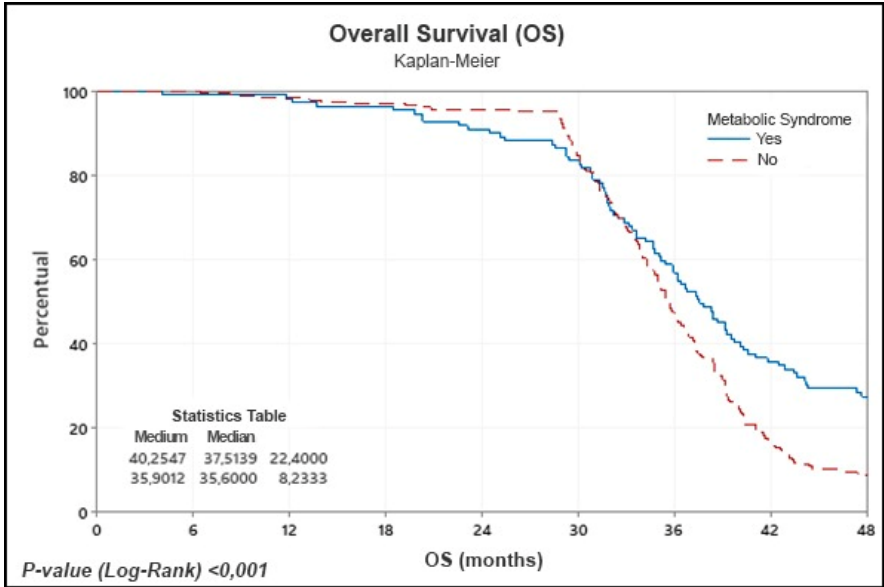
Objectives: To evaluate the relationship between metabolic syndrome at the diagnosis of breast cancer and overall survival, disease-free survival and invasive disease-free survival.

Methodology: Retrospective longitudinal observational study of the cohort type carried out in the Mastology sector of the Gynecology and Obstetrics Service of the Hospital do Servidor Público Estadual de São Paulo "Francisco Morato Oliveira. We evaluated the rates of local recurrence, distant metastases and overall survival of patients with malignant breast cancer in each group.

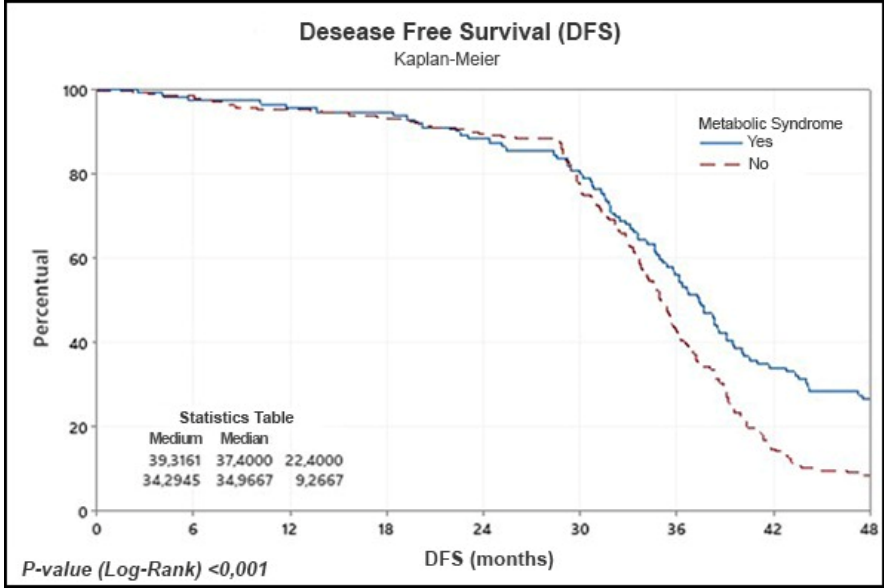
Results: From January 2017 to December 2020, 375 patients underwent surgical treatment for breast cancer at the Hospital do Servidor Público Estadual, of which 25 were excluded due to loss of follow-up, 10 due to incomplete data and 5 due to diagnosis of metastases. Thus, 335 patients were eligible for the study, with a mean age of 63.4 ± 1.4 years, and a mean follow-up time of 48 ± 1.4 years. Metabolic syndrome (MS) is present in 109 (32.5%) patients, while 226 (67.5%) do not have MS. Regarding the characteristics of prognostic factors, that is, KI 67, molecular classification and staging, in table 3 we can observe that patients with metabolic syndrome have a very similar distribution, while those without MS have a KI 67 $\geq 14\%$ in 62.4% of the patients. patients with a significant difference. The molecular profile in MS patients is 39.4% Luminal A patients and 42.5% Luminal B patients without MS, with a significant difference in distribution. Regarding clinical staging, patients with MS have initial clinical stage I and IIA in 54.1%, and advanced stage IIB 20.2% III 25.7%, while patients without MS have initial clinical stage 65%, advanced stage IIB 11.1% III 23.9, results with a significant difference. When we evaluated the presence of obesity as a factor of worsening of prognostic factors, we did not find significant differences. We evaluated the temporal outcomes of overall survival, disease-free survival, and invasive disease-free survival. The overall sample survival was 37.3 years with a CI 1.1 years, disease-free survival was 35.9 years with a CI 1.2 years, and invasive disease-free survival was 36.9 years with CI 1.3 years. When we compared these outcomes with the presence of MS, we observed a significant difference in all outcomes.

Conclusions: The presence of MS at diagnosis does not worsen overall survival, disease-free survival or invasive disease-free survival.

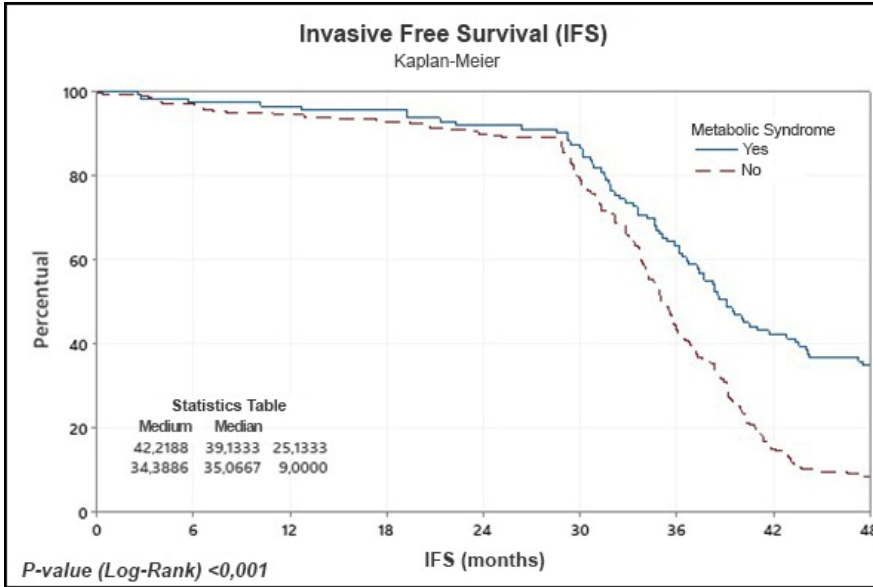
Overall Survival (OS) for Breast Cancer and Metabolic Syndrome



Disease Free Survival (DFS) for Breast Cancer and Metabolic Syndrome



Invasive Free Survival (IFS) for Breast Cancer and Metabolic Syndrome



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5:00 PM - 6:15 PM

P3-05-14

Clinicopathological features of early breast cancer in Japanese premenopausal women

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Background

Breast cancer incidence is constantly increasing in Japan. The age-specific incidence rates (ASIRs) of breast cancer shows two peaks, at ages 45-49 and 60-64, in Japan. Therefore, the incidence rate of breast cancer in Japanese premenopausal women is higher compared to the Western countries. In our study, we clarified the clinicopathological characteristics of Japanese premenopausal breast cancer.

Patients and Methods

The total of 1,220 premenopausal breast cancer patients treated for early breast cancer, at stage 0-III, between 2010 and 2021. The patients were divided into three age groups; aged under 40 (group A, n=258, 21.1%), aged 40 to 45 (group B, n=428, 35.1 %), and aged 46 and over (group C, n=533, 43.7%). Information regarding the clinicopathological characteristics was collected from the medical records.

Result

Significantly longer periods from menarche to the breast cancer onset ($p < 0.0001$), larger number of history of pregnancy ($p < 0.0001$), and higher BMI (25 or higher) ($p = 0.0091$), and more habitual drinking histories ($p = 0.0029$) were recognized in group C. In premenopausal onset, ER-positive status is higher ($p = 0.0022$), the histological grade is lower ($p = 0.0094$), as age increases, and more negative PgR status ($p = 0.0019$), and more triple negative breast cancer ($p = 0.0002$) were shown in group A. Hormone receptor-positive HER2-negative breast cancers under 45 years of age (group A, B) were more likely to receive neoadjuvant chemotherapy than those aged 46 years and older (group C) ($p = 0.0077$), but there was no age-related difference for other subtypes. The association between clinicopathological factors and

distant relapse-free survival (DRFS) in each age group was analyzed. is associated with higher grades (group A, p=0.0638 , group B, p=0.0208, group C, p=0.0006) , negative PgR status (group A, p=0.0379,group B, p=0.0683,group C, p=0.0042), and lower ER expression (group B, p=0.0395 group C, p=0.0021) were significantly associated with poor DRFS. Similarly, in overall survival, higher grades (group A, p=0.0257,group B, p=0.0027,group C, p=0.0111) ,negative PgR status (group A, p=0.0162,group B, p< 0.0001,group C, p=0.0003), and lower ER expression (group C, p=0.0003) were significantly poor prognosis. In univariate analyses, higher grade, negative PgR status, and ER negative/low-positives were risk factors, and in multivariate analyses, higher grade was a risk factor for poor prognosis

Conclusion

We found that there are many clinicopathological characteristics related to poor prognosis in premenopausal breast cancer patients aged under 40, such as low or negative ER expression, higher histological grade, and negative PgR status.

clinicopathological characteristics-1

premenopausal N=1220				
	age<40 n=258 (21.1)	40-45 n=428 (35.1)	46- n=533 (43.7)	p
median age (range)	36 (21-39)	43 (40-45)	49 (46-60)	
from menarche to onset (median age range)				
>20 years (31: 21-35)	57 (22.2)	0	0	<0.0001
21-30 years (40: 31-45)	200 (77.8)	241 (56.8)	0	
31years < (48: 41-60)	0	183 (43.2)	526 (100)	
Number of pregnancy				
median number of pregnancy (range)	1 (0-7)	2 (0-8)	2 (0-8)	
done	156 (60.5)	318 (74.5)	432 (81.1)	<0.0001
none	99 (38.4)	107 (25.1)	99 (18.6)	
unknown	3 (1.2)	2 (0.5)	2 (0.4)	
Number of birth				
median number of birth (range)	1 (0-5)	1 (0-5)	2 (0-5)	<0.0001
0	114 (44.2)	129 (30.2)	118 (22.1)	
1,2	116 (45.0)	234 (54.8)	327 (61.4)	
3,4	25 (9.7)	61 (14.3)	86 (16.1)	
5-	2 (0.8)	2 (0.5)	2 (0.4)	
unknown	1 (0.4)	1 (0.2)	0	
BMI				
-18.4	34 (13.2)	57 (13.4)	53 (9.9)	0.0091
18.5-24.9	193 (74.8)	316 (74.0)	370 (69.4)	
25.0-29.9	22 (8.5)	40 (9.4)	85 (16.0)	
30-	9 (3.5)	14 (3.3)	25 (4.7)	
History of smoke				
past	60 (23.3)	72 (16.9)	87 (16.3)	0.219
continuation	23 (8.9)	35 (8.2)	45 (8.4)	
none	175 (67.8)	317 (74.4)	400 (75.1)	
unknown	0	2 (0.5)	1 (0.2)	
Alcohole				
habitually	26 (10.1)	56 (13.1)	100 (18.8)	0.0029
sometimes	113 (43.8)	167 (39.1)	185 (34.7)	
totally not	118 (45.7)	198 (46.4)	247 (46.3)	
unknown	1 (0.4)	6 (1.4)	1 (0.2)	
Breast cancer family history				
have	184 (71.3)	325 (76.1)	422 (79.2)	0.0486
no	70 (27.1)	99 (23.2)	101 (19.0)	
unknown	4 (1.6)	3 (0.7)	10 (1.9)	
ER status (PS)				
negative (<1%)	22 (8.5)	40 (9.4)	44 (8.3)	0.0022
low-positive (1-10%)	14 (5.4)	7 (1.6)	10 (1.9)	
positive (11%-)	205 (79.5)	361 (84.5)	468 (87.8)	
unknown	17 (6.6)	19 (4.5)	11 (2.1)	
PgR status (PS)				
negative	47 (18)	49 (11.5)	70 (13.1)	0.0019
positive	194 (75.2)	360 (84.3)	452 (84.8)	
unknown	17 (6.6)	18 (4.2)	11 (2.1)	
HG				
1	53 (26.1)	88 (27.9)	141 (32.3)	0.0094
2	82 (40.4)	142 (44.9)	205 (47.0)	
3	68 (33.5)	86 (27.2)	88 (20.2)	
unknown	0	0	2 (0.5)	
Subtype				
HR+ /HER2-	118 (45.7)	226 (52.9)	310 (58.2)	0.0002
HR+ /HER2+	35 (13.6)	45 (10.5)	33 (6.2)	
HR- /HER2+	13 (5.0)	9 (2.1)	15 (2.8)	
HR- /HER2-	24 (9.3)	20 (4.7)	21 (3.9)	
unknown	68 (26.4)	127 (29.7)	154 (28.9)	

clinicopathological characteristics-2

pathological tumor size (prior surgery)					
	pTis	27 (13.7)	71 (19.9)	69 (14.5)	0.4185
	pT1	116 (58.9)	202 (56.7)	280 (59.0)	
	pT2	49 (24.9)	77 (21.6)	116 (24.4)	
	pT3-	5 (2.5)	6 (1.7)	10 (2.1)	
NAC trial rate		60 (23.3)	68 (16.0)	55 (10.4)	<0.0001
pathological tumor size (NAC)					
	pTis	17 (28.3)	21 (31.8)	13 (23.6)	0.6114
	pT1	27 (45.0)	25 (37.9)	31 (56.4)	
	pT2	10 (16.7)	14 (21.2)	7 (12.7)	
	pT3-	6 (10.0)	6 (9.1)	4 (7.3)	
pathological node status (prior surgery)					
	pN0, pN1mi	149 (76.6)	279 (79.7)	366 (78.5)	0.7065
	pN1	34 (17.7)	54 (15.4)	67 (14.4)	
	pN2	9 (4.7)	12 (3.4)	22 (4.7)	
	pN3	2 (1.0)	5 (1.4)	11 (2.4)	
pathological node status (NAC)					
	pN0, pN1mi	31 (51.7)	46 (67.7)	34 (63.0)	0.0874
	pN1	14 (23.3)	16 (23.5)	14 (25.9)	
	pN2	11 (18.3)	4 (5.9)	6 (11.1)	
	pN3	4 (6.7)	2 (2.9)	0	
NAC (HR+/HER2-)					
	done	22 (18.6)	37 (16.4)	28 (9.1)	0.0077
	none	96 (81.4)	189 (83.6)	281 (90.9)	
	pCR	4 (18.2)	5 (13.5)	1 (3.3)	0.164
	non-pCR	18 (81.8)	32 (86.5)	29 (96.7)	
NAC (HR+/HER2+)					
	done	18 (51.4)	18 (40.0)	13 (39.4)	0.5117
	none	17 (48.6)	27 (60.0)	20 (60.6)	
	pCR	6 (33.3)	12 (66.7)	6 (46.2)	0.1266
	non-pCR	12 (66.7)	6 (33.3)	7 (53.9)	
NAC (HR-/HER2-)					
	done	8 (61.5)	4 (44.5)	8 (53.3)	0.7286
	none	5 (38.5)	5 (55.6)	7 (46.7)	
	pCR	4 (50.0)	1 (25.0)	5 (62.5)	0.4603
	non-pCR	4 (50.0)	3 (75.0)	3 (37.5)	
NAC (HR-/HER2+)					
	done	12 (50.0)	9 (45.0)	6 (28.6)	0.3143
	none	12 (50.0)	11 (55.0)	15 (71.4)	
	pCR	3 (25.0)	3 (33.3)	0	0.1612
	non-pCR	9 (75.0)	6 (66.7)	6 (100)	
Adjuvant chemotherapy					
	done	115 (44.6)	158 (37.0)	191 (35.8)	0.0526
	none	143 (55.4)	269 (63.0)	342 (64.2)	
Adjuvant endocrine therapy					
	done	188 (72.9)	300 (70.3)	409 (76.7)	0.073
	none	70 (27.1)	127 (29.7)	124 (23.3)	
Ovarian function suppression (ER+)					
	done	23 (9.8)	19 (5.0)	4 (0.8)	<0.0001
	none	211 (90.2)	364 (95.0)	477 (99.2)	

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5:00 PM - 6:15 PM

P3-05-15

Clinical significance of breast cancer resistance protein (BCRP) quantified by fluorescence nanoparticle in breast cancer patients undergoing neoadjuvant chemotherapy

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Breast cancer resistance protein (BCRP), also known as ATP-binding cassette transporter G2 (ABCG2), is associated with chemotherapy resistance. BCRP is also implicated in breast cancer stem cells and has been reported as a poor prognostic factor. However, the relationship of BCRP levels in breast cancer tissues with chemotherapy resistance and prognosis has not been clarified to date. Our laboratory recently developed nanoparticles suitable for the quantitative immunohistochemical (IHC) method called phosphor-integrated dots (PIDs). Using PID-based IHC (IHC-PIDs), many biomarker proteins can be visualized and quantitatively analyzed at the single-particle level in paraffine-embedded, formalin-fixed tumor samples. We aimed to evaluate the correlation between quantitatively analyzed BCRP expression and prognosis in breast cancer tissue samples using immunohistochemistry with IHC-PIDs. Thirty-seven Japanese patients diagnosed with invasive ductal carcinoma of the breast who underwent mastectomy and lymph node dissection at Tohoku University Hospital (Sendai, Japan) between 2004 and 2010 were included. All patients had undergone NAC and were pathologically diagnosed with non-pathological complete response or progressive disease and

lymph node metastasis postoperatively. The patients were followed up within a median of 10.1 years (range, 1.1–18.2 years). Among the thirty-seven patients, twenty-eight patients had core needle biopsy specimens taken before NAC. BCRP levels in breast cancer tissue and metastatic lymph nodes were quantitatively detected after preoperative chemotherapy and core needle biopsy. Biomarker assay with IHC-PIDs showed high accuracy for quantitative assessment of BCRP with low expression. The optimal PT+LN BCRP cut-off score for predicting survival was 27.4, with a sensitivity of 60.6% and a specificity of 77.3%. BCRP expression in PT+LN samples was dichotomized into high and low groups at this cutoff value, and OS was compared between these group. The results showed that OS was significantly worse in the high BCRP-expression group (log-rank $p=0.0089$). In conclusion, high BCRP levels are associated with poor prognosis in patients with breast cancer with residual tumors within the primary tumor and lymph nodes after preoperative chemotherapy. These findings provide a basis for further appropriate adjuvant therapy in these patients.

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P3-05-18

Unravelling the clinicopathological and functional significance of Replication Protein A (RPA) heterotrimeric complex in sporadic breast cancers

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Unravelling the clinicopathological and functional significance of Replication Protein A (RPA) heterotrimeric complex in sporadic breast cancers Mashael Algethami¹, Michael S Toss^{1,4}, Juliette Brownlie¹, Corinne L Woodcock^{1,2}, Chandar Jaipal¹, Ahmed Shoqafi¹, Katia A Mesquita¹, Adel Alblihy^{1,3}, Andrew R Green¹, Nigel P Mongan^{1,5}, Emad A Rakha^{1,4}, Jennie N Jeyapalan^{1,2} and Srinivasan Madhusudan^{1,6} ¹ Nottingham Biodiscovery Institute, Academic Unit for Translational Medical Sciences, School of Medicine, University of Nottingham, University Park, Nottingham NG7 2RD, UK. ² Faculty of Medicine and Health Sciences, Centre for Cancer Sciences, University of Nottingham, Sutton Bonington Campus, Sutton Bonington, Leicestershire LE12 5RD, UK ³ Medical Center, King Fahad Security College (KFSC), Riyadh 11461, Saudi Arabia. ⁴ Department of Pathology, Nottingham University Hospital, City Campus, Hucknall Road, Nottingham NG5 1PB, UK. ⁵ Department of Pharmacology, Weill Cornell Medicine, New York, NY, 10065, USA ⁶ Department of Oncology, Nottingham University Hospitals, Nottingham NG5 1PB, UK.

Introduction: Replication Protein A (RPA) is a critical single-stranded DNA (ssDNA)-binding protein that coats and protects exposed ssDNA from endogenous nucleases. RPA is a heterotrimeric complex consisting of RPA1 (70kDa), RPA2 (32kDa), and RPA3 (14kDa) subunits. RPA provides a platform for recruitment of factors required during replication, checkpoint regulation, DNA repair [including homologous recombination (HR), nucleotide excision repair (NER), base excision repair (BER) and mismatch repair (MMR)], telomere maintenance and retro-transposition. To understand the role of RPA in breast cancer pathogenesis we conducted a comprehensive genomic, transcriptomic, bioinformatic, proteomic and preclinical study. **Patients and methods:** RPA1, RPA2 and RPA3 protein expression was evaluated in 4221 primary invasive breast carcinomas and 776 breast ductal carcinoma in situ (DCIS). Transcriptomic investigation was completed in the METABRIC cohort (n=1980). Detailed bioinformatics was conducted in the TCGA cohort (n=1090). RPA deficient breast cancer cell lines were tested for Cisplatin, Palbociclib and Olaparib sensitivity. **Results:** RPA1, RPA2 and RPA3 loss is frequent in DCIS and linked to aggressive phenotype (including high grade, ER and PR negativity) (all p values < 0.01). DCIS with low RPA1 was also associated with poor local recurrence-free interval (p< 0.00001). In invasive breast cancers, low RPA1, low RPA2 and low RPA3 were all associated with larger size, lympho-vascular invasion, higher histological grade, high stage, ER negativity and poor breast cancer specific survival. Transcriptomic alterations in low RPA tumors included those genes involved in steroid hormone biosynthesis, chemical carcinogenesis, and drug metabolism. Pre-clinically, RPA deficient breast cancer cells were sensitive to Cisplatin and Palbociclib (CDK4/6 inhibitor) therapy compared to controls. Additionally, the PARP1 inhibitor Olaparib was synthetically lethal in RPA1 and RPA2 deficient cells compared to controls. Increased Olaparib sensitivity was associated with double strand breaks, S-phase cell cycle arrest and increased apoptosis. **Conclusions:** We provide the first comprehensive evidence that RPA loss is an early event during breast cancer pathogenesis and promotes aggressive phenotypes. Pre-clinically RPA deficient breast cancer cells were selectively toxic to Cisplatin, Palbociclib and Olaparib.

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P3-05-20

Low 21-Gene Recurrence Score Is Not Associated with a High Axillary Nodal Burden in Post-Menopausal Women Presenting with a Clinically Negative Axilla

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Background: The predictive and prognostic value of the 21-gene recurrence score (RS) has emphasized the importance of tumor biology and minimized the credence of a limited (1-3 positive) nodal burden. The practice changing results of RxPonder demonstrated that post-menopausal women with 1-3 positive lymph nodes (pN1) and a RS of ≤ 25 did not necessarily benefit from adjuvant chemotherapy. Given that RS influences adjuvant therapy decision-making more significantly than nodal status, it is unclear whether axillary staging with sentinel lymph node biopsy (SLNB) has a continued role in the surgical care of post-menopausal patients otherwise presenting with early stage, clinically node negative (cN0) hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) invasive breast cancer. In this context, the de-escalation of axillary staging, especially in the presence of a low RS, is an area of active investigation. To help elucidate this further, we sought to estimate the association of RS with pathologic nodal stage.

Methods: Using the 2004-2019 National Cancer Database (NCDB) Patient User File (2022 release), we evaluated the association of RS with the incidence of pN0, pN1 and pN2-3 disease. Only female patients diagnosed who were age 50 and older with HR+/HER2- invasive breast cancer were eligible, and only those presenting with cT1-T2N0 who underwent upfront surgery with a SLNB comprised our study population. Those with Oncotype DX testing performed with an available RS were included. Given the limitations within the dataset, age 50 and over was selected as a surrogate for post-menopausal status. Categorical variables were compared between RS groups (≤ 25 vs. > 25) using chi-square tests and continuous variables were compared using t-tests. A logistic regression analysis was performed to estimate the association between RS (≤ 25 vs. > 25) and nodal burden (pN2-3 vs pN0-1).

Results: There were 151,447 patients with an invasive breast cancer diagnosis between 2015 and 2019 who met inclusion criteria. The average age at diagnosis was 64.1 (IQR 58-69) and almost 75% of tumors displayed ductal histology. There were 130,568 (86.2%) patients with a RS ≤ 25 and 20,879 (13.8%) with a RS > 25 . On final pathology, 85.2% were pN0 and 14.8% were pN1-3. For those with a RS ≤ 25 , 84.9% were pN0, 14.8% were pN1 and 0.3% were pN2-3. For those with a RS > 25 , 86.8% were pN0, 12.9% were pN1 and 0.3% were pN2-3. Overall, 14.5% demonstrated pN1 disease, of which 12.3% yielded a RS > 25 . Of the 461 patients with pN2-3 disease for whom RS was available, 12.4% (57 patients) had RS > 25 . After adjustment, RS > 25 was associated with reduced incidence of pN2-3 compared to pN0-1 (OR=0.64, 95% CI 0.47-0.87, $p=0.004$).

Conclusion: In this population of post-menopausal patients with cT1-T2N0, HR+/HER2- invasive breast cancer and an available RS, almost 86% displayed pN0 or pN1 disease in conjunction with a RS ≤ 25 . Based on the current available literature, less than 5% of cT1-2N0 patients are thought to harbor $> pN1$ disease. These data add further support, suggesting that this patient population is unlikely to harbor a higher than limited nodal burden given a clinically negative axilla. Though less than 0.5% of the studied patient population demonstrated pN2-3 disease, an important caveat to make is that these patients would not have met criteria for RS, and it's likely this low number reflects the absence of testing. Given that RS has not been validated for this higher nodal stage, we cannot make recommendations to omit axillary surgery in this cohort of patients. The data presented here provides further rationale for the two large prospective studies addressing whether SLNB could be eliminated in patients with otherwise small HR+/HER2- tumors which are currently ongoing.

Pathologic Nodal Staging Based on Recurrence Score

Table 1: Pathologic Nodal Staging Based on Recurrence Score

Recurrence Score	Final Pathologic Nodal Status				P-Value
	pN0 N(%)	pN1 N (%)	pN2 N(%)	pN3 N (%)	
RS ≤25 (N=130568)	110872 (84.9)	19292 (14.8)	331 (0.3)	73 (0.06)	<0.001
RS >25 (N=20879)	18123 (86.8)	2699 (12.9)	44 (0.2)	13 (0.06)	
Total (N=151447)	128995 (85.2)	21991 (14.5)	375 (0.2)	86 (0.06)	

Data presented as N (row percentage). pN: pathologic nodal status, pN0: node negative, pN1: 1-3 positive nodes, pN2: 4-9 positive nodes, pN3: 10 or more positives nodes, RS: Recurrence Score

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5:00 PM - 6:15 PM

P3-05-21

A novel AI-digital Test with an automated approach for grading and phenotyping breast cancer enriches recurrence score risk prediction in an Oncotype evaluated cohort.

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Background

Genomic testing such as OncotypeDx remains an important component of the treatment decision process for many breast cancer (BC) patients. Evidence from Sparano et al. JCO 2021;39:557-564 demonstrated the importance of combining clinical features such as tumor grade, size and age with the 21-gene recurrence score (i.e., RSclin). Given the challenges associated with reliability of BC grading as a prognostic feature, we sought to develop a broadly accessible AI-digital test (PDxBr) which included a BC AI-grade combined with clinical features (i.e., age, tumor size, stage and lymph node status) to predict recurrence risk in an Oncotype categorized cohort.

Methods

We evaluated performance of the PDxBr test along with the AI-grade, clinical feature (i.e., age, size, tumor stage and LN status) and histology grade models in a subgroup analysis from a retrospective longitudinal clinical development validation study utilizing samples from breast cancer (BC) patients in the Mount Sinai Health Care System (NYC, NY) from 2004-2016.

Eligible

participants were ≥ 23 years old with infiltrating ductal or mixed ductal and lobular carcinoma of the breast (IDC) and all with an Oncotype RS, and a median 6-year follow-up. All participants had H&E slides or paraffin blocks (for slide generation) from the resected BC specimen. H&E slides were digitized (40X magnification) using a Philips UltraFast Digital slide scanner (Netherlands) and a single whole slide image (WSI) was selected for model development. The AUC/C-index was used to demonstrate performance.

Results

599 patients with Oncotype RS results were interrogated: 57% white, mean age 57, mean tumor size 1.3cm, 100% T1/2 and HR+ve, 55% grade 2, 26% grade 3 and 18% grade 1; 95% pN0

with 36 events (6%). 21 (60%) of events were local-regional recurrences. Of note, there were 55% histologic Grade 2 cases in this population. Combining Oncotype RS with assorted sub-models including histologic grade, clinical features, AI-grade, or PDxBr model in a SVRc analysis

demonstrated incremental improvement in the C-index for predicting BC recurrence (Table 1).

Conclusions

Both PDxBr test and AI-grade when combined with Oncotype were superior to Oncotype alone, or Oncotype with grade or clinical features suggesting that the incorporation of an improved BC grade with Oncotype RS enhances overall risk discrimination. PDxBr is the first digital BC test combining automated AI-BC prognostic grade with clinical-pathologic features to predict risk of early-stage BC recurrence. Additional validation studies are underway to confirm these results.

AUC comparison of Oncotype alone and then combined with histology grade, clinical data (age, stage, tumor size and LN pos), AI-grade, and the PDxBr model.

Model	C-index	CI Lower Limit	CI Upper Limit
Oncotype Rs	0.35	0.26	0.48
Oncotype + grade	0.51	0.42	0.60
Oncotype + Clinical	0.64	0.57	0.71
Oncotype + AI grade	0.72	0.67	0.79
Oncotype + PDX Br	0.76	0.70	0.82

Disclosure(s):

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5:00 PM - 6:15 PM

P3-05-22

Serum S100A8/S100A9 levels are associated with increased risk of brain metastasis in patients with aggressive breast cancer

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Background: Inflammatory breast cancer (IBC) is a rare and extremely aggressive form of breast cancer with an increased propensity to disseminate to distant organs such as the brain; indeed, a previous study reported that 37% of patients with HER2+ IBC present with brain metastasis as the first site of relapse. Our group recently generated new sublines from HER2+ IBC that exhibited a high brain metastatic propensity and further demonstrated that the stress response protein N-myc downstream regulated gene 1 (NDRG1) is a driver of breast cancer brain metastasis. Transcriptome analysis comparing NDRG1-expressing brain-metastasizing and NDRG1-depleted brain-non-metastasizing cells revealed prominent downregulation of two

S100 calcium binding proteins, S100A8 and S100A9, in NDRG1-depleted cells. S100A8/S100A9 are known to facilitate the homing of tumor cells to the brain and lung pre-metastatic niche. Recent studies elegantly demonstrated a critical role for S100A9 in brain relapse and radioresistance in brain metastasis mouse models. The purpose of the present study was to evaluate whether S100A8/S100A9 serum levels predict the risk of brain metastasis in aggressive breast cancers. Methods: In a retrospective cohort of 304 IBC patients, we measured serum S100A8/S100A9 levels by using ELISA. Overall survival (OS) and breast cancer-specific survival (BCSS) were analyzed using Kaplan-Meier curves, log-rank test, and Cox proportional hazard regression. Results: The overall median follow-up time was 64 months. Forty-six percent of patients had estrogen receptor (ER)-negative tumors, 61.3% were stage III-IV, 77% high grade, 16.8% received adjuvant chemotherapy and 53.6% received adjuvant radiation. On univariate analysis, S100A8/S100A9 levels, disease stage, ER status, PR status, HER2 status, adjuvant chemotherapy, and adjuvant radiation therapy were significantly associated with OS and BCSS. Patients with high S100A8/S100A9 serum levels (>3rd quartile vs. ≤ 3rd quartile) had poor OS ($p=0.01$) and BCSS ($p=0.006$). Also, patients with high S100A8/S100A9 serum levels had a higher risk of developing brain metastasis ($p=0.01$). S100A8/S100A9 serum levels was not significantly correlated with any other metastasis. On multivariate analysis, high S100A8/S100A9 serum levels was independently associated with reduced OS (hazard ratio [HR] = 1.8, 95% CI 1.1 to 3.0, $p=0.01$), reduced BCSS (HR = 1.8, 95% CI 1.2 to 2.8, $p=0.006$) and increased risk of developing brain metastasis (HR = 2.1, 95% CI 1.2 to 3.8, $p=0.01$). Conclusions: We found that having high levels of serum S100A8/S100A9 is an independent prognostic factor for reduced OS and BCSS and for the development of brain metastasis in patients with IBC. Thus, S100A8/ S100A9 may represent a biomarker for unfavorable clinical outcome and brain metastasis in patients with aggressive breast cancers.

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5:00 PM - 6:15 PM

P3-05-23

Pathological complete response rate and disease-free survival after neoadjuvant chemotherapy in patients with HER2-low and HER2-0 breast cancers

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ABSTRACT Background: Half of HER2-negative breast cancers (BC) show HER2-low expression. The strong efficacy of recent anti-HER2 antibody-drug conjugates (ADC) in HER2-low tumors has risen the interest of HER2-low as a proper BC subtype. Chemosensitivity and prognosis of this subtype are not clear when compared to HER2-0 tumors. We investigated the pathological complete response (pCR) and disease-free survival (DFS) rates in BC patients receiving neoadjuvant chemotherapy for HER2-low or HER2-0 tumors. Methods: Data were collected from the Institut Paoli-Calmettes European Comprehensive Cancer Center database. HER2-low tumors were defined by HER2 IHC score of 1+ or 2+ with negative FISH, and HER2-0 by IHC score of 0+. Clinicopathological characteristics, pCR (defined as [ypT0/ypTis] and [pN0sn or ypN0]) and DFS rates were compared between the two cohorts. Results: From Jan/2005 to Jun/2021, 1,111 patients receiving neoadjuvant chemotherapy were evaluable. The incidence of HER2-low was 41%, including 63% of hormone receptor (HR)-positive and 37% of HR-negative tumors ($p < 0.001$). In the whole population, the pCR rate was lower in HER2-low (23%) versus HER2-0 (30%) tumors ($p = 0.013$), but this association was lost in multivariate analysis. In HR-positive patients, HER2-low negatively impacted pCR rates when compared to HER2-0 (10% vs. 16%, $p = 0.046$), but not in HR-negatives (46% vs. 42%), and this result was maintained in multivariate analysis (OR 0.60 [95CI 0.36-1.00]; $p = 0.049$, and OR 1.15 [95CI 0.77-1.71]; $p = 0.490$, respectively). No correlation existed between DFS and HER2-status. Conclusion: HER2-low is associated with HR positivity. HER2 status did not impact pCR in HR-negative patients, whereas HER2-low was associated with lower pCR rate in HR-positive patients, supporting the development of anti-HER2 ADC in this setting.

Disclosure(s):

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5:00 PM - 6:15 PM

P3-05-24

Correlation between the expression of JCAD in plasma exosomes and breast cancer

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Background: Breast cancer is the most common cancer in women. The five-year survival rate of patients with stage 0 and stage I breast cancer is more than 95%, that of patients with stage II breast cancer is 80%, that of patients with stage III breast cancer is about 50%, and that of stage IV breast cancer is less than 30%. The stage of breast cancer is closely related to the prognosis. Exosomes are membrane vesicles secreted by living cells, which carry donor cell specific genetic information. They can exist stably in the circulatory system, so they are ideal biomarkers. Method: We collected 128 breast cancer patients (17 benign cases, 26 stage I cases, 36 stage II cases, 15 stage III cases and 34 stage IV cases) treated in our center from 2018 to 2019. We collected patients' plasma and extracted exosomes, then we sent them for

sequencing. We analyzed the difference between benign cases' and stage IV cases' sequencing results, and then we screen them by comprehensively considering the change trend of gene expression from benign cases to stage IV cases, the survival curve of patients and the lymph node metastasis. The clinicopathological factors and progression free survival (PFS) of breast cancer patients were analyzed by Cox regression. Finally, JCAD was selected. Using virus to stably overexpress JCAD and shRNA technology to knock down JCAD, the function of JCAD for the proliferation and metastasis of breast cancer was discussed through CCK8 cell proliferation experiment, EdU cell proliferation experiment, plate cloning experiment, transwell cell migration experiment. T-test and chi square test were performed on the data. $P < 0.05$ showed that the difference was statistically significant. Kaplan-Meier survival was used to analyze the long-term efficacy. Result 1. The expression of JCAD mRNA in exosomes increased from benign to stage 4 ($P < 0.001$). In addition, patients with lymph node metastasis had significantly higher expression of exosome JCAD ($p=0.009$), and the prognosis of patients with high expression of exosome JCAD was poor ($p=0.003$). This conclusion has also been verified in TCGA database. Finally, Cox regression analysis showed that JCAD was an independent prognostic factor affecting PFS ($p=0.005$). 2. JCAD is transmitted between cells in the form of exosomes: In breast cancer cells, stable transgenic strains with overexpression of JCAD and shRNA knockdown strains of JCAD were constructed. The exosomes were extracted by ultracentrifugation for RNA and protein level verification. It shows that there was a difference in the expression of JCAD in the exosomes of overexpression and knockdown strains. After adding exosome inhibitor GW4869 to culture cells, it was found that the level of JCAD mRNA secreted by exosomes decreased significantly. In addition, through PKH26 exosome fluorescence labeling method, it was found that JCAD was transmitted between cells in the form of exosomes. 3. JCAD can promote the proliferation and migration of breast cancer cells: This experiment verified the ability of JCAD to promote the proliferation of breast cancer cells through CCK8 cell proliferation experiment, EdU cell proliferation experiment, plate cloning experiment. Then the ability of JCAD to promote the migration of breast cancer cells was verified by transwell cell migration experiment. The exosomes were added to wild type cells for co-culture. It was further found that the exosomes with high expression of JCAD could promote the proliferation and migration of breast cancer cells. Conclusion JCAD is significantly overexpressed in stage IV patients and patients with lymph node metastasis. Moreover, JCAD is an independent prognostic factor affecting PFS, and the exosome JCAD is expected to become a potential prognostic liquid biopsy marker. Further cell experiments showed that JCAD can be transmitted between breast cancer cells through exosomes and promote the proliferation and metastasis of breast cancer cells.

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5:00 PM - 6:15 PM

P3-05-25

Clinical Factors associated with Survival Outcomes in Patients with Metaplastic Breast Cancer

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Background Metaplastic breast cancer (MBC) is a rare and aggressive subtype of breast cancer (BC) defined by presence of both epithelial and mesenchymal components. Most are

triple negative but are often chemo-refractory and associated with poor survival outcomes compared to non-metaplastic triple negative BC. Advances in therapy have led to improvements in survival outcomes of patients (pts) with BC over the last decade. Our multicenter retrospective study aims to assess (1) progression free survival (PFS) and overall survival (OS) (2) factors predictive of survival outcomes in MBC pts

Methods We performed a retrospective analysis of pts diagnosed with MBC from 1997-2021 at Mayo Clinic (Florida, Arizona and Rochester) under IRB approval. Kaplan-Meier method was used to estimate OS and PFS at 1, 3 and 5 years. Cox regression models were used to examine the association between risk factors and survival outcomes. All tests were two-sided with p value < 0.05 considered statistically significant

Results We evaluated 158 pts with MBC. Median age and tumor size was 61 (range: 20-91) years and 2.8 (range: 0.5-21) cm, respectively, with 80% of pts being postmenopausal. At diagnosis, 14.6% of pts had clinical T3/T4 disease, 16.4% were clinically node-positive, and 6.3% (10 pts) had distant metastases (DM). Spindle cell histology was seen in 36 pts. Most MBC pts were triple-negative (68.3%), high grade (77.2%) and high Ki-67 (36/47; 76.5%). Of the 61 pts tested for germline mutation, 8 (13.1%) were positive, with BRCA1/2, PTEN, NBN, CHEK2, and BARD1 mutations. Most pts had lumpectomy (53.8%), followed by simple mastectomy (38.5), and modified radical mastectomy (7.7%). Majority of pts had sentinel lymph node biopsy (71.8%). Adjuvant radiation therapy was performed in 65.6% of pts. Pathologic complete response (pCR) was noted in 4/38 (10.5%) evaluable pts who received neoadjuvant chemotherapy (NACT). Residual cancer burden (RCB) scores of 2 and 3 were seen in 76.2% of evaluable pts. Median follow-up time was 2.2 years (range: 6 days-24.6 years). Overall, 1-, 3-, and 5-year OS was 93.3%, 81.7%, and 76.0%, while PFS was 80.8%, 67.9%, and 60.9%, respectively. The presence of DM at diagnosis [HR 38.55 (11.18, 132.93), p < 0.001] and spindle cell histology (SC) [HR 2.57 (1.19, 5.53), p = 0.02] predicted worse OS in multivariable analysis. Inferior PFS was predicted by DM [HR 18.84 (6.53, 54.35), p < 0.001], SC [HR 2.46 (1.25, 4.86), p = 0.009], and node-positivity at diagnosis [HR 3.65 (1.5, 8.89), p = 0.004]. The 5-year OS and PFS were 22.2% and 0% for DM pts versus 80.0% and 65.6% for non-DM pts. The 5-year OS and PFS were 71.5% and 54.7% for SC pts versus 81% and 66.6% for non-SC pts. 5-year OS and PFS for NACT pts was 67.3% and 52.6% for NACT pts versus 78.2% and 62.8% for non-NACT pts. Age at diagnosis, menopausal status, family history of BC, grade, stage, tumor size, hormone-receptor and HER2 status, and use of NACT were not found to be significantly associated with OS or PFS in multivariate analysis.

Conclusion This study is one of the largest and most recent review of institutional experiences with MBC. Overall, OS at 5 years was improved compared to prior older studies of MBC but still remains very low for those with DM, representing an area of unmet clinical need. SC and DM correlated with worse outcomes for both PFS and OS. Additionally, node positivity at diagnosis was a predictor of worse PFS. In contrast, no association was seen between survival and tumor size, stage, hormone receptor-positivity, HER2 receptor-positivity. The low pCR rates following NACT in our study are consistent with reported literature. Further, use of NACT does not impact survival, suggesting pts with resectable disease should proceed with surgery first.

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Association of muscle mass and density with outcomes in patients with ER positive metastatic breast cancer: correlative analysis of ECOG-ACRIN 2112

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Introduction: Observational data investigating the relationship between body habitus and survival or toxicity in breast cancer has been largely centered in the curative setting and focused on weight- based metrics, with variable and inconsistent results. Muscle is a large, active endocrine organ that affects physical function, drug metabolism, inflammation, and quality of life, but is not adequately measured by body weight alone. Very few studies have evaluated muscle measures in metastatic breast cancer (MBC) and have been focused on patients receiving cytotoxic chemotherapy. Here, we evaluate the impact of muscle mass and muscle density measured on CT scan on outcomes in patients with MBC receiving endocrine-based therapy. Methods: Baseline CT scans done at the time of study enrollment were centrally collected from participants in ECOG-ACRIN E2112, a randomized phase III study of exemestane with or without entinostat in MBC, which ultimately did not impact survival. A transverse cut at the L3 level was extracted and processed using semi-automated SliceOmatic software (Tomovision) by two independent investigators to obtain total body skeletal muscle mass and muscle attenuation. Low muscle mass was defined as skeletal muscle index (SMI, lean muscle area/height, cm²/m²) less than 41 and low skeletal muscle attenuation (SMA) was defined as average muscle density less than 41 HU, or less than 33 HU if the patient is overweight or obese by BMI. Chi-square tests were used to determine the association between

SMI and SMA and other clinical characteristics, including body weight, race, and performance status. Multivariable Cox proportional hazard models were used to determine the association between low SMI or low SMA and overall survival (OS), progression free survival (PFS), and patient-reported outcomes. Results: Of the 608 patients randomized in E2112, 546 had analyzable CT scans and follow up data available. 45% (n=246) of participants had obesity by BMI (≥ 30); 39% (n=212) had low SMI and 56% (n=305) had low SMA. Obese patients were more likely to have higher SMI ($p < 0.001$); however, 9.5% (n=52) of the study population had both obesity and low SMI. Low SMA was associated with higher rate of obesity and worse performance status ($p < 0.001$), consistent with muscle quality being a predictor of functional status. Low SMI was not associated with survival outcomes (OS HR 1.04 95%CI 0.83-1.30, PFS HR 1.12 95% CI 0.92-1.36), nor was low SMA (OS HR 1.02 95%CI 0.81-1.28; PFS HR 1.02 95%CI 0.84-1.23). In addition, BMI was not related to survival outcomes. Conclusions: Low muscle mass and low muscle density are prevalent in estrogen receptor positive MBC patients. Muscle measures correlated with obesity and performance status; however, neither low SMI nor low SMA were associated with worse prognosis in this population. Further work is needed to refine body composition measurements and select optimal cutoffs and meaningful endpoints in specific breast cancer populations, particularly in those living with metastatic disease.

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The impact of co-existing ductal carcinoma in situ in invasive early hormone receptor positive breast cancer on the genomic and clinical risk of recurrence

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Background: Invasive early breast cancer (IBC) often presents with a co-existing ductal carcinoma in situ (DCIS) component, while about 5% of the cases present with an extensive (>25%) intraductal component (EIC). The presence of a DCIS component was previously shown to be associated with favorable clinico-pathological characteristics and survival outcomes. However, the association between co-existing DCIS and genomic risk of recurrence is unclear. Methods: Patients with early hormone receptor positive (HR+) HER2neu-negative (HER2-) breast cancer and known OncotypeDX breast recurrence score (RS), who underwent breast surgery in our institute, were included. A natural language processing (NLP) algorithm was used to identify co-existence of extensive DCIS (DCIS-H) and non-extensive DCIS (DCIS-L) in surgical pathological reports. Genomic risk was determined using OncotypeDX RS, while clinical risk was calculated according to the MINDACT criteria, based on tumor size and grade. The genomic and clinical risks of DCIS-H, DCIS-L and pure IBC (No-DCIS) were compared. Results: A total of 45 (5%) DCIS-H cases, 468 (56%) DCIS-L cases and 328 (39%) No-DCIS

cases were identified. DCIS-H cases presented with less aggressive clinico-pathological characteristics, such as lower proportions of histologic grade III (10% vs 26% vs 21%) and lower proportions of node-positive disease (13% vs 18% vs 21%), compared to DCIS-L and No-DCIS cases, respectively. The distribution of OncotypeDX RS significantly varied between the groups. DCIS-H tumors were less likely to have a high RS and more likely to have a low or intermediate RS compared to DCIS-L and No-DCIS tumors (High RS: 4% vs 20% vs 20%, Low + intermediate RS: 96% vs 80% vs 80%, respectively; $p=0.04$). Additionally, the proportions of high clinical risk cases were lower in the DCIS-H group compared to the DCIS-L and No-DCIS groups (42% vs 53% vs 50%, respectively; $p=0.002$). Based on genomic and clinical risk and current guidelines, we found that women presented with an extensive DCIS component (DCIS-H) had a lower probability of receiving an adjuvant chemotherapy recommendation compared to women presented with a non-extensive DCIS component (DCIS-L) or pure IBC (No-DCIS) (11% vs 29% vs 25%, respectively; $p=.035$). No differences in disease recurrence were detected between the groups. Conclusions: Co-existing extensive DCIS in invasive early HR+Her2- breast cancer is significantly correlated with lower genomic and clinical risk of recurrence and a smaller chance for chemotherapy recommendation. The rarity of this condition (5% of cases) limited our ability to detect differences in outcomes. These findings warrant future studies of the underlying genomic landscape of co-existing extensive DCIS.

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Impact of increased adiposity on extended aromatase inhibitor treatment in postmenopausal patients with estrogen receptor positive (ER+) breast cancer: a retrospective analysis of the SOLE trial

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Background: The risk of late distant recurrence (≥ 5 years) in post-menopausal patients with ER+ BC remains significant even after standard adjuvant endocrine therapy (ET). Obesity, which has reached high proportions in Western Countries, is one of the modifiable factors that can contribute to BC recurrences. While body mass index (BMI) is an easily available surrogate measure of adiposity, it might not reflect accurately patient adiposity, especially in post-menopausal patients. We therefore hypothesize that mammary adipocyte measurements might better capture the adiposity of the patient. In this study, we retrospectively evaluated the prognostic role of both BMI and adipocyte measurements in the SOLE trial.

Patients & Methods: The SOLE trial (NCT00553410) consisted of 4,884 postmenopausal women with hormone receptor positive, lymph node-positive BC treated with 5 years of letrozole after having completed 4-6 years of adjuvant ET. BMI was available for 3,606 patients with ER+/HER2- BC and categorized according to the WHO classification (underweight: < 18.5 , normal weight $18.5 - 24.9$, overweight $25 - 29.9$, obesity ≥ 30 kg/m²). Considering the small

sample size, patients with underweight (n=35) were grouped together with patients with normal weight for the subsequent analyses. We evaluated the association between clinico-pathological characteristics and BMI using Fisher exact test and Kruskal-Wallis test. Given the previously reported association of BMI with distant recurrences (PMID: 21115856), we considered distant-relapse free interval (DRFI) as the main study endpoint. Cox regression analyses were adjusted for histology, chemotherapy (yes/no), type of local therapy, in addition to previously reported clinico-pathological variables (PMID: 29158011). Then, we conducted a stratified case-cohort study consisting of 311 patients (97 with distant relapse-cases) with successful digital assessment of adipocytes on normal mammary adipose tissue sample collected at surgery, as previously described (PMID: 33120083). Stratification factors were treatment arm and type of prior ET. Weighted Cox regression models (PMID: 17554753, 18712477) were used to evaluate prognostic association with adipocyte size (area in μm^2) categorized in quartile of the 75th percentile (Q4 vs Q1-3), as done previously (PMID: 33753731).

Results: 1392 (39%) patients were normal weight, 1315 (36%) were overweight and 899 (25%) were obese. Older age at diagnosis, lymph node involvement (≥ 4), large tumor size and menopausal status were associated with overweight and obesity. After a median follow-up of 84 months, no associations were found between DRFI and BMI in the univariable and multivariable analysis (adjusted HR overweight vs normal=0.99, 95%CI: 0.76 – 1.29, p=0.977 and HR obese vs normal=1.11, 95%CI: 0.84 - 1.47, p=0.425). In the case-cohort study, patients with larger adipocytes had an increased hazard of distant recurrence in the univariable and multivariable analysis (see table 1).

Conclusion: In this study, we did not detect any association between BMI and survival outcomes. We however found that larger mammary adipocytes were independently associated with an increased hazard of distant recurrence. These results suggest that mammary adipocytes, which can be easily evaluated on H&E slides using digital pathology, should be considered as a novel marker to evaluate the risk of late recurrence in patients with breast cancer.

DRFI	HR (95%CI)	P-value
Adipocyte area^{75th}		
Quartile 1-3 (2720 – 8425 μm^2)	1.00 (reference)	
Quartile 4 (8426 – 13485 μm^2)	2.58 (1.42 – 4.70)	0.001
Age group, years		
<55	1.00 (reference)	
55-59	3.15 (1.42 – 6.98)	0.004
60-64	1.13 (0.47 – 2.69)	0.782
65-69	1.08 (0.41 – 2.87)	0.865
70+	1.40 (0.58 – 3.36)	0.446
Treatment arm		
Continuous letrozole	1.00 (reference)	
Intermittent letrozole	1.03 (0.68 – 1.54)	0.879
Prior endocrine therapy		
SERMs only	1.00 (reference)	
AIs only	0.94 (0.49 – 1.80)	0.857
Both SERMs and AIs	1.00 (0.57 – 1.78)	0.974
Tumour grade		
G1	1.00 (reference)	
G2	1.32 (0.43 – 3.98)	0.618
G3	2.29 (0.71 – 7.40)	0.164
Tumour size		
≤ 2 cm	1.00 (reference)	
> 2 cm	1.85 (0.97 – 3.5)	0.059
Number of positive nodes		
1-3	1.00 (reference)	
4+	4.52 (2.44 – 8.35)	< 0.001
Tumour histology		
Invasive carcinoma of no-special type (NST)	1.00 (reference)	
Invasive lobular carcinoma (ILC)	1.36 (0.70 – 2.63)	0.355
Mixed NST/ILC	0.63 (0.16 – 2.46)	0.511
Other	0.56 (0.05 – 6.08)	0.637
Hormone receptor		
ER+/PgR+	1.00 (reference)	
ER+/PgR-	0.58 (0.20 – 1.64)	0.309
Duration of prior endocrine therapy		
< 4.5 years	1.00 (reference)	
4.5 – 5.5 years	0.51 (0.24 – 1.07)	0.076
> 5.5 years	0.25 (0.05 – 1.09)	0.065
Duration from end of prior ET to randomization		
≤ 1 month	1.00 (reference)	
> 1 month	0.90 (0.47 – 1.70)	0.749
Prior chemotherapy		
No	1.00 (reference)	
Yes	0.77 (0.37 – 1.62)	0.505
Local therapy		
Mastectomy with radiotherapy	1.00 (reference)	
Mastectomy without radiotherapy	0.70 (0.27 – 1.81)	0.468
Breast conservative surgery with radiotherapy	0.75 (0.39 – 1.44)	0.388

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5:00 PM - 6:15 PM

P3-05-29

Use of Bioimpedance Spectroscopy as a Surrogate for Bone Mineral Content in Oncology Patients: Practical Application of the SOZO Device

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Background: Many cancer patients, particularly those with breast or prostate cancer, receive hormonal manipulation therapies that can significantly impact their bone mineral content (BMC), potentially leading to osteoporotic associated life-threatening fractures, particularly given the median age of patients diagnosed with these malignancies. Bioimpedance spectroscopy (BIS) is a non-invasive tool that measures fluid and body composition values including skeletal muscle mass (SMM) and fat free mass (FFM). BIS devices can be used easily and quickly at point-of-care at the time of vital signs, with the patient standing on the device placing their hands and feet on metal electrodes and a reading obtained in less than a minute. Multiple previous studies have shown strong correlation between SMM and BMC, suggesting that a BIS reading can provide a reproducible, simple and quick estimate of BMC. To that end, we present initial findings correlating BIS readings obtained with a SOZO device (ImpediMed) with dual x-ray absorptiometry (DXA) to determine if BIS readings can be applied as an accurate point of care surrogate measure of BMC. Materials and Methods: Concurrent BIS measures and DXA scans, were performed in 75 healthy volunteers and 93 cancer patients (during and after cancer treatment) Group 1: 75 healthy volunteers (32 male, 43 female), mean age 27.4 (18-66 years); Group 2: 44 patients undergoing cancer treatment (11 male, 33 female; 18 breast, 7 lung, 4 endometrial, 4 colorectal, 4 prostate, 7 other), mean age 61.3 (38-79 years); and Group 3: 49 patients participating in a 12-week exercise program after cancer treatment (15 males, 34 females; 22 breast, 6 prostate, 3 colorectal, 3 endometrial, 2 lung, 13 other), mean age 57.8 (19-79 years). The healthy volunteers in Group 1 were further randomized into two subsets. Group A was used to develop a BIS predicted BMC algorithm and Group B was used to validate the algorithm. Results: The Pearson correlation coefficients (R) for DXA BMC and SOZO SMM were strong for all 3 groups (R=0.92, 0.85, and 0.80 for Groups 1, 2, and 3, respectively). Stepwise multiple linear regression for BMC was performed for Group A based on BIS parameters. For Group A, SMM resulted in a multiple correlation coefficient of 0.94 (P< 0.0001). The correlation coefficient between the BIS predicted BMC and DXA BMC of Group B was 0.87 (P< 0.0001, 95%CI 0.78-0.93). For Groups 2 and 3 combined, the correlation coefficient between the BIS predicted BMC and DXA BMC was 0.82 (P< 0.0001, 95%CI 0.73-0.87). Conclusions: Concurrent measures of SMM obtained with BIS using SOZO correlated strongly with DXA BMC, demonstrating that SOZO SMM may be a useful surrogate in the clinic to provide a quick, easy, and reproducible indicator of change in BMC, particularly for those patients undergoing treatments that may affect BMC. Tracking SMM during or after cancer treatment with SOZO may provide an estimate of changes in BMC allowing clinicians to obtain additional diagnostic testing and/or consider treatment modifications.

Disclosure(s):

Frank Vicini, n/a: Impedimed: Consulting Fees (e.g., advisory boards) (Ongoing); Prelude: Consulting Fees (e.g., advisory boards) (Ongoing)

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P3-05-30

Survival after Development of Contralateral Breast Cancer

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Purpose There are many studies reporting survival after development of contralateral breast cancer(CBC) but with inconsistent results. Also, many studies were based on European or North American population and few on Asian population. However, Korean breast cancer patients have different characteristics such as age distribution. Therefore, purpose of this study is to investigate whether development of CBC has influence on survival in Korean breast cancer population. **Methods** In this retrospective study, we included patients who were diagnosed with a first primary unilateral non-metastatic breast cancer at Asan Medical Center, Korea, between 1999-2013 followed through 2018. In this population, patients who developed CBC during the follow-up period were divided into the CBC cohort, and who did not into the non-CBC cohort. Survival of CBC cohort and non-CBC cohort was compared in the whole study population and in subgroup analysis by interval of CBC development, and breast cancer subtype. **Results** Over median follow-up of 107 months, 418 patients developed CBC out of

16,251 patients. Development of CBC did not influence overall survival or breast cancer-specific survival. In subgroup analysis by interval of CBC development, patients who developed CBC within one year after diagnosis of the first breast cancer had higher risk for overall death in CBC cohort (hazard ratio 2.58; 95% CI 1.28-5.18), and patients who developed CBC after one year showed no significant difference in survival compared with non-CBC cohort. In subgroup analysis by the subtype, patients with hormone receptor-positive/human epidermal growth factor receptor 2-negative subtype for the first breast cancer showed higher risk for overall death in CBC cohort (hazard ratio 1.88; 95% CI 1.14-3.10) whereas patients with triple negative subtype for the first breast cancer showed lower risk for overall survival in CBC cohort (hazard ratio 0.42; 95% CI 0.19-0.95). Conclusion Development of CBC in Korean breast cancer patients did not have significant impact on survival. However, development of CBC early after diagnosis of first breast or having certain subtype of breast cancer may have affect on survival. Such information can be important information when counseling patients who are considering contralateral prophylactic mastectomy.

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P3-05-31

PVT1, CASC16, TNFRSF13B and NAMPT may be the key genes correlated with recurrence and metastasis of breast cancer

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Background: It is vital to find the risk genes and loci related to recurrence and metastasis in breast cancer (BC) patients. The Genome-wide association study (GWAS) can detect the risk of single nucleotide polymorphism (SNP) and help us understand the mechanism of disease progression by analyzing the SNP information of the whole genome. At present, GWAS have identified several genetic susceptibility SNPs for BC, but it is unclear about its significance in the recurrence and metastasis of BC patients. Therefore, in this study we aimed to identify the risk SNPs related to recurrence and metastasis of BC based on GWAS analysis. Methods: This study adopts a two-stage GWAS research strategy. In the first stage, according to propensity score matching, we chose 97 pairs of BC patients with or without recurrence and metastasis who were treated in Shandong Cancer Hospital and Institute from November 2013 to April 2014. Their peripheral blood samples were collected and DNA was extracted for genome-wide detection by Illumina ASA chip. The SNP loci related to recurrence and metastasis of BC were obtained by logistic regression analysis of GWAS. In the second stage, 854 BC patients from the same hospital were verified from May 2014 to June 2015. The SNP genotyping was detected by time-of-flight mass spectrometry to verify its correlation with recurrence and metastasis of BC. The SNP loci and their corresponding genes and pathways were analyzed using DAVID (<https://david.ncifcrf.gov/>) online enrichment analysis website. Results: In the first stage, 191 SNPs were obtained from GWAS analysis ($P < 0.001$). Based on these SNPs and their corresponding genes, we further found that glutamatergic synaptic transmission may be related to BC recurrence and metastasis through GO analysis. Similar results were found in

calcium signaling pathway and insulin secretion pathway through KEGG enrichment analysis. And 21 SNPs were screened for their association with the tumor evolution process and whether they are located in the gene coding functional region. In the second stage, Cox regression analysis showed that the genotyping of the four SNPs was consistent with the results of GWAS analysis, and these SNPs are located in the intron region of the gene. Specifically, compared with homozygous AA, BC patients carrying TNFRSF13B rs4273077(AG/GG) and PVT1 rs10108514(AG/GG) had a 26% (HR: 0.74, 95%CI: 0.54-1.01) and 27% (HR: 0.73, 95%CI: 0.54-0.98) reduced risk of recurrence and metastasis, respectively; compared with homozygous CC, patients with BC carrying NAMPT rs4730155(CT/TT) had a 35% (HR: 0.65, 95%CI: 0.45-0.93) reduced risk of recurrence and metastasis; while compared with CASC16 rs12920540(CA/AA), BC patients with homozygous CC has a 52% (HR: 1.52, 95%CI: 1.06-2.18) increased risk of recurrence and metastasis. Analysis of TCGA and GTEx databases showed that the expression levels of PVT1 and CASC16 in breast tumors were significantly higher than those in normal tissues and matched para-cancerous tissues ($P < 0.001$), whereas the expression level of NAMPT in breast tumors was significantly lower than that in normal tissues ($P < 0.001$). No significant difference was shown about the expression level of TNFRSF13B between breast tumor and normal tissues or matched para-cancerous tissues ($P \geq 0.05$). Conclusion: Our study suggested that PVT1, CASC16, TNFRSF13B and NAMPT may be correlated with the risk of recurrence and metastasis of BC. Glutamatergic synaptic transmission, calcium signaling pathway and insulin secretion pathway may be involved in BC recurrence and metastasis.

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P3-05-32

Positive sentinel lymph node does not affect prognosis in T1 breast cancer patients who undergo breast conserving surgery with sentinel lymph node biopsy.

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Backgrounds: The ACOSOG Z0011 trial revealed oncologic outcomes in patients who underwent breast conserving surgery (BCS) and sentinel lymph node biopsy only versus completion axillary dissection to be equivalent. It was also reported that axillary recurrence rate to be not different between axillary dissection group and SLNB only group, despite the positive rate of over 20% in non-sentinel lymph nodes. It led to suspicion that the role of SLNB in local control to be less significant than previously recognized. Currently trials such as SOUND trial and NAUTILUS trial are being conducted in cT1N0 breast cancer undergoing BCS to compare the outcomes between the current standard surgery and no axillary surgery.

Purposes: This study aimed to investigate the factors associated with positive SLN in patients with T1 breast cancer, including T substages. We also evaluated the oncologic outcomes according to SLN positivity.

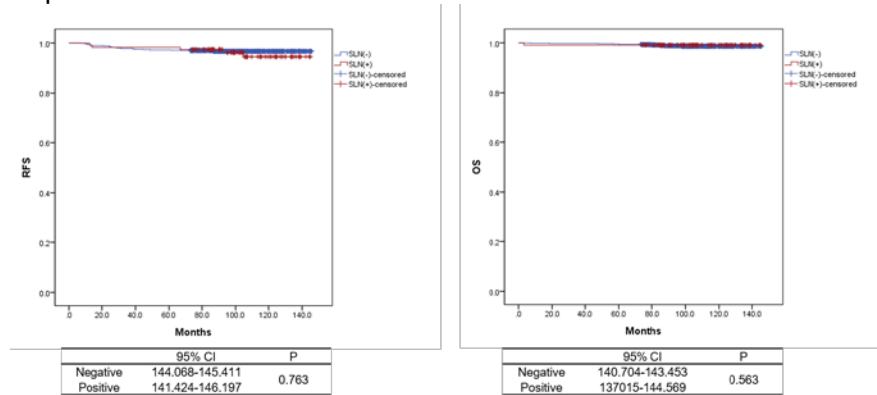
Method: We retrospectively reviewed medical records of patients with pT1 breast cancer who underwent BCS including SLNB at Seoul National University Bundang Hospital from 2010 to 2015 (n=986). SLN positive was defined as one or more micro- to macro-metastasis in axillary lymph node specimen. Overall, regional, and systemic recurrence-free survival (RFS, RRFS, SRFS) and overall survival (OS) were estimated by the Kaplan-Meier analysis.

Result: Of 986 patients, positive SLN was observed in 116 patients (11.8%). Regarding T substages, T1mic, T1a, and T1b groups showed SLN positive rate of 0%, 3.4%, and 8.5% respectively whereas T1c showed 15.3%. Multivariable logistic regression analyses revealed clinical T stage (OR 1.791, 95% CI 1.061-3.023, P=0.029), >C2 finding in preoperative axillary ultrasonography (OR 3.021, 95% CI 1.740-5.248, P< 0.001), usual histologic type including invasive ductal carcinoma, invasive lobular carcinoma, and metaplastic carcinoma confirmed in preoperative biopsy (OR 4.406, 95% CI 1.357-14.305, P=0.014) to be independent predictive factors for SLN positivity. The median follow-up period was 103.03 months. The 5 year RFS, RRFS, SRFS, and OS showed no statistical difference between SLN positive group and

negative group. In multivariable Cox regression analysis, serum CEA level higher than 5ng/ml at diagnosis (HR 7.534, 95% CI 3.336-17.019, P=0.002) and Ki-67 level higher than 20% (HR 7.534, 95% CI 3.336-17.019, P< 0.001) were shown to be the independent prognostic factors for RFS.

Conclusion: Our data implicates that patients with T1c breast cancer should undergo SLNB at all times presently, considering substantially higher SLN positive rate compared to other T1 substages (16.8% vs. 6.1%, P< 0.001) although no survival difference was observed between SLN positive group and negative group.

Kaplan-Meier curve of recurrence-free survival and overall survival



Kaplan-Meier analyses revealed no difference of recurrence-free survival, overall survival between SLN-positive and SLN-negative group.

Univariable and multivariable model for recurrence-free survival

	Univariable OR	95%CI	P value	Multivariable OR	95%CI	P value
SLN positivity						
Negative	Ref					
Positive	1.323	0.511-3.427	0.564			
Preop ALN (US)						
Negative	Ref					
>C2	1.185	0.362-3.882	0.780			
Preop ALN (MRI)						
Negative	Ref					
>C2	0.584	0.139-2.442	0.461			
Preop ALN (CT)						
Negative	Ref					
>C2	2.285	0.966-5.405	0.060			
Pathologic T stage						
T1mi-T1b	Ref					
T1c	1.031	0.513-2.072	0.933			
Pathologic N stage						
N0	Ref					
N+	1.323	0.511-3.427	0.564			
Grade						
Low grade	Ref			Ref		
High grade	4.484	2.160-9.310	<0.001	1.235	0.444-3.432	0.686
Ki-67						
<20	Ref			Ref		
≥20	7.614	3.523-16.456	<0.001	4.654	1.531-14.149	0.007
ER status						
Negative	Ref					
Weak positive	0.735	0.097-5.566	0.766			
Positive	0.241	0.120-0.483	<0.001			
PR status						
Negative	Ref					
Weak positive	0	0	0.975			
Positive	0.396	0.200-0.785	0.008			
HER2 status						
Negative	Ref					
Positive	1.529	1.036-2.256	0.032			
Pathologic subtype						
Luminal	Ref			Ref		
HER2+	3.952	1.590-9.827	0.003	1.34	0.445-4.037	0.603
TNBC	6.785	2.994-15.377	<0.001	2.154	0.755-6.146	0.161
RTx						
No	Ref					
Yes	0.396	0.153-1.025	0.056			
CTx						
No	Ref					
Yes	1.601	0.802-3.194	0.182			
HTx						
No	Ref					
Yes	0.208	0.105-0.412	<0.001			

Higher Ki-67 expression, ER negativity, PR negativity, HER2 positivity were shown to be independent risk factors associated with shorter RFS. Multivariable analysis showed higher Ki-67 expression as the sole independent risk factor for shorter RFS.

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5:00 PM - 6:15 PM

P3-05-33

High expression of MiR-99b in breast cancer is associated with cell proliferation signaling and worse patient survivals in breast cancer

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Background: MicroRNA (miR) is single stranded RNA which regulates the gene expression epigenetically by inhibiting the mRNA translation as well as promoting mRNA degradation. MiR-99b is known as a regulator of mechanistic target of rapamycin (mTOR) signaling and was reported as both onco-miR that promote cell proliferation and tumor suppressor-miR in multiple cancers. We hypothesized that there is a complex interaction between miR-99b and cancer signaling pathways as well as tumor microenvironment, which may influence outcomes.

Methods: We studied the clinical relevance of miR-99b expression by performing in silico analyses of 1,961 breast cancer patients using two independent large cohorts; METABRIC and TCGA. Results: We found that high miR-99b breast cancer enriched MTORC1 signaling gene set (normalized enrichment score (NES)>1.50 in both cohorts), but not epithelial mesenchymal transition, NF- κ B, nor TGF- β signaling gene sets (all false discovery rate (FDR)>0.40). High miR-99b breast cancer was significantly associated with high rates of mutation scores; silent- and non-silent-mutation rate, fraction altered, single-nucleotide variant neoantigens, as well as intratumor heterogeneity and homologous recombination defects. MiR-99b high tumors also enriched several cell proliferation-related gene sets; E2F targets, G2M checkpoint, and Mitotic spindle signaling, and was significantly associated with pathological grade, but not with subtype nor AJCC stage. High miR-99b breast cancer was significantly associated with low fraction of several stromal cells, including adipocytes cells, keratinocytes cells, and lymphatic endothelial

cells in tumor microenvironment (all $p < 0.001$). On the other hand, miR-99b expression was not associated with immune function nor immune cell infiltration in breast cancer, except for dendritic cells ($p=0.006$ and 0.020 , respectively). Finally, breast cancer with high miR-99b expression was significantly associated with worse overall survival (OS) (hazard ratio (HR)=1.23 ($p < 0.001$) and 1.26 ($p=0.027$), respectively) and disease-specific survival (DSS) (HR=1.28 ($p < 0.001$) and 1.39 ($p=0.022$), respectively), particularly DSS for ER-positive/HER2-negative breast cancer (HR=1.29 ($p < 0.001$) and 1.82 ($p=0.017$), respectively), consistently in two cohorts. In conclusion, we found that high miR-99b expressing breast cancer was significantly associated with not only MTORC1 but also cell proliferation and worse patient outcomes particularly in ER-positive/HER2-negative breast cancer.

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5:00 PM - 6:15 PM

P3-05-34

CANTO-RT: Skin toxicities evaluation of a multicenter prospective cohort of irradiated patients for early-stage breast cancer.

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Purpose:

Skin damage is the most common and most important toxicity during and after radiotherapy. Its assessment and understanding of the factors influencing its occurrence, is a major issue in the management of patients irradiated for an early breast cancer (BC).

Method:

CANTO (NCT01993498) is a prospective clinical cohort study of 10 150 patients with stage I-III BC treated from 2012-2017 in 26 cancer centers.

In this study, we used CANTO-RT, a sub-cohort of CANTO, including 3480 patients who received RT. We are focus on specifical skin toxicities: Erythema, fibrosis, telangectasia and skin color change (CTCAE v4.0). These toxicities were assessed at baseline 0-3-6 (M0), 12 (M12), 36 (M36) months.

The RT-related variables were independent variables. Multivariable logistic regression models

assessed associations between RT-related variables and skin toxicities of interest.

Results:

We studied 3480 patients from 2012 to 2017. Patients had a median age of 56.8 years and a mean BMI of 26. The majority of patients had SBR grade 1-2, TNM 1-2, RH+/HER2- breast cancer. Most patients had conservative surgery and 52.7% received chemotherapy. All the patients received radiotherapy mainly normofractionated 50Gy in 25 fractions, in 3D, with a boost of 16Gy in 8fractions.

The prevalence of toxicities of interest varied over time, so at M0, 41.1% of patients had erythema while 24.8% of patients had fibrosis.

At M12 and M36, the prevalence of erythema decreased from 8.8% to 2.9% respectively while fibrosis remains stable from 25.1% to 22.5%.

The prevalence of telangiectasia increases from 1% to 7.1% from M0 to M36. The prevalence of the skin color change decreased from 31.7% to 17.5% from M12 to M36. After adjustments, at M0 and M12, we showed a statistically significant association between the occurrence of skin erythema and obesity (OR: 1.3 p < 0.003); the presence of axillary dissection (OR: 1.33 p < 0.003); the type of surgery (OR: 0.71 p < 0.001); the use of taxane- based chemotherapy (OR: 1.46 p < 0.005) and the 3DvsIMRT irradiation technique (OR: 0.42 p < 0.001). However, no radiotherapy factors were statistically related to erythema from M12.

Regarding fibrosis, a statistically significant association is found, at M0, with age at diagnosis (OR: 1.43 p < 0.018), obesity (OR: 1.44 p < 0.001), tobacco (OR: 1.4 p < 0.008), and the use of boost (OR: 1.61 p < 0.001). Only obesity and the type of surgery received by the patient remained statistically significant factors at M12 and M36.

Obesity and age at diagnosis represented at M12 and M36 a risk associated with the onset of telangiectasias.

The skin color change is consistently correlated at M12-M36 with obesity and smoking. The use of a boost increases the skin color change at M36.

Conclusion:

In this study we identified several risk factors for acute and late skin toxicity such as obesity in the occurrence of skin erythema, fibrosis or telangiectasia. The use of a boost was mainly related to the occurrence of skin color change while the use of IMRT-type technique decreased the occurrence of skin erythema. The knowledge of its predictive factors allows a personalized management of the patient by adapting our treatments and our monitoring according to these different factors.

Relationship between radiation therapy parameters and the occurrence of skin toxicity

		M3-6 (n=3380)			M12 (n=3088)		
		N	OR [IC95%]	P-value	N	OR [IC95%]	P-value
Obesity	No	2696	1 (ref)	0.003	2470	1 (ref)	<0.001
	Yes	684	1.30 [1.09 ; 1.54]		618	1.79 [1.35 ; 2.36]	
Type of surgery	Conservative surgery	2744	1 (ref)	0.001	2517	1 (ref)	<0.001
	Mastectomy	636	0.71 [0.57 ; 0.87]		571	0.34 [0.20 ; 0.57]	
Axillary dissection	No	2177	1 (ref)	0.003	2029	1 (ref)	0.008
	Yes	1203	1.31 [1.09 ; 1.56]		1059	1.50 [1.11 ; 2.01]	
Type of chemotherapy	No chemotherapy	1599	1 (ref)	0.005	-	-	
	Neoadjuvant chemotherapy	375	1.51 [1.18 ; 1.95]		-	-	
	Adjuvant chemotherapy	1406	1.08 [0.92 ; 1.27]		-	-	
Taxanes chemotherapy	No	-	-		1517	1 (ref)	0.009
	Yes	-	-		1571	1.46 [1.10 ; 1.93]	
RT technique	3D	3246	1 (ref)	<0.002	-	-	
	IMRT	134	0.42 [0.28 ; 0.62]		-	-	

Table 2a. Skin toxicity of interest: Erythema at M0 and M12 (multivariate analysis)

Evolution of skin toxicities of interest over time for a given patient (Sankey plot)

		M36 (n=3006)			M12 (n=1569)			M36 (n=1523)		
		N	OR [IC95%]	P-value	N	OR [IC95%]	P-value	N	OR [IC95%]	P-value
Smoking status	Non smoker	1873	1 (ref)	0.008	-	-	-	-	-	-
	Former smoker	623	1.40 [1.13 ; 1.72]		-	-	-	-	-	-
	Smoker	510	1.06 [0.83 ; 1.35]		-	-	-	-	-	-
Age at diagnosis	<50 yrs	862	1 (ref)	0.018	458	1 (ref)	0.127	431	1 (ref)	0.127
	50-65 yrs	1340	1.17 [0.95 ; 1.45]		700	1.02 [0.91 ; 1.60]		686	1.09 [0.79 ; 1.52]	
	>65 yrs	804	1.43 [1.12 ; 1.84]		411	1.40 [1.03 ; 1.94]		406	1.44 [0.99 ; 2.09]	
Obesity	No	2381	1 (ref)	<0.001	1206	1 (ref)	<0.001	1229	1 (ref)	<0.001
	Yes	625	1.44 [1.17 ; 1.75]		363	1.56 [1.21 ; 2.01]		294	1.71 [1.26 ; 2.31]	
Axillary dissection	No	1944	1 (ref)	0.075	1070	1 (ref)	0.433	1036	1 (ref)	0.373
	Yes	1062	1.20 [0.98 ; 1.47]		499	1.12 [0.84 ; 1.50]		487	0.84 [0.57 ; 1.24]	
Type of surgery	Conservative surgery	2458	1 (ref)	<0.001	1357	1 (ref)	<0.001	1267	1 (ref)	0.007
	Mastectomy	548	0.44 [0.30 ; 0.64]		212	1.09 [0.85 ; 1.40]		256	0.45 [0.24 ; 0.80]	
Boost	No	911	1 (ref)	<0.001	358	1 (ref)	0.993	460	1 (ref)	0.172
	Yes	2095	1.61 [1.24 ; 2.11]		1211	1.00 [0.59 ; 1.68]		1063	1.30 [0.89 ; 1.91]	
Fractionation	Normofractionation	-	-	-	1428	1 (ref)	0.194	-	-	-
	Hypofractionation	-	-	-	141	1.46 [0.82 ; 2.57]		-	-	-
Technique RT	3D	-	-	-	-	-	-	1478	1 (ref)	0.102
	IMRT	-	-	-	-	-	-	45	0.45 [0.13 ; 1.16]	

Table 2b. Skin toxicity of interest: Fibrosis at M0, M12 and M36 [multivariate analysis]

* A= erythema. B= fibrosis, C= telangiectasia, D=skin color

Table 3. Grade CTCAEv4 of toxicities of interest

	M0 (n=3480)			M12 (n=3210)			M36 (n=2449)		
	Grade 0	Grade 1-2	Grade 3-4	Grade 0	Grade 1-2	Grade 3-4	Grade 0	Grade 1-2	Grade 3-4
Erythema	2009 (58.7)	1385 (40.5)	27 (0.8)	2848 (91.2)	271 (8.7)	4 (0.1)	2309 (97.1)	65 (2.8)	4 (0.2)
Fibrosis	2366 (75.2)	764 (24.2)	16 (0.5)	2346 (74.9)	780 (24.9)	7 (0.2)	1873 (77.5)	540 (22.3)	5 (0.2)
Telangiectasia	3061 (99.0)	32 (1.0)	0 (0)	2993 (97.4)	80 (2.6)	0 (0)	2212 (92.9)	169 (7.1)	0 (0)
Skin coloration	1229 (35.4)	2211 (63.7)	28 (0.8)	2170 (68.3)	1004 (31.6)	5 (0.2)	1990 (82.5)	417 (17.3)	5 (0.2)

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The impact of parity and age of first full term pregnancy on the prevalence of invasive lobular carcinoma in patients with breast cancer

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Background: The impact of reproductive factors on breast cancer has proven to be complex. The risk for estrogen receptor positive/ HER2-negative (ER+/HER2-) breast cancer is estimated to be transiently augmented in the years after giving birth (up to 20 years) while later in life high parity and early first full-term pregnancy (1st FTP) seem to protect against ER+/HER2- breast cancer (BC). Invasive lobular carcinomas (ILC) represents the second most common histological subtype of BC and >90% are ER+/HER2-. In this study, we aimed at investigating whether parity and age at 1st FTP are associated with: 1) the prevalence of ER+/HER2- pure ILC (i.e., not mixed) in an ER+/HER2- BC cohort (overall and according to the age at breast cancer diagnosis), and, 2) standard clinical and pathological features of pure ILC.

Patients and methods: We performed a single center retrospective study in UZ Leuven, Belgium of patients diagnosed with non-metastatic ER+/HER2- breast cancer between January 2000 and November 2020. Both patient and tumor characteristics were collected from clinical files. Firth's logistic regression was performed to investigate the association of BC histology (pure ILC vs all other BC histological subtypes = control group) with parity (yes vs. no and nulliparous, 1 child, 2 children, >2 children) in univariable models and multivariable models adjusted for age group at diagnosis (< 30, 31-40, 41-50, 51-60, 61-70, >70), age at 1st FTP (continuous and per age group: < 21, 21-25, 26-30, >30), Interval between 1st FTP and diagnosis (continuous), year of birth and BMI. Analyses were done in the overall group as well as per age group at diagnosis. Similarly, regression analyses were performed in patients with ER+/HER2- ILC to assess the association of parity (yes vs. no and nulliparous, 1 child, 2 children, >2 children) with the following variables: age at diagnosis, BMI, histological grade, tumor size, nodal involvement and progesterone receptor positivity.

Results: 7360 patients were included of which 1121 (15.2%) were diagnosed with pure ER+/HER2- ILC, the remaining 6239 (84.8%) patients were considered as the control group. Overall, in multivariable analyses, parity with >2 children was associated with a higher prevalence of pure ILC as compared to uniparous patients (odds ratio, OR 1.257, 95CI 1.039-1.521, p= 0.019). No significant association was seen for age at 1st FTP and interval 1st FTP – diagnosis. The subgroup analyses per age group are summarized in Table 1. Only for the age group 41-50, an increased age 1st FTP was associated with an increased prevalence of pure ILC.

In patients with pure ER+/HER2- ILC, nulliparous women were less likely to have a progesterone receptor (PR)-positive tumor as compared to parous women (OR 0.477, 95CI 0.224-0.907, p= 0.022). No other significant associations were seen for clinicopathological features between nulliparous and parous women, and between uniparous and multiparous women in the overall cohort nor any age group.

Conclusions: Within an ER+/HER2- breast cancer cohort, higher parity seems to be associated with a higher prevalence of pure ILC, which is especially seen in the patients diagnosed with

breast cancer between the age of 51 and 60. Increased age at the 1st FTP only seems to increase the incidence of ILC in the age group 41-50. With the exception of nulliparous women having less PR positive tumors, parity does not seem to affect the clinicopathological features of ER+/HER2- pure ILC.

Table 1: subgroup analyses per age group of association of histology (pure ILC vs control group) with parity, age 1st FTP and interval 1st FTP – diagnosis

Variables	31-40		41-50		51-60		61-70		>70	
	OR (95CI)	p-value	OR (95CI)	p-value	OR (95CI)	p-value	OR (95CI)	p-value	OR (95CI)	p-value
Parity (2 vs. 1 child)	0.672 (0.227-2.015)	0.471	1.097 (0.749-1.628)	0.638	1.111 (0.805-1.543)	0.525	1.294 (0.938-1.798)	0.117	1.009 (0.674-1.521)	0.965
Parity (≥2 vs. 1 child)	0.635 (0.140-2.432)	0.516	1.394 (0.895-2.180)	0.142	1.592 (1.120-2.270)	0.010	1.299 (0.911-1.860)	0.149	0.972 (0.643-1.482)	0.893
Age 1 st FTP (21-25 vs. <21)	0.992 (0.095-15.619)	0.995	1.544 (0.759-3.395)	0.239	1.083 (0.670-1.796)	0.749	0.710 (0.465-1.094)	0.119	1.459 (0.863-2.571)	0.162
Age 1 st FTP (26-30 vs. <21)	1.589 (0.099-40.579)	0.755	2.358 (1.039-5.705)	0.040	0.978 (0.532-1.824)	0.942	0.777 (0.440-1.374)	0.384	1.410 (0.737-2.767)	0.302
Age 1 st FTP (≥31 vs. <21)	3.642 (0.118-200.742)	0.477	3.372 (1.273-9.411)	0.014	0.918 (0.415-2.039)	0.834	1.358 (0.837-2.891)	0.428	1.580 (0.696-3.611)	0.274
Interval 1 st FTP - diagnosis	1.05 (0.836-1.361)	0.685	1.027 (0.970-1.088)	0.363	0.968 (0.924-1.014)	0.168	1.002 (0.956-1.050)	0.930	1.001 (0.962-1.041)	0.963
Year of birth	0.841 (0.75-0.927)	0	0.978 (0.952-1.005)	0.107	0.997 (0.974-1.021)	0.818	0.998 (0.977-1.020)	0.871	1.020 (0.993-1.049)	0.152
BMI	1.016 (0.902-1.119)	0.775	0.973 (0.936-0.140)	0.140	1.000 (0.972-1.027)	0.973	0.980 (0.955-1.006)	0.139	0.976 (0.949-1.010)	0.164

Multivariable model adjusted for all variables
No results for age group ≤30 since no ER+/HER2- pure ILC in that age group

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Prognostic factors in non-metastatic hormone receptor-positive HER2-negative mucinous breast cancer: an international multicentre cohort study

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Background: Mucinous carcinoma is the third most common histological subtype of breast cancer after ductal and lobular carcinomas, accounting for approximately 3% of invasive breast cancers. Although considered a favourable subtype with de-escalation of treatment recommended in the National Comprehensive Cancer Network guidelines, recurrence can occur and supporting data is limited. We thus examined prognostic factors of pure mucinous breast cancer (PMBC) in an international multicentre cohort study. Methods: Patients diagnosed between January 2000 to December 2015 with hormone receptor-positive HER2-negative stage I to III PMBC, invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC) at 6 centers in Singapore, Taiwan, Korea and Japan were evaluated. Cox proportional hazards regression analyses were used to compare relapse-free survival (RFS), distant relapse-free survival (DRFS) and overall survival (OS) by histological subtypes, and to identify prognostic factors for PMBC. Results: Of 23,105 women eligible for analysis, 20,684 had IDC, 1,475 had ILC and 946 had PMBC. The median follow-up was 6.6 years; 5-year RFS, DRFS and OS for PMBC were 94.6%, 96.5% and 98.1% respectively. On multivariable cox regression analyses, PMBC demonstrated superior RFS (hazard ratio [HR] = 0.70, 95% CI: 0.56 - 0.88), DRFS (HR = 0.69, 95% CI: 0.53 - 0.89) and OS (HR = 0.70, 95% CI: 0.52 - 0.93) compared to IDC, while ILC had comparable survival outcomes as IDC. When restricted to only PMBC, significant independent prognostic factors for RFS included ethnicity (vs Chinese, "Others" [non-Chinese/Japanese/Korean, mainly Malay and Indian]: HR = 2.62, 95% CI 1.23 – 5.57),

older age (vs < 40 years, >70 years: HR = 3.53, 95% CI 1.67 – 7.46), tumor size (vs T1, T3-4: HR = 2.79, 95% CI 1.45 – 5.37), positive lymph nodes (HR = 2.04, 95% CI: 1.10 – 3.77), use of radiotherapy (HR = 0.54, 95% CI 0.33 – 0.91) and endocrine therapy (HR = 0.31, 95% CI 0.12 – 0.77). On further analysis, the inferior RFS, DRFS and OS in older patients (>70 years) were driven largely by non-breast cancer deaths rather than relapses. Use of endocrine therapy was also associated with superior DRFS (HR = 0.26, 95% CI 0.09 – 0.73) but not OS. In a subgroup analysis, use of chemotherapy was associated with improved DRFS (HR = 0.25, 95% CI 0.08 – 0.82) and OS (HR = 0.07, 95% CI 0.01 – 0.37) with a trend in RFS (HR = 0.41, 95% CI 0.14 – 1.24) for lymph node-positive PMBC; no differences in outcomes were observed for the lymph node-negative subgroup. Conclusions: Larger tumor size, lymph node positivity and ethnicity were significant factors for RFS in PMBC. Use of endocrine therapy was associated with superior RFS and DRFS, while chemotherapy was associated with better DRFS and OS for lymph-node positive PMBC.

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5:00 PM - 6:15 PM

P3-05-37

Influence of Clinical Heterogeneity on Pregnancy Associated Breast Cancer survival: Systematic Review with Metanalysis

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Objective: Pregnancy-associated breast cancer (PABC) is defined as diagnosed during pregnancy or within one year of childbirth, in which current evidence associates with poor prognosis, without showing what clinical characteristics could impact in survival. We aim to explore the impact of heterogeneity in risks on death and disease relapse, suggesting clinical characteristics that might improve PABC clinical outcomes.

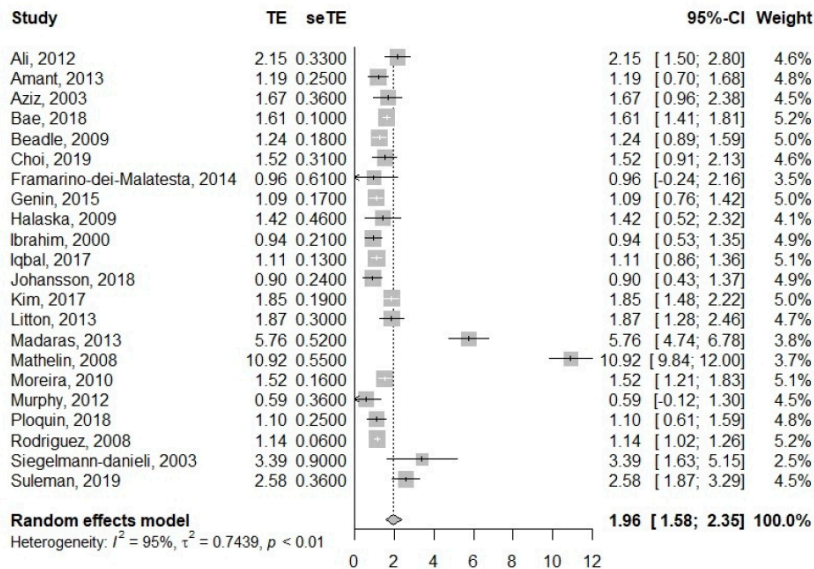
Methods: Medline, Embase, Cochrane, Lilacs and congress abstracts published since 2000 were used as data sources. Two reviewers independently selected manuscripts and extracted data and a third reviewer solved discrepancies. The primary outcome was overall survival (death), and secondary outcome was disease-free survival (death or relapse). Summarized hazard ratios were recalculated based on reported data. All metaanalyses used a random-effects model and heterogeneity was reported using the I² method.

Results: A total of 7143 studies were identified and 30 studies were included for metaanalyses. PABC is associated with a 96% (HR=1.96, 95%CI 1.58;2.35) higher risk of death and an additional 82% (HR=1.82, 95%CI 1.45;2.20) risk of death or disease relapse in comparison to a population of non-PABC or nulliparous BC. Through sensitivity analyses, we identified that

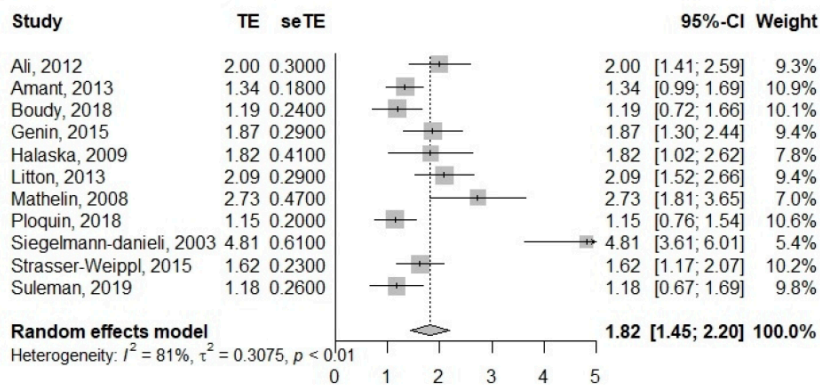
clinical outcomes was impacted, possibly due to Ki-67 levels, poorly differentiated tumors, and triple negative breast cancer (TNBC) frequency in the study.

Conclusions: PABC is correlated with poorer prognosis, suggesting that besides early diagnosis, Ki-67 levels, poorly differentiated tumors and TNBC might be relevant sources of inconsistency. So, such clinical sources of heterogeneity should be better investigated regarding the potential to evaluate alternative therapeutic strategies.

PABC deaths compared to non-PABC population, represented as hazard ratio



PABC deaths or disease relapse compared to non-PABC population, represented as hazard ratio



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Biology and clinical course of lobular cancer in breast cancer (BC)

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Biology and clinical course of lobular cancer in breast cancer (BC)

Background: Invasive lobular carcinoma (ILC) accounts for 10–15% of all breast cancers. Due to its distinctive growth pattern and biology, lobular carcinoma often fails to form distinct masses that can be easily detected by palpation or mammography. Because it is substantially less common than infiltrating ductal carcinoma (IDC), knowledge about clinical outcomes of ILC has been based on studies including relatively small patient (pt) numbers. Thus, we sought to assess the biologic and genomic features of ILC in the context of clinical outcomes.

Methods: Eligible pts were adults with metastatic lobular or ductal BC seen at MD Anderson between 1997 and 2020. Overall survival (OS), progression-free survival (PFS), and disease-free interval (DFI) from the initial diagnosis were estimated using the Kaplan-Meier method. Survival distributions were compared using the log-rank test. Multivariate Cox proportional hazards regression models were applied to assess effect of covariates of interest on OS and DFS. No statistical adjustment was made for multiple testing.

Results: A total of 7642 IDC and 1159 ILC female metastatic BC pts were included in the analysis. Clinical characteristics are presented in the table. Pts with ILC were on average older, had fewer metastases, and were more likely to have a family history of breast or ovarian cancer than pts with IDC. Lobular cases were less likely to be HER2+, had lower Ki-67, and lower nuclear grade than ductal cancer cases.

The median follow-up was 4.37 years. The median OS for all pts from initial diagnosis was 5.38 years; 5.21 years and 6.57 years for IDC and ILC, respectively. ER positivity was associated with longer OS in both IDC [Hazard ratio (HR) 0.47, 95% confidence interval (CI): 0.45 - 0.49, $P < 0.0001$] and ILC (HR 0.63, 95% CI: 0.54 - 0.75, $P < 0.0001$). In de novo metastatic disease,

the median OS was 3.74 years in IDC and 4.15 years in ILC. In recurrent IDC and ILC, the median OS was 5.84 and 7.89 years, respectively. De novo presentation had better OS from time of metastatic disease diagnosis for pts with both ILC and IDC than those presenting with recurrent cancer; however, de novo presentation was associated with worse PFS on 1st line therapy. In ILC, grade III had a poorer prognosis than grade I/II; (HR 1.47, 95% CI: 1.30 - 1.68, P< 0:0001). Among pts with IDC, grade I had the best outcomes, followed by grade II, then grade III. In IDC, significantly improved OS was observed in HER2+ BC (HR 0.85, 95% CI: 0.79 - 0.92), P< 0:0001). The median PFS for all pts was 0.53 years and the median DFI was 2.61 years. In both ILC and IDC, PFS and DFI were better in cancers that were ER+ or grade I/II. Conclusions: In metastatic BC pts, the biologic phenotypes and clinical behavior of ILC and IDC differ. More complete and reliable characterization of ILC may yield useful information regarding the biologic nature of ILC resulting in discovery of actionable findings leading to more personalized therapy. Further analyses of genomic features and patterns of metastatic sites between IDC and ILC will be presented.

Biology and clinical course of lobular cancer in breast cancer (BC)

Variable	Levels	Ductal (%)	Lobular (%)
Race	Asian/Pacific Is	4.4	2.6
	Black	13	7.8
	Native American	0.2	0.1
	Other	1.3	1.1
	Spanish/Hispanic	10.4	10.3
	White	70.7	78.1
Site of Metastasis at First Dx	Non-visceral	42.7	55.4
	Visceral	57.3	44.6
De Novo/Recurrent	De Novo	29.2	34.6
	Recurrent	70.8	65.4
ER %	0-9%	28.4	8.6
	10-55%	10.8	11.2
	56-94%	30.3	40.4
	>=95%	30.5	39.8

Patient characteristics of ILC and IDC

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5:00 PM - 6:15 PM

P3-05-39

Expert consensus on the definition of high risk of recurrence in HER2-negative early breast cancer: a modified Delphi panel

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PURPOSE: There is currently no standardised definition for patients at high risk of recurrence of HER2-negative early breast cancer (eBC, stages 1–3) after surgery. Recognising that the assessment of high risk is often multifactorial, the aim of this modified Delphi panel was to establish expert UK consensus on this definition, separately considering HR-positive and triple-negative (TN) patients. **METHODS:** A total of 45 UK-based clinicians, including breast cancer oncologists and surgeons, were invited to participate. The number of respondents in each of three rounds was 29, 24 and 22 respectively. Statements were developed using the results

from a targeted literature review and the guidance of a lead clinician, and comprised free-text, single-choice or numerical formats. The first round aimed to determine which factors are currently used in clinical practice to assess risk of recurrence in the populations of interest. In the subsequent rounds, the objective was to establish thresholds indicative of high risk in a 10-year timeframe for each of the factors retained in Round 1. Between each round, statements were refined, considering the distribution of responses and free-text notes provided by participants. Consensus for single-choice questions was set at a pre-defined threshold of $\geq 70\%$ of respondents. **RESULTS:** Consensus was achieved on the need to assess age, tumour size, tumour grade, number of positive nodes, presence of inflammatory breast cancer and one or more risk prediction tools to define high risk of recurrence in all HER2-negative patients. In HR-positive patients, there was agreement on the use of one or more tumour profiling tests and biomarkers to define high risk of recurrence. However, there was no consensus on biomarker use in TN patients, and support for specific biomarkers (such as Ki-67) was conflicting for both sub-populations based on the analysis of free-text notes. Similarly, while there was consensus on the use of pCR status/residual disease to indicate high risk in TN patients, this factor failed to reach consensus for the HR-positive sub-population. Germline BRCA status and menopausal status were not considered to be key factors for risk of recurrence in either biological subtype. In the second and third rounds, thresholds indicative of high recurrence risk were agreed; it should be noted that the free-text responses provided by the participants frequently highlighted that many of the factors should be considered along a continuous scale when assessing the risk of individual patients. In HR-positive patients, these thresholds included: age < 35 years, tumour size > 5 cm (each when considered independently from other risk factors); tumour grade 3 (independently or in combination with other factors); number of positive lymph nodes ≥ 4 when considered independently or ≥ 1 in combination with other factors. For patients with TN tumours, the following thresholds reached consensus, whether considered independently or in combination with other factors: tumour size > 2 cm, tumour grade 3, number of positive lymph nodes ≥ 1 . In several cases, however, no consensus could be reached on the appropriate threshold indicating high risk of recurrence. In the HR-positive sub-population, these included thresholds for age and tumour size, when considered in combination with other factors. In the TN sub-population, this included age, whether independently or in combination with other factors. **CONCLUSIONS:** The expert consensus reached in this panel highlights that an integrated model is important in assessing recurrence risk in eBC and that definitions of high risk differ according to biological subtype. The results may serve as a valuable reference point for clinicians to use in assessing risk of disease recurrence and in making treatment decisions after surgery in the HER2-negative eBC population. **FUNDING:** AstraZeneca UK Ltd. Writing support: Costello Medical.

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Association of body mass index with clinicopathological features and survival in patients with primary ER+/HER2- invasive lobular breast cancer

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Background: Invasive lobular carcinoma (ILC) represents up to 15% of all breast carcinomas. The majority of ILC express the estrogen receptor (ER) and have no amplification/overexpression of the human epidermal growth factor receptor 2 (HER2). A high body mass index (BMI) has been associated with an increased risk of developing ILC in postmenopausal women, similar to what is seen for breast cancer of no special type (NST). It is however unknown if BMI impacts the clinicopathological features and the prognosis of ILC.

Methods: We performed a multicentric retrospective study in 5 European centers of patients diagnosed between January 2000 and December 2020 with ER+/HER2- non-metastatic pure (i.e., not mixed) ILC. Patient and tumor characteristics and event-related data were collected. BMI was categorized into underweight ($\leq 18.5 \text{ kg/m}^2$), lean ($> 18.5 \text{ kg/m}^2$ and $< 25 \text{ kg/m}^2$), overweight ($\geq 25 \text{ kg/m}^2$ and $< 30 \text{ kg/m}^2$) and obese ($\geq 30 \text{ kg/m}^2$). The association of BMI as either a continuous or a categorical variable with clinicopathological variables was assessed using linear regression or ordinal logistic regression, respectively. Median follow-up was calculated using the reverse Kaplan-Meier estimator. Survival analyses using univariable (stratified by center) and multivariable (adjusted for all included variables and stratified by center) Cox regression were performed to evaluate the association of BMI with disease free survival (DFS), distant recurrence free survival (DRFS) and overall survival (OS). DFS and DRFS were analyzed in the presence of death without event as the competing risk.

Results: The data of 2476 patients were collected and BMI was available for 2346 patients. In total, 1299 (55%) patients were lean, 638 (27%) overweight and 339 (14%) obese. Underweight patients only represented 3% of all patients and were thus excluded from further analyses. A higher age at diagnosis, higher grade, larger tumor size, nodal involvement and multifocality were significantly associated with higher BMI (Table 1). The median follow-up was 8,5 years (interquartile range 59.24 – 142.13 months). In univariable analysis, higher BMI was associated with worse survival outcomes (Table 2). However, this association was not seen in multivariable analysis while grade, tumor size and nodal involvement were still prognostic for all endpoints. Similar results were seen with BMI as a continuous variable.

Conclusion: Larger tumors and nodal involvement were more likely to be found in patients with ER+/HER2- ILC with higher BMI which might be explained by a delayed diagnosis in these patients. Higher grade also seemed to be associated with higher BMI. In multivariable analyses, BMI was not found to be an independent prognostic factor. Tumor grade, tumor size, and nodal

status remained strongly prognostic for survival outcomes in multivariable survival analyses which is consistent with their known prognostic importance in luminal tumors. We hypothesize that the prognostic effect of BMI is mediated through these variables for patients with ER+/HER2- ILC.

Table 1: Association of clinicopathological features of ER+/HER2- ILC with categorical BMI

	Model 1		Model 2	
	OR (95CI)	p-value	OR (95CI)	p-value
Age (>50 vs ≤50)	2.25 (1.83-2.77)	<0.01	2.70 (2.08-5.53)	<0.01
Grade (G3 vs G1/2)	1.89 (1.41-2.51)	<0.01	1.54 (1.09-2.17)	0.01
Tumor size (≥2cm vs <2cm)	1.81 (1.53-2.13)	<0.01	1.52 (1.22-1.91)	<0.01
Nodal involvement (yes vs no)	1.68 (1.42-1.98)	<0.01	1.45 (1.16-1.83)	<0.01
Multifocality (multi vs unifocal)	1.30 (1.05-1.60)	0.01	1.44 (1.15-1.80)	<0.01
PR-positivity (yes vs no)	1.30 (1.02-1.68)	0.04	1.51 (1.11-2.08)	0.01

Model 1: stratified by center
 Model 2: adjusted for all other variables and stratified by center
 95CI: 95% coincidence interval; G: grade; OR: odds ratio; PR: progesterone receptor

Table 2: Association of categorical BMI and other clinicopathological features of ER+/HER2- ILC with survival

Variable	DRFS				DFS				OS			
	Model 1		Model 2		Model 1		Model 2		Model 1		Model 2	
	HR (95CI)	p-value	HR (95CI)	p-value	HR (95CI)	p-value	HR (95CI)	p-value	HR (95CI)	p-value	HR (95CI)	p-value
BMI (Overweight vs Lean)	1.45 (1.09-1.93)	0.01	1.13 (0.83-1.54)	0.45	1.25 (0.98-1.59)	0.08	1.04 (0.80-1.36)	0.77	1.49 (1.19-1.87)	<0.01	1.17 (0.91-1.50)	0.22
BMI (Obese vs Lean)	1.59 (1.13-2.42)	<0.01	1.01 (0.68-1.49)	0.97	1.43 (1.07-1.92)	0.02	1.00 (0.71-1.40)	0.99	1.61 (1.23-2.11)	<0.01	1.19 (0.88-1.63)	0.25
Age (>50 vs ≤50)	1.00 (0.75-1.33)	0.99	1.34 (0.96-1.87)	0.08	1.06 (0.83-1.35)	0.64	1.24 (0.94-1.64)	0.13	2.08 (1.58-2.73)	<0.01	2.02 (1.48-2.75)	<0.01
Grade (G3 vs G1/2)	2.02 (1.41-2.88)	<0.01	1.65 (1.11-2.45)	0.01	1.70 (1.24-2.33)	<0.01	1.55 (1.09-2.19)	0.01	2.11 (1.60-2.78)	<0.01	1.84 (1.36-2.51)	<0.01
Tumor size (≥2cm vs <2cm)	4.20 (2.94-5.99)	<0.01	2.63 (1.69-4.10)	<0.01	2.58 (2.00-3.32)	<0.01	1.76 (1.28-2.42)	<0.01	2.18 (1.72-2.76)	<0.01	1.54 (1.16-2.04)	<0.01
Nodal involvement (yes vs no)	6.28 (4.59-8.58)	<0.01	4.86 (3.33-7.09)	<0.01	4.11 (3.25-5.19)	<0.01	4.24 (3.13-5.72)	<0.01	2.44 (1.99-3.00)	<0.01	2.89 (2.22-3.75)	<0.01
PR-positivity (yes vs no)	0.79 (0.55-1.13)	0.20	0.76 (0.52-1.10)	0.15	0.92 (0.67-1.27)	0.61	0.88 (0.64-1.23)	0.46	0.76 (0.58-1.01)	0.06	0.82 (0.61-1.10)	0.18
Radiotherapy (yes vs no)	1.72 (1.13-2.62)	0.01	1.09 (0.66-1.80)	0.74	1.46 (1.04-2.04)	0.03	0.99 (0.67-1.46)	0.95	0.91 (0.70-1.19)	0.49	0.75 (0.55-1.02)	0.06
Chemotherapy (yes vs no)	2.70 (2.10-3.48)	<0.01	1.04 (0.79-1.43)	0.79	1.87 (1.51-2.32)	<0.01	0.83 (0.63-1.08)	0.17	1.08 (0.87-1.33)	0.50	0.64 (0.49-0.83)	<0.01
Endocrine therapy (yes vs no)	2.21 (0.82-5.99)	0.12	1.53 (0.48-4.86)	0.47	1.00 (0.58-1.72)	1.00	0.69 (0.44-1.12)	0.69	1.45 (0.77-2.74)	0.25	1.39 (0.67-2.88)	0.38

Model 1: stratified by center
 Model 2: adjusted for all other variables and stratified by center
 95CI: 95% coincidence interval; BMI: body mass index; G: grade; HR: hazard ratio; PR: progesterone receptor

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P3-05-42

Identification of subpopulation of breast cancer patients with poor clinical outcome using CUB domain containing protein-1 (CDCP1)/CD318 and its interactive proteins SRC and the HGF axis

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Introduction. The CUB domain containing protein 1, also known as TRASK (Transmembrane and associated with Src kinases) or CD318, has been suggested as a biomarker for stem cells or stem like cells. The transmembrane CDCP1 protein is known to activate the Src kinase and has recently shown to play a key part in the aggressiveness of breast cancer cells including migration, invasiveness and possibly growth induced by the motogenic Hepatocyte Growth Factor (HGF) and its receptor MET (Kawase et al 2022), a process requires Rho-GEF, PI3K and STAT5. This appears to allow identification of a subset of cancer cells that are aggressive in their biological behaviours. Here, we examined the expression profile of CDCP1, SRC, the HGF/HGF receptor complex and HGF activation regulators in a cohort of breast cancer and attempt to establish if such protein axis is able to identify patients with high risk of poor clinical outcome. Methods. Using an establish breast cancer cohort which is comprised of both normal mammary tissues and breast cancer tissues freshly obtained after surgery, we quantified the gene transcripts of CDCP1/CD318 and examined its clinical and pathological relevance. Integrated analysis was conducted for CDCP1 and the expression profile of SRC, PI3K, HGF, the HGF receptor cMET, HGF activator (HGFA), HGF activation regulators including HAI-1, HAI2, matriptase-1 and matriptase-2, and STAT family members. This was done against the clinical outcome of the patients as well as the clinical and pathological factors. Results. Breast cancer tissues expressed high levels of CDCP1 compared with normal mammary tissues. CDCP1 itself had a weak yet significant value in predicting the overall survival of the patients

($p=0.047$). The expression levels of these CDCP1 related molecules aren't significantly correlated with CDCP1. However, integrated analyses revealed that CDCP1, together with its pathway regulators SRC, HGF, the HGF receptor (MET) and the HGF activation regulators matriptases form a power prognostic indicator for the clinical outcome of the patients ($p < 0.0001$, HR=1.8 for overall survival (OS) and $p=0.002$, HR=1.5 for disease-free survival (DFS)). This integrated profile has also identified subgroups of patients with highly favourable and very poor clinical outcomes over a ten-year follow-up period, with the respective survival at 100% and 36% respectively. The predictive power for OS and DFS is highly independent of other clinical and pathological factors in a multivariate analysis ($p=0.003$ and $p=0.017$ respectively). The predictive power is applicable to ER negative and HER2 positive tumours. Discussion. CDCP1/CD318, a factor known to stimulate cancer cell aggressiveness, together with its pathway kinase SRC and newly identified extracellular activator HGF and the HGF regulators forms a significant independent prognostic factor. It identifies subgroups of patients with favourable and poor prognosis, allowing consideration of targeted therapies for the patients. Reference Kawase N, Sugihara A, Kajiwara K, Hiroshima M, Akamatsu K, Nada S, Matsumoto K, Ueda M, Okada M. SRC kinase activator CDCP1 promotes hepatocyte growth factor-induced cell migration/invasion of a subset of breast cancer cells. *J Biol Chem*, 2022, 298:101630. doi: 10.1016/j.jbc.2022.101630

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Germline Testing Results in Patients with Genomic Tumor Profiling

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Background: With the rise of genomic testing, more clinicians are using panels to understand the genetic profile of breast cancer to help aid in clinical management. However, little is known about the relationship between the results of genomic tests and the likelihood of identifying an underlying germline variant, and how this should integrate into clinical decision making.

Methods: Data was obtained from the Informed Genetics Annotated Patient Registry (iGAP), an IRB-approved, multi-centered longitudinal registry designed to capture biomarker test results and their impact on treatment practices and outcomes. Two genomic tumor profiling tests were studied - MammaPrint recurrence risk and Blueprint molecular subtypes, including Luminal type A, Luminal type B, Basal, and HER 2 type. Of the 3400 patients currently enrolled in the registry, 528 have been diagnosed with breast cancer and underwent tumor profiling by both MammaPrint and BluePrint as well as germline genetic testing, including analyses of 24 cancer susceptibility genes (ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, NBN, PALB2, PTEN, STK11, TP53, APC, BMPR1A, CDK4, EPCAM, MLH1, MSH2, MSH6, MUTYH, PMS2, RAD51C, RAD51D, SMAD4). Differences in positive germline variant rates were tested for with two-sided, Chi-Square tests using the prop.test function in R. Results: 231 (44.17%) were classified as High-Risk for recurrence on MammaPrint, with a 0.13 PVs detected per patient tested (positive germline variant (PV) Rate), 269 (51.34%) were identified as having a Low-Risk, with a 0.0849 PV rate, and 23 (4.4%) Ultra-Low-Risk, with a 0.0455 PV rate. There is not a significant difference between the High-Risk and Low-Risk for recurrence ($p=0.09$). 45 (8.54%) Basal molecular subtype identified by BluePrint panel, with a 0.1778 PV rate, 292 (55.41%) classified as Luminal A type, with a 0.0819 PV rate, 171 (32.45%) Luminal B with 0.1078 PV rate, and 13 (2.47%) HER2 Type with 0.07 PV rate. There was a significant difference between Basal and Luminal A PV rates ($p=0.042$), but no other statistically significant differences were found.

Conclusions: Patients with a Basal molecular subtype have a significantly higher likelihood of having a germline pathogenic variant compared to Luminal A subtype. There was a trend that did not reach statistical significance for MammaPrint High Risk to have a higher likelihood of germline pathogenic result compared to MammaPrint Low Risk. This data adds another parameter for germline testing in those breast cancer patients who fall outside of current NCCN testing criteria.

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Genomic testing and Ki-67 Percentage: Two puzzle pieces being undervalued in breast cancer treatment

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Background: Genetic resources are underutilized when it comes to being incorporated into a breast cancer patient's treatment, but that isn't the only piece being overlooked. The Ki-67 proliferation index expressed (Ki-67%) is an established marker of tumor proliferation and aggressive behavior. We hypothesized that Ki-67% could have increased clinical utility when correlated with genomic testing results. Methods: Data was obtained from the Informed Genetics Annotated Patient Registry (iGAP), an IRB-approved, multi-center longitudinal registry designed to capture biomarker test results and their impact on treatment practices and outcomes. Tumor grades and Ki-67% were taken from patient pathology reports. The average Ki-67% was then calculated and compared for each tumor grade, MammaPrint genomic recurrence risk category (ultra low risk, low risk, and high risk), and Blueprint molecular subtype (Luminal type A, Luminal type B, Basal, and HER 2 type). ANOVA statistical analysis was performed for significance values. Results: Of 3102 patients enrolled in the iGAP Registry, 733 were diagnosed with breast cancer and had available tumor grade and Ki-67% data. Among these patients, 357 had genomic recurrence risk (MammaPrint) and 220 genomic molecular subtyping (BluePrint) reports. As expected, tumor grades were significantly positively correlated with Ki-67% ($p < 0.0001$ between all 3 tumor grade groups). Average Ki-67% in each genomic recurrence risk revealed a significant difference between Low Risk (14%, range 1-70%) and High Risk (36%, range 1-95%, $p < 0.0001$). Among the genomic molecular subtypes, there were significant differences in Ki-67% between Basal (avg 69%, 17-95%) and Luminal type A (avg 13%, 1-70%, $p < 0.0001$) and all other subtypes, while Luminal type B (avg 24%, 1-80%) and HER 2 (avg 38%, 29-45%) were not significantly different from each other ($p = 0.2817$), but still significantly different to all other subtypes. Conclusion: From these results, we can deduce that molecular subtype correlates with, but is clinically distinct from, Ki-67 proliferation index. These results also indicate that molecular subtype correlates with higher tumor grades, possibly due to increased cell proliferation. Achieving truly personalized clinical decision making requires utilizing multiple modalities and biomarkers, integrating the results into management.

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Circulating tumor cells, immunohistochemical subtypes, and genes mutation as prognostic markers in HER2 negative metastatic breast cancer patients candidates to chemotherapy

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Background: In the era of targeted therapies, chemotherapy (CT) is still a valuable treatment option for patients (pts) with HER2 negative metastatic breast cancer (MBC). The identification of predictive and prognostic markers might improve treatment response and survival. Here we investigated the role of tumor subtypes, circulating tumor cells (CTCs), and mutations in genes or pathways of interest, in predicting response to CT and prognosis of HER2 negative MBC pts within AARES trial. Methods: AARES is an open label multicentric randomised phase 2 trial comparing a DNA-damaging (arm A: cisplatin 25 mg/m²/day, day 1-3 + cyclophosphamide 600 mg/m² day 1) versus (vs) a non-DNA-damaging (arm B: capecitabine 1000 mg/m² bid/day, day 1-14 + vinorelbine 60 mg/m²/day, day 1,8) CT regimen in pts with HER2 negative MBC. Archival tumor tissue samples and blood samples were collected at baseline. The Cell SearchTM system was used for CTCs isolation and enumeration and a cut-off of 5 CTC/7,5 ml was used. Tumor subtypes were based on locally assessed hormone receptors and HER2 status. The luminal-like subtype (Lum) was defined by ER or PR positivity, while the triple negative subtype (TN) by ER, PR, and HER2 negativity. Tissue samples were used for DNA extraction and next generation sequencing analysis using a target enrichment panel of 170 genes (TruSight 170, Illumina). Primary endpoint was objective response rate (ORR) assessed for the two treatment arms. Progression free survival (PFS) and overall survival (OS) were evaluated as secondary endpoints, and estimated with the Kaplan-Meier method. ORR, PFS and OS were correlated with CTC counts, tumor subtypes, and mutational status of genes/pathway of interest (PIK3CA, TP53, BRCA1, BRCA2, PI3K/AKT pathway (PI3K/AKT)). Results: AARES enrolled 102 pts from 2011 to 2016 across 9 Italian centers. Of these, 77 pts were evaluable for ORR. Median follow up was 32 months. Overall, median age was 57. The majority of pts had Lum tumors (73%), while 27% had TN. 86% of pts had visceral metastases, and 52% had 3 or more metastatic sites. 48% of pts received the study treatment as 1st line,

32% as 2nd line, and 19% as 3rd line. Out of the 77 pts with ORR data, 41 (53%) were CTC- and 36 (47%) CTC+. A larger proportion of pts with Lum tumors were CTC+ (54% n=30), while TN tumors were mainly CTC- (71% n=15). 49 pts had adequate tumor tissue for sequencing analysis. TP53 mutations (mut) were found in 33% of pts, BRCA1/2 mut in 14%, PIK3CA mut in 35%, and PI3K/AKT mut in 47%. ORR was 24% and 37% in arm A vs arm B, respectively (p=0.2), and no difference in ORR was observed by tumor subtypes (Lum vs TN), and CTCs count (+ vs -). PFS and OS were assessable on the whole population (n=102) and did not significantly differ by treatment arms. Median OS (mOS) was higher in Lum pts compared to TN (24 months (mo) vs 15.4 mo, p=0.048) while median PFS (mPFS) did not differ according to tumor subtypes (p=0.28). Overall, CTCs count was not significantly associated with mPFS or OS however in pts with TN tumors and CTC-, mPFS and mOS were significantly longer (mPFS: 4.44 mo vs 2.56 mo in CTC- and CTC+ subgroups, respectively, p=0.00087 and mOS: 22.07 mo vs 3.57 mo in CTC- and CTC+ subgroups, respectively, p<0.0001). On the other hand, no differences were observed in Lum pts categorized according to CTC status (p=0.83 for mPFS, p=0.54 for mOS). Finally, pts with PI3K/AKT mut had a significantly worse PFS compared to wild type in the overall population (p=0.0091) as well as in Lum (p=0.034) and TN pts (p=0.0052). Conclusions: CTCs and tumor subtypes were not predictive of response to CT regimens in HER2 negative MBC pts. A number of CTC >5 in TN MBC, and mutations in the PI3K/AKT pathway, identified a subgroup of pts with worse prognosis, potentially candidates for alternative treatments. Further studies are needed to confirm these results in a larger population.

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scRNA-seq profiling reveals different tumor immune-microenvironment in triple negative breast cancer and decodes pivotal role of THBS1- SDC1 axis in tumor metastasis

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ABSTRACT Background: Breast cancer has become the most common cancer worldwide and triple-negative breast cancer (TNBC) is the most aggressive subtype due to the lacks of hormone receptors and HER2 expression. Increasing rate of breast cancer metastasis also need to be solved. Nearly one in four breast cancer patients developed metastasis after treatment, which attributed to 90% cancer related death. Considering highly aggressive pattern of TNBC, TNBC showed higher metastasis probability rather than other subtypes. Therefore, exploring more biomarkers and therapeutic targets are on urgent. Methods: We profiled the transcriptomes of 59646 cells from 12 primary and 4 metastatic tumor samples from Gene Expression Omnibus (GEO) database (<https://www.ncbi.nlm.nih.gov/geo/>). Results: Comparing with primary site, metastatic site was predominated with immunosuppressive tumor microenvironment. In brief, metastatic samples showed increasing numbers of macrophages, lower anti-tumor microenvironment scores, higher malignant cell properties scores, less effective T cells and macrophages, enhanced immune escape potential tumor cells and a later pseudotime state of malignant cells, compared with primary samples. Remarkably, metastatic samples exhibited a stronger interaction of THBS1-SDC1 axis between macrophage subcluster named angiogenesis-1 and malignant cell subcluster named CDKN2A epithelial cells. We subsequently confirmed that higher THBS1-SDC1 expression indicated with poor overall survival and distant metastatic free survival of TNBC patients in The Cancer Genome Atlas (TCGA) TNBC cohort. Conclusion: Our immune landscape of TNBC ecosystem provide deeper insights into tumor metastasis and offer potential biomarkers and therapeutic target for TNBC. Key words: Breast cancer; immune-microenvironment; THBS1; SDC1; metastasis

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Regional Lymph node percutaneous analysis in patients with breast cancer

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Background: The evaluation of regional lymph nodes in patients with breast cancer is one of the main predictive and prognostic factors for treatment. The most frequently methods of percutaneous evaluation for suspicious lymph nodes are fine needle aspiration (FNA) and core needle biopsy (CNB). According to the international literature, CNB and FNA are considered diagnostic methods with high specificity (98% vs. 99%), however FNA can present up to 21% of inconclusive results due to insufficient material, which leads to recall and delay in treatment approach. Although CNB is well established as a percutaneous method for the diagnostic evaluation of suspicious breast lesions, the literature is still scarce regarding the use of this method for the evaluation of suspicious regional lymph nodes in patients with breast cancer. **Objectives:** To analyze the results of percutaneous biopsies performed in suspected lymph nodes according to the topography and the type of needle used, and to verify the preferred method used. **Methods:** This was a retrospective study evaluating a public Hospital in São Paulo – Brazil (Pérola Byington Hospital database). Patients who underwent ultrasound-guided percutaneous lymph node biopsy from May 2015 to November 2017 were included. Data were analyzed and the type of biopsy (FNA or CNB) and the results were analyzed. **Results:** 106 medical records of patients with previous breast cancer and that underwent lymph node biopsy were reviewed. The mean age was 54.7 years (SD±12.4) in the CNB group and 54.7 years (SD±10.8) in the FNA group. Most of the patients were submitted to CNB (66% - 71 patients) and 34% were evaluated with FNA (35 patients). According to the topography of the lymph nodes, 80% were in the axilla (n=84), 10% in the supraclavicular region (n=11) and 10% in the

cervical region (n=11). When analyzing the FNA results, 31% did not present sufficient material (n=11), 37% were malignant (n=13), 20% were benign (n=7) and 12% showed cellular atypia (n=12). Among the CNB performed in suspected lymph nodes, 53% were malignant (n=38) and 31% were benign (n=33), and no one had insufficient material. There were no reports of complications related to the procedures. In the insufficient material group, 27% (n=3) of the patients underwent a new percutaneous biopsy (2 CNB with malignant result and 1 FNA with inconclusive result) and 73% (8) were maintained in follow-up. The mean follow-up time was 24 months, and clinical and imaging stability was confirmed after this period. In the CNB group with malignant result, 10% (4) were diagnosed with neoplasia of other sites (cervix, lymphoma, melanoma and gastrointestinal), 78% (30) presented immunohistochemistry in agreement with that of the breast, 3% (1) presented different immunohistochemistry and in 9% (3) this evaluation was not performed. Conclusion: CNB was the preferred diagnostic method in our Hospital (66% vs 34%), being considered a viable procedure to evaluate lymph nodes in various topographies and with low rates of inconclusive results. Besides that, immunohistochemistry was done in 91% of the cases showing the importance of this analysis in the treatment of the recurrence or even in the diagnosis of other primary tumors. In the future, studies that assess indirect costs may confirm the applicability of CNB in patients with suspicious lymph nodes in terms of achieving greater agility and resolution.

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Prediction of disease recurrence in low risk Oncotype Dx breast cancers from digital H&E-stained whole slide images of pre-treatment resections alone

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Background Breast cancer patients with estrogen receptor (ER)+/HER2- (and usually node-negative) tumors can avail themselves of Oncotype DX Breast Recurrence Score[®] (ODXRS) testing to predict their risk of distant recurrence within 9 years and, consequently, putative chemotherapy benefit. However, ODXRS testing requires sufficient tumour availability and specimen shipping, which imposes time and financial burdens to testing which have to be met by healthcare systems. The advent of digital pathology offers a potential avenue for exploring computer-aided diagnostic solutions which may overcome these hurdles by extracting the requisite information from hematoxylin and eosin (H&E)-stained tissue whole slide images (WSIs) alone. In turn, this technology could significantly reduce diagnostic turnaround times and cost, and improve accessibility and test reproducibility, thereby enabling healthcare systems to run more efficiently and offer patients more timely results. Ideally, such a platform should incorporate a measure of the underlying tumor biology to provide a fully explainable, white box solution, and may offer further insights into the identification of early recurrence events. Aims The aim of this study was to establish whether our computer-aided solution's (Q-Plasia OncoReader Breast, QPORB) digital biomarker representing G1/S cell cycle deformations extracted from H&E WSIs was prognostic for disease-free survival (DFS) and

could predict disease recurrence, particularly in the setting of low risk ODXRS breast cancers. Methods Primary breast cancer resection/excision specimens (n=70 cases) sent for ODXRS testing from St James's University Hospital, UK (2016-2019) were collected. Anonymised diagnostic glass slides (n=198 slides) of H&E-stained tumors were scanned at x20 magnification on an Aperio AT2 scanner. In parallel, relevant clinical and histological data were collected from pathology reports and electronic patient records, including both ODXRS and recurrence events during follow-up. The QPORB recurrence scale (QPORB-RS), which combines statistical physics and tumor biology to identify image-based malignant cell cycle deformation, extracts prognostic information from WSIs. The contribution of potential confounders (age, stage, grade, lesion size, Nottingham prognostic index and Charlson score) were accounted for. Results The QPORB-RS was prognostic for DFS for patients with predominantly node-negative (including node micro-metastases) HR+/HER2- tumors over a median follow-up period of 5 years (P=0.02; dichotomized Kaplan Meyer with median cut-off). The QPORB-RS concurred with ODXRS's high vs. low recurrence risk in 73% (19/26) and 61% (27/44) of cases, respectively, with an overall agreement of 66% (46/70). Moreover, the QPORB-RS identified all 5 patients who had recurrences (with ODXRS of 6, 9, 10, 21 and 26, and ages of 55, 66, 42, 35 and 50 years, respectively) as being high risk in the subset of those given a low (including historically intermediate) ODXRS and who did not receive chemotherapy. Conclusion The QPORB-RS is a good prognostic test of risk of disease recurrence in breast cancer patients with predominantly node-negative (including node micro-metastases) HR+/HER2- tumors within a median 5-year follow-up period. Our efforts are now focussed on extending this cohort and establishing the prognostic value of the QPORB-RS across all breast carcinomas, regardless of molecular subtype, stage/node positivity and menopausal status.

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Number of involved organs at baseline is prognostic for overall survival in patients with metastatic breast cancer: Results from the AGMT_MBC-Registry

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Background: Hormone-receptor (HR) status, HER2 Status, de novo metastatic disease, distant recurrence-free interval (DRFI), and visceral disease are known prognostic factors in metastatic breast cancer (MBC). Therefore, in the majority of clinical trials, randomization is stratified for these parameters. Whether the number of involved organs at baseline has an additional prognostic value was examined in this analysis.

Patients and methods: The AGMT-MBC-Registry is a multicenter nationwide ongoing retrospective and prospective registry for MBC patients in Austria. In this analysis, patients with known HR status, HER2 status, and available survival data were included. Multivariable hazard ratios were estimated by COX proportional hazard models. For variable selection a backward stepwise model selection using the Akaike information criterion was performed.

Results: As of 04/05/2022, 2,235 patients have been included in the registry, of which 1,840 patients fulfilled the inclusion criteria. In two different multivariable COX proportional hazard models for overall survival, the number of involved organs was a highly statistically significant independent prognostic factor: (1) a model including the number of involved organs at baseline together with known prognostic factors (see Table 1); (2) a stepwise selection model additionally including menopausal status and involved metastatic organ sites (bone, liver, lung, brain, and lymph nodes) separately. This effect was maintained in sensitivity analysis taking different breast cancer subtypes as well as visceral and non-visceral disease into account.

Table 1: Multivariable Model for overall survival

Conclusion: The number of involved organs at baseline is an independent prognostic factor in MBC and should be considered as a stratification factor in randomized trials.

Table 1: Multivariable Model for overall survival

Characteristic	HR ¹	95% CI ¹	p-value
Subtype			
HR+/HER2- (reference level)			
HR-/HER2+	1.09	0.88, 1.35	0.4
HR+/HER2+	0.80	0.67, 0.96	0.017
TNBC	2.54	2.19, 2.93	<0.001
Age at diagnosis of metastatic disease (cont.)	1.02	1.01, 1.02	<0.001
Distant recurrence-free interval category			
DRFI < 24 months (reference level)			
DRFI ≥ 24 months	0.69	0.60, 0.80	<0.001
<i>de novo</i> metastatic disease	0.64	0.55, 0.73	<0.001
Visceral disease			
yes (reference level)			
no	0.77	0.68, 0.88	<0.001
Number of involved organs			
1 (reference level)			
2-3	1.27	1.12, 1.45	<0.001
>3	1.86	1.49, 2.33	<0.001

¹HR = Hazard Ratio, CI = Confidence Interval, DRFI = distant recurrence-free interval

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P3-05-50

Comprehensive Analysis of Pyroptotic Gene Prognostic Signatures Associated with Tumor Immune Microenvironment and Genomic Mutation in Breast Cancer

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Background: Breast cancer is becoming a tumor with the highest morbidity rate, and inflammation-induced cell death namely pyroptosis reportedly plays dual roles in cancers. However, the specific mechanism between pyroptosis and the clinical prognosis of breast cancer patients is indistinct. Hence, novel pyroptosis-related biomarkers and their contributing factors deserve further exploration to predict the prognosis in breast cancer. Methods: Pearson's correlation analysis, and univariate and multivariate Cox regression analysis were utilized to obtain six optimal pyroptosis-related gene prognostic signatures (Pyro-GPS). The risk score of each breast cancer patient was calculated. Next, a Pyro-GPS risk model was constructed and verified in TCGA cohort (n=1,089) and GSE20711 cohort (n=88). Then analyses of immune microenvironment, genomic variation, functional enrichment, drug response and clinicopathologic feature stratification associated with the risk score of Pyro-GPS were performed. Ultimately, a nomogram based on the risk score and several significant clinicopathologic features was established. Results: The low-risk breast cancer patients have better survival outcomes than the high-risk patients. The low-risk patients also show higher immune cell infiltration levels and immune-oncology target expression levels. There is no significant difference in genetic variation between the two risk groups, but the frequency of gene mutations varies. Functional enrichment analysis shows that the low-risk patients are prominently correlated with immune-related pathways, whereas the high-risk patients are enriched in cell cycle, ubiquitination, mismatch repair, homologous recombination and biosynthesis-related pathways. Pyro-GPS is positively correlated with the IC50 of anti-tumor drugs. Furthermore, comprehensive analyses based on risk score and clinicopathological features were performed to predict the prognosis of breast cancer patients. Conclusions: The risk score of Pyro-GPS can serve as a promising hallmark to predict the prognosis of BRCA patients. Risk score evaluation may assist to acquire relevant information of tumor immune microenvironment, genomic mutation status, functional pathways and drug sensitivity, and thus provide more effective personalized strategies.

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Junzhe Yang, n/a: No financial relationships to disclose

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Patients with low expression of BCL 2 experience more late recurrence than patients who do not, which neutralized the protective effect of low BCL2 expression in patients with estrogen receptor positive breast cancer

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Background) BCL2 is a key factor for the regulation of cellular apoptosis and its overexpression inhibits apoptotic cell death and activates cellular proliferation, resulting tumor progression. Although BCL2 are expected to be associated with an adverse prognosis in breast cancer, previous studies have reported inconsistent results and some reported even favorable features. The aim of this study is to investigate what characteristics of BCL2 yield this discrepant result in patients with breast cancer. Materials and methods) Female patients with breast cancer who completed primary treatment against breast cancer between 2003 and 2018 at Wonju Severance Hospital, Korea, were included. Clinicopathological characteristics including BCL2 expression were collected. Patients were categorized into two groups, BCL2 expression in more or less than 10% of tumor cells. Kaplan-Meier curves were generated to compare recurrence-free interval (RFI) and overall survival (OS). Result) The final cohort included 616 patients with a mean age of 54.79 ± 11.2 (25-86) years. Patients with estrogen receptor positive breast cancer were more frequent in patients with tumor in which BCL2 was expressed in less than 10% of tumor cells (70.7% vs. 57.7%). Patients with tumor in which BCL2 was expressed in less than 10% of tumor cells showed better survival than their counterpart. Subgroup analysis according to the estrogen receptor and HER2 overexpression status was done. In patients with tumor in which HER2 was not overexpressed, patients with tumors in which BCL2 expressed less than 10% of tumor cells showed better survival ($p=0.007$). Survival difference maintained in patients with triple negative disease ($p=0.010$). However, in patients with estrogen receptor positive breast cancer, survival of two groups of patients with high and low BCL2 expression become not significant over time as late recurrence occurred ($p=0.227$). In contrast, patients with HER2 positive disease breast cancer showed worse prognosis than their counterpart when their tumor showed BCL2 expression in less than 10% of tumor cells. Conclusion) BCL2 overexpression showed different contribution to the patients' survival according to the subtypes. Patients with HER2 overexpression showed better survival when BCL2 was overexpressed and patients with HER2 negative disease does not. First, similar survival was resulted from late recurrence in patients with estrogen receptor positive disease.

Second, apoptotic capacity of tumor cells may not be major survival factor if tumor cells are exactly targeted.

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Sarcopenia and Post-Mastectomy Breast Reconstruction Outcomes after Radiation Therapy

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Background: Sarcopenia, characterized by the loss of muscle mass, has emerged as a negative prognostic factor in cancer patients. It has been associated with poorer outcomes and increased treatment-related morbidity. Post-mastectomy breast radiation therapy (RT) increases the likelihood of reconstructive complication, with up to 20% of reconstructed women requiring implant removal. The factors that lead to these complications are poorly understood and likely multifaceted. We investigated the relationship between pre-radiation therapy sarcopenia and post-mastectomy reconstruction outcomes. Methods: Chart review was performed to determine demographic, medical, and treatment variables, including reconstruction complication events and failures in breasts treated with mastectomy, immediate reconstruction, and RT. Reconstruction failure was defined as tissue expander or implant removal, resulting in no final reconstruction or autologous reconstruction only. Reconstruction

complications included surgical site infection, late infection (1 year post-RT), seroma development, flap necrosis, nipple necrosis, wound dehiscence, capsular contracture, hematoma, extrusion, leak, venous congestion, and unplanned reoperation. An axial slice at the L2 or L3 vertebral body from the radiation therapy planning CT scan was analyzed for skeletal muscle area using a previously validated algorithm, with manual review and adjustment as indicated. Sarcopenia was defined by skeletal muscle index (SMI, skeletal muscle area in cm² divided by patient's height squared) below 34.4 cm²/m². Chi-square, Kaplan Meier, and univariate Cox regression tests were used for analysis. Results: Ninety-nine women with breast cancer who underwent mastectomy, reconstruction, and RT were included in this study. All women had immediate reconstruction: 93 women had tissue expander placement while six women had permanent implant placement. Mean age was 47.5 years (SD 10.6) at diagnosis and median BMI was 24.8. Seventy-six percent were non-smokers, 24% were former smokers, and only 16 (16.2%) and 3 (3.0%) had hypertension or diabetes, respectively. Median follow-up was 2.7 years. Median SMI was 38 cm²/m² and 18 (18%) met criteria for sarcopenia (SMI < 34.4 cm²/m²). Mastectomy was bilateral in 79 women, skin-sparing in 61, and nipple sparing in 31. Bilateral mastectomy was less frequent amongst women with sarcopenia (61%) compared to 84% of those without sarcopenia (p=0.03). After RT, twenty-three women required unplanned reoperation. Within these 23 women, there were 45 total complications. Complications included surgical site infection (n=18), capsular contracture (n=12), seroma (n=4), wound dehiscence (n=3), and others (n=8). However, only 8 women had reconstructive failure and none were sarcopenic at the time of the RT planning scan. Any complication or failure after RT occurred in similar proportions of patients with and without sarcopenia: 38% and 30%, respectively. Kaplan-Meier curves and univariate Cox regression models showed no significant difference in time to failure (p = 0.380) or time to any event (complication or failure) (p=0.53), between sarcopenic and non-sarcopenic patients. Conclusion: Sarcopenia, using SMI < 34.4 cm²/m² on pre-radiotherapy planning scans, was not associated with an increased risk of post-radiotherapy reconstructive complication or failure in this selected cohort of non-smokers. Few women had sarcopenia at the time of operation, and results should be validated in a larger series.

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IMPACT OF THE BODY MASS INDEX (BMI) ON THE SURVIVAL OF BREAST CANCER WOMEN WHO ACHIEVED A COMPLETE PATHOLOGICAL RESPONSE (pCR) AFTER NEOADJUVANT CHEMOTHERAPY (NACT) IN BRAZIL

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Introduction

Breast cancer (BC) it is highly prevalent in the world with a significant mortality rate despite advances in systemic therapies. Obesity increases the risk of this cancer specially in post-menopause women and may even affect the prognosis at all ages.

Objective

To evaluate the impact of BMI on overall (OS) and disease free interval (DFI) of Brazilian women with BC undergoing NACT and who achieved pCR.

Methods

This is a retrospective study that included patients with confirmed breast cancer clinical stage I to III, age more than 18 years old and complete records that were submitted to NACT. These patients were divided in four groups based on their BMI by the World Health Organization definition BMI < 18,5 kg/m²: underweight; BMI 18,5 to < 25 kg/m²: healthy weight; BMI 25 a < 30 kg/m²: overweight; BMI ≥30kg/m²: obesity. pCR was defined as absent of invasive tumor in the breast or axilla. Student t test or chi-square test were used to analyze the association of each variable between groups with and without pCR. Univariate and multivariate analyzes were used to calculate odds ratios (OR) and 95% of confidence intervals (CI) of the independent

variables BMI, age, clinical stage, immunohistochemistry and correlated with pCR (p value < 0.05 was assumed as statistically significant). The study was approved by local ethics committee.

Results

A total of 1.481 patients from a single reference center between January 2011 to May 2020 were included. The mean age was 50 years and mean BMI was 28,08 (SD 5,59). Most of the patients presented clinical stage III (67,3%) at diagnosis. Invasive carcinoma nonspecial type was the most frequent (95,11%). After NACT 1.138 (76.84%) still had invasive disease and only 343 (23.16%) had pCR. BMI ratio was 1.6% underweight, 30.5% healthy weight, 34.9% overweight and 33.0% obese. Regarding survival analyses, there was no statistical significance for the different BMI categories for both OS (p=0.43) and DFS (p=0.7) and no statistical significance when evaluated pCR and BMI OS (p=0.26) and DFS (p=0.22). OS was estimated for three groups (healthy weigh: 109 months, overweight: 105 months, obese: 79 months). For patients with underweight, the median OS was not reached. The 5-year OS rate in Brazil, according to this study, was 85.4%. Of these 1,481 women, 387 relapsed after surgery (22 cases: local relapse; 355: systemic relapse; 10: both relapses). Only the underweight reached the median (58 months) but this group is very small, and the other categories still have immature data because the median was not reached to define DFS.

The association of the most aggressive subtypes of cancer as predictors of pCR was statistically significant (Luminal B: p=0.019; HER 2: p< 0.001; Triple negative: p< 0.001, in relation to Luminal A). There wasn't any statistical significance for the different BMI categories.

Conclusion

This study did not show interference of BMI on OS and/or DFS in Brazilian women with BC undergoing NAC. Few patients reached pCR (23.16%) probably due to the advanced initial stage. On the other hand, pCR was much more frequent in the more aggressive subtypes (Triple negative, HER 2 and Luminal B). Obesity as an independent chronic condition and despite not having an impact on survival in these analyses, most women were overweight or obese (72.85%), showing the frequency of obesity in Brazilian women, which should be understood as a public health problem in the country. In addition, following these women for 10 years can help to understand better the real impact of obesity in breast cancer survival.

Table 1. Percentual of breast cancer in different clinical stages

STAGE	PATIENTS (number)	PATIENTES (%)
I	37	2.5
II	447	30.2
III	997	67.3
TOTAL	1481	100

Table 1. Percentual of breast cancer in different clinical stages

Table 2. Logistic regression considering pCR as an outcome

SUBTYPE BC	OR	IC 95%	P- value
Luminal A	1.00	-	-
Luminal B	1.97	1.15-3.58	0.019
HER 2	5.65	3.36-10.11	<0.001
Triple negative	6.09	3.66-10.83	<0.001

Table 2. Logistic regression considering pCR as an outcome

Disclosure(s):

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P3-05-55

The Effects of Comorbidities on the Effectiveness of Neoadjuvant Chemotherapy in Breast Cancer

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Background: Neoadjuvant chemotherapy has been used in a variety of cancer treatments to transform inoperable tumors to operable tumors. Within breast cancer treatment, it has successfully been used to increase the rates of breast conservation therapy. Neoadjuvant chemotherapy is being used to downgrade locally advanced breast cancer, as well as treat inflammatory breast cancer, and node negative breast cancers with genetic expression profiling results that predict the need for adjuvant chemotherapy. There have been several studies that have evaluated the effects of age and comorbidities of patients with breast cancer on treatment decisions, particularly chemotherapy. However, very few studies have reviewed additional factors outside of tumor characteristics for predicting complete response to neoadjuvant chemotherapy. The purpose of this study is to determine if there are any patient factors, particularly comorbidities, that play a role in modifying chemotherapy regimens and if that affects the patient's response to chemotherapy. Methods: A retrospective chart review was performed on patients between 18-89 years of age at the time of their breast cancer diagnosis, who underwent neoadjuvant between 1/1/2014 and 1/1/2019. Patients included were treated by Dr. Kara Friend or Dr. Jennifer Reed at Sentara Leigh Memorial Hospital. Data collected included demographics, tumor characteristics, treatment regimens (chemotherapy, radiation therapy, antihormone therapy, and surgery), noting when chemotherapy regimens had to be modified, pathologic response to neoadjuvant chemotherapy, and long term outcomes. Comorbidities were identified and used to calculate the Charlson Comorbidity Index (CCI), which was used to categorize patients. Results: A total of 111 patients were reviewed. All patients were female and ages ranged from 24 to 84, with most patients being in their fourth or fifth decade. 30% of the patients had triple negative tumors, and 48% had HER2+ tumors. Most patients had invasive ductal carcinoma, with only 6 patients (5.4%) having invasive lobular carcinoma. 26 patients had positive genetic panels, 10 of which were BRCA positive. 28 patients had negative panels, and 57 were not tested. The most common chemotherapy regimens were TCHP, AC/T, and TCH. Two patient's cycles were reduced from the beginning due to low ejection fractions, 3 were modified due to pulmonary reactions, 1 for renal failure, 1 for Hepatitis C activation, and 10 for neutropenia or infections. One patient self-discontinued chemotherapy in favor of alternative medicine. 65.7% of the patients underwent antihormone therapy. 27% of the patients underwent radiation. Most patients had CCI scores of 0. Of those with a CCI score of 0, 4 needed modified regimens (8.3%). Of those with a CCI score of 1,

three needed modified regimens (10.3%). Of those with a CCI score of 2, three patients needed modified regimens (23.3%). Of those with a CCI score of 3 or greater, 8 needed modified regimens (38.1%) When evaluating the effect of a CCI of 0-2 compared to 3 or greater on likelihood of reduced chemotherapy, there was not a statistically significant result ($p = 0.99$). However, there appeared to be a trend of increasing need for modified regimens with increasing CCI score. When evaluating if a reduced chemotherapy regimen led to progression during neoadjuvant chemotherapy or no response, the result was not statistically significant ($p=0.24$). Conclusion: Our study suggests that an increasing CCI score corresponds to an increased likelihood of needing a modified regimen, however this result was not statistically significant. Increased comorbidities and the need for modifying chemotherapy regimens do not appear to have an effect on pathologic response to neoadjuvant chemotherapy. This study is limited by the sample size, and a greater sample size will be necessary to make further conclusions.

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The clinical impact of preoperatively needle-aspiration biopsy for axillary lymph nodes in T1-T2 breast cancer patients with axillary lymph node metastasis

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Introduction: More than half of the results of axillary lymph node dissection followed by metastasis in sentinel lymph node(SLN) biopsy are negative. For deescalating axillary surgery, it is necessary to predict the non-SLN metastasis state, where metastasis was confirmed in the SLN biopsy. Method: Breast cancer patients with T1 and T2 stage were retrospectively reviewed from January 2008 to December 2016. A total of 818 patients underwent surgery as the primary treatment and the result of SLN biopsy was positive for metastasis. Patients who skipped SLN biopsy procedure and were proven metastatic axillary lymph nodes by needle-aspiration biopsy (NAB) were excluded. SLN was defined as lymph nodes detected by the dual method with hot-uptake by radioisotope and dyed by blue dye, or lymph nodes with palpable or suspected metastatic findings during SLN biopsy. Clinicopathological factors including and extra-nodal invasiveness were analyzed. Result: The median follow-up period was 73 months. Non-SLN metastasis was significantly seen in patients with older than 50 years, positive node metastases by preoperative NAB, high T stage, and extra-nodal invasion. In subgroup analysis, patients who underwent total mastectomy had the similar patterns of the increased risk of having non-SLN. Poor overall survival was observed in the patients with the presence of non-SLN metastasis. Conclusion: We confirmed predictive factors with a high probability of non-SLN metastasis. Axillary lymph node dissection cannot be overlooked in the patients proven the metastatic result of preoperative NAB.

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Lymphatico-venous communications and rhythmic, respiratory pressure changes influence the incidence of metastatic disease at presentation in solid tumours

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Background-

Dissemination of cancer cells and their colonization at distant sites (metastases) is the primary cause of death in patients with solid tumors. Despite of popular theories of cancer metastases, there are several lacunae in our understanding of extent of Metastatic Disease at Presentation (MDP). The aim of this study was to evaluate if organ sites could be grouped together based on the available knowledge extent of lympho-vascular communication (LVC) and probable respiratory pressure changes they undergo and whether this correlated with incidence of MDP.

Methods-

We analyzed a prospectively maintained database of patients with solid tumors presenting between January and December 2017 at our tertiary care cancer center. The tumors were hypothetically divided into four regions (R) depending on extent of LVC and respiratory pressure changes. All patients had clinico-radiological staging after pathological confirmation of cancer. The hypothetical region grouping R1-R4 was independently evaluated by unsupervised k-means clustering. The incidence of MDP was compared in subgroups defined by primary tumor stage, anatomical region, histology, gender, and age using logistic regression.

Results-

Of 17,467 patients included with median age 54 years, 6714 (38.4%) had MDP. The incidence of M1 disease in R1 vs R2 vs R3 vs R4 regions, older (>50 years) vs younger (Conclusion- Primary anatomical regions defined by LVC and respiratory pressure changes; primary tumor histology (type and grade) and male gender are significant determinants of MDP in solid tumors.

Region grouping of solid organs based on extent of lymphaticovenous communications and rhythmic respiratory pressure changes and % MDP

Region	LV communication	Pressure changes	Anatomical sites	Sample size N	MDP (%)	95% CI
R1	None	None	Head and neck region Pelvic viscera below levator ani- cervix, vulva, vagina and anal canal	3219	148 (4.6)	3.93 – 5.38
R2	Few, open with lymphatic blockade	None	Breast, extremities, chest and abdominal wall, skin	4116	841 (20.4)	19.23 – 21.69
R3	Present	Low	Pelvic viscera within peritoneal reflection- colorectal, small intestine, ovary, urinary bladder, body uterus, prostate, testis	3673	1609 (43.8)	42.21 – 45.42
R4	Present	High	Intra-thoracic and intra-abdominal organs- lung, oesophagus, mediastinum, liver, gall bladder, kidney, stomach	6459	4116 (63.7)	62.55 – 64.89
Overall	-	-	-	17467	6714 (38.4)	37.72 – 39.16

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Frequency and prognosis of HER2-low status in Mexican patients with metastatic breast cancer

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Background

Breast cancer (BC) is the leading cause of cancer and cancer-related death in Mexican women. Recently, low expression of HER2 (HER2-low), defined as immunohistochemically 1+ or 2+ and lack of HER2 gene amplification, has gained increased attention as a promising new predictive biomarker for treatment with antibody-drug conjugates, such as trastuzumab-deruxtecan, not currently available in Mexico. To date, the frequency and prognostic value of HER2-low status in the Mexican population with metastatic BC remains unknown.

Methods

Single center retrospective cohort of patients diagnosed with metastatic BC between 2017 and 2020. Only patients with known HER2 status and available survival data were included. Patients' sociodemographic and clinicopathological characteristics, and outcomes were collected from medical records. Descriptive statistics were used to analyze sociodemographic and clinicopathological characteristics. X2 tests were used to evaluate associations between HER2 status and other characteristics. Progression-free survival (PFS) and overall survival (OS) were calculated using the Kaplan-Meier method and compared by the log-rank test according to HER2 status. Multivariable adjusted hazard ratios were estimated by Cox regression models. A p value of < 0.05 was considered statistically significant.

Results

Among 55 patients with metastatic BC, median age at diagnosis was 51 years, 56.4% were postmenopausal and 25.5% had family history of BC. The most frequent histologic subtype was ductal (65.5%), followed by lobular (20%). Approximately 2/3 presented with metastatic disease de novo (67.3%), 69.1% presented with visceral metastases and the median number of lines of treatment was 2. According to intrinsic subtypes 54.5% were luminal HER2-negative (HER2-), 16.4% luminal HER2-positive (HER2+), 10.9% HER2 enriched, and 18.2% triple negative. According to HER2 status, 11 (20%) were HER2+, 26 (47.3%) were HER2-low, and 18 (32.7%) were HER2-. HER2-low expression was more frequent in the hormone-receptor positive (HR+) (51.3%) than in HR negative (HR-) (31.3%), however, this difference was not statistically significant ($p = 0.11$). Patients' characteristics according to HER2 status are shown in Table 1.

With a median follow-up of 39.9 months, there were no differences in PFS and OS according to HER2 status. Median OS was 45, 30.8, and 46.4 months, for HER2+, HER2-low, and HER2-, respectively ($p = 0.48$). On univariate analysis, age, menopausal status, RH status, HER2 status, disease presentation and visceral metastases were not associated with improved OS. In patients with HER2-low status, median OS was 36.6 and 15.8 months for patients with HR+ and HR- disease ($p = 0.009$). In the HER2-low subgroup, multivariate analysis showed that HR status (hazard ratio 10.96 [95% CI 2.11-56.92], $p = 0.004$) and having received ≥ 2 lines of treatment (hazard ratio 13.34 [95% CI 1.97-90.37], $p = 0.008$) were statistically associated with better OS.

Conclusion

Our findings show that almost half of patients with metastatic BC have a low HER2 expression. Although HER2-low status did not impact survival in a small cohort of Mexican patients, HR status and lines of treatment were associated with better prognosis in patients with HER2-low disease. These results demonstrate the high burden of Mexican patients with HER2-low disease who could benefit from targeted therapies after first line therapy, and the importance of ensuring access to effective treatment options.

Table 1

Characteristic	HER2+		HER2-low		HER2-		<i>p</i>
	n = 12	%	n = 25	%	n = 18	%	
Age							
<65 years	10	83.3	20	80.0	16	88.9	0.74
≥ 65 years	2	16.7	5	20.0	2	11.1	
Menopausal status							
Premenopausal	4	33.3	10	40.0	10	55.6	0.43
Postmenopausal	8	66.7	15	60.0	8	44.4	
RH status							
Positive	6	50.0	20	80.0	13	72.2	0.11
Negative	6	50.0	5	20.0	5	27.8	
Disease presentation							
De novo	10	83.3	14	56.0	13	72.2	0.22
Recurrence	2	16.7	11	44.0	5	27.8	
Visceral metastases							
Yes	8	66.7	18	72.0	12	88.9	0.91
No	4	33.3	7	28.0	6	11.1	
Lines of treatment							
<2 lines	7	58.3	9	36.0	6	11.1	0.34
≥ 2 lines	5	41.7	16	64.0	12	88.9	

Patient characteristics

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ER+ HER2-negative mBRCA1/2 carriers breast cancer patients (n=81): Clinical outcomes and molecular characterization via the 21-gene Breast Recurrence Score (RS) test vs the general RS-tested population (799,986 samples)

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Background: The RS assay is a validated prognosticator/predictor of chemotherapy (CT) benefit in ER+ HER2-negative early-stage breast cancer (BC). It is offered to pts irrespective of BRCA1/2 status. We compared RS results, single-gene expression and gene group scores, between pts with germline BRCA1/2 mutations and the general BC pt population undergoing RS testing. Treatments/outcomes in the mBRCA1/2 cohort were also examined.

Methods: This real-life retrospective cohort study included consecutive ER+ HER2-negative mBRCA1/2 female carriers BC pts who had RS testing in 2004-2015. RS and gene expression data were compared to a previously described commercial use database (DB) (J Surg Oncol. 2020;122:611). Chi-square test and 1-sample t-test were used to compare RS distribution and single gene/gene group scores, respectively, between the cohort and the DB. Independent sample t-test was used to compare gene expression/gene group scores across pt subgroups within the mBRCA1/2 cohort. Fisher's test/logistic regression were used to identify variables associated with distant recurrence in the mBRCA1/2 cohort.

Results: The analysis included 81 pts in the mBRCA1/2 cohort and 799,986 BC samples in the DB. Age at diagnosis was younger in the mBRCA1/2 pts vs the DB (median [IQR], 56 [47-61.5] vs 60 [51-67] yrs; $P < .001$). In mBRCA1 and mBRCA2 pts (32 and 48 pts, respectively; for 1 pt, the BRCA gene involved was unknown), RS distribution shifted towards the high RS category when compared to the DB (Table). Comparing single-gene expression and gene group scores in mBRCA1 pts vs the DB, revealed statistically significant differences in 12 of the 16 cancer genes in the RS assay, and in 2 gene group scores, all in a direction contributing to higher RS results. Similar analysis with mBRCA2 pts, revealed significant differences in expression of 10 genes and 3 gene group scores, all in a direction contributing to higher RS results. The only statistically significant difference in gene expression between the mBRCA1 and mBRCA2 pts was in the ESR (higher in mBRCA2 pts; $P = .0407$) and MYBL2 gene (higher in mBRCA1 pts; $P = .0365$) (Table). Of the 32 mBRCA1 pts, 18 (56%) received CT (RS 0-25, 1/14 [7%]; RS 26-100, 17/18 [94%]; treatment information was unavailable for 1 pt). Of the 48 mBRCA2 pts, 19 (40%) received CT (RS 0-25, 5/27 [19%]; RS 26-100, 14/21 [67%]). With a median (IQR) follow up of 8.2 (5.6-9.7) yrs from diagnosis, 9 pts had distant recurrence (1 mBRCA1 pt, 8 mBRCA2 pts). Their median RS result was 25 (range, 16-41), and 4 received adjuvant CT. No statistically significant differences were observed between these 9 pts and the 72 non-recurring pts in terms of pt/disease characteristics and CT treatment. A trend towards significance was observed with respect to the BRCA gene involved (recurrence rate of 3.1% in mBRCA1 pts vs 16.7% in mBRCA2 pts, $P = .078$). A statistically significant association was found between the proliferation and invasion gene group scores and the odds of having distant recurrence (proliferation group score: odds ratio [OR], 23.60 [95% CI, 1.4-397], $P = .0281$; invasion group score: OR, 5.1 [95% CI, 1.1-23], $P = .0339$). The ER and HER2 gene groups scores were not associated with distant recurrence.

Conclusions: Both mBRCA1 and mBRCA2 carriers are characterized by higher RS results that stem from a distinct gene expression profile of most genes in the RS assay.

Single Gene Expression and Gene Group Scores vs the Commercial Use DB

	DB N = 799,986	mBRCA1 pts n = 32	P-value mBRCA1 vs DB	mBRCA2 pts n = 48	P-value mBRCA2 vs DB
RS group, %					
0-10	22%	6%		10%	
11-25	62%	38%	<.001	46%	<.001
26-100	16%	56%		44%	
Gene expression, mean (SD)					
<i>ER group</i>					
ESR	10.0	9.4 (1.5)	.018	10.0 (1.2)	.83
PGR	7.3	6.1 (1.8)	<.001	6.4 (1.6)	<.001
BCL2	8.5	8.3 (1.1)	.32	8.7 (1.0)	.23
SCUBE2	8.8	7.9 (2.0)	.013	8.4 (1.6)	.054
Group score	8.5	7.8 (1.2)	<.001	8.2 (1.0)	.019
<i>Proliferation group</i>					
CCNB1	5.7	6.0 (0.4)	<.001	5.9 (0.6)	.023
KIF7	6.4	7.2 (0.7)	<.001	7.0 (0.9)	<.001
STK15	5.6	6.5 (0.8)	<.001	6.3 (0.8)	<.001
SURV	5.0	6.2 (0.9)	<.001	6.0 (1.3)	<.001
MYBL2	4.5	5.8 (0.8)	<.001	5.4 (1.0)	<.001
Group score	5.4	6.3 (0.6)	<.001	6.1 (0.8)	<.001
<i>HER2 group</i>					
ERBB2	9.2	8.9 (0.9)	.12	9.2 (0.6)	.92
GRB7	6.7	6.7 (0.8)	.68	6.9 (0.7)	.031
Group score	6.9	7.0 (0.8)	.84	7.1 (0.7)	.047
<i>Invasion group</i>					
STMY3	10.0	9.7 (1.4)	.22	10.0 (1.3)	.64
CTSL2	3.8	4.4 (0.9)	.0026	4.3 (0.8)	<.001
Group score	6.9	7.0 (0.7)	.34	7.1 (0.8)	.76
<i>Individual</i>					
CD68	8.8	9.1 (0.6)	.035	9.0 (0.5)	.11
GSTM1	7.8	6.7 (1.6)	<.001	7.0 (1.2)	<.001
BAG1	8.5	8.1 (0.7)	.0014	8.3 (0.6)	.018

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P3-05-60

Understanding Ethnoracial Differences in Oncotype DX Recurrence Scores in Patients with Early-Stage Breast Cancer: An Analysis Based on Hispanic Ethnicity

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Background: Recent studies suggest racial and ethnic differences in tumor genomics and receipt of systemic treatment may be drivers of racial and ethnic disparities in clinical outcomes (e.g., mortality, recurrence) in patients with breast cancer (BC). For patients of Hispanic ethnicity, the relationship between ethnoracial categories (i.e., Hispanic Black, Hispanic White), tumor genomics, and receipt of systemic has not been well elucidated. The objective of this study is to examine implications of ethnoracial categories on Oncotype DX recurrence score (RS), receipt of chemotherapy for high risk RS and endocrine therapy (ET) use in the National Cancer Database (NCDB). **Materials/Methods:** Patients diagnosed from 2004-2017 with stage I or stage II HR+/HER2- BC with RS available in the NCDB were identified. The data was divided into Black and White patients then stratified by ethnicity. Study ethnoracial categories included non-Hispanic White (NHW), Hispanic White (HW), non-Hispanic Black (NHB) and Hispanic Black (HB). High-risk RS was defined using the original definition of RS>30. On univariable analysis, intra-racial differences in RS score (t-test) and the proportion of patients with high-risk RS (chi-square test) were examined by ethnicity. Systemic therapy (chemotherapy and ET) were assessed with univariable analysis within racial groups by ethnicity (chi-square test). **Results:** The ethnoracial composition of the cohort was 220,490 (87.5%) NHW, 20,690 (8.2%) HB, 10,477(4.2%) HW and 296 (< 1%) HB. Overall, Hispanic patients had higher mean RS relative to non-Hispanic patients (18.4 [11.8] vs. 18.0 [10.8], p=0.0004) and a higher proportion of RS>30 (10.4% vs. 9.6%, p=0.0028). Amongst White patients, Hispanic ethnicity was

associated with higher mean RS (18.3 [11.7] HW vs. 17.8 [10.6] NHW) and higher rate of RS>30 (10.4% HW vs. 9.1% NHW, $p < 0.0001$). There was no significant difference in mean RS between NHB and HB patients (19.0 [13.5] HB vs. 20.0 [12.7], $p = 0.1855$) but there was a trend towards a lower proportion of RS>30 in HB patients (10.8% HB vs. 14.6% NHB, $p = 0.0688$). In patients with RS>30, the proportion that received chemotherapy was similar based on ethnicity within White (80.7% HW vs. 82.3% NHW, $p = 0.1843$) and Black (78.1% HB vs. 81.2% NHB, $p = 0.6601$) patients. ET use was slightly lower in HW vs. NHW patients (90.6% vs. 91.7%, $p < 0.0001$). There was no significant difference in ET use in NHB vs HB patients (89.9% vs. 89.9%, $p = 0.9651$). Conclusions: In our examination of the early-stage breast cancer patients in the NCDB, Hispanic ethnicity was associated with higher RS amongst White patients with an opposite trend in Black women. Systemic therapy use was largely similar across ethnoracial categories. Future, studies should disaggregate Hispanic ethnicity by race to better understand tumor characteristics and clinical outcomes in this population.

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Unleashing NK- and CD8 T cells by combining monalizumab (anti-NKG2A) and trastuzumab for metastatic HER2+ breast cancer: first results MIMOSA trial

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Background Although treatment options and survival of HER2+ metastatic breast cancer (MBC) patients have greatly improved, the majority of MBC-patients still die of this disease. The relatively high levels of TILs observed in this BC subtype provide a rationale for immunomodulatory strategies, however, PD1-blockade has only shown modest response rates in this setting. While PD-1 blockade mainly acts on T cells, monalizumab targets the inhibitory immune checkpoint NKG2A which interacts with HLA-E on tumor cells, thereby unleashing NK- as well as CD8 T cells. We hypothesize that monalizumab can promote antibody-dependent

cell-mediated cytotoxicity (ADCC) which is critical for trastuzumab efficacy. Clinical activity was shown in patients with head and neck cancer when monalizumab was combined with cetuximab (anti-EGFR). Here, we present the first results of the MIMOSA-trial investigating the efficacy of the novel combination monalizumab and trastuzumab in patients with HER2+ MBC. Methods In the phase II MIMOSA-trial (NTC04307329), HER2+ MBC patients were treated biweekly with 4mg/kg trastuzumab and 750mg monalizumab. Key eligibility criteria were progressive disease despite anti-HER2 therapy, had received a minimum of one and a maximum of three lines of palliative chemotherapy, had measurable disease according to RECIST1.1, and a serum LDH-level below 500U/L. Primary endpoint was objective response rate according to RECIST1.1. Secondary endpoints included clinical benefit rate (complete response CR, partial response PR or stable disease SD for at least 6 months) according to RECIST1.1, progression-free survival, overall survival and safety. Dose-limiting toxicities were continuously monitored throughout the trial and evaluated using a pre-defined Pocock-type boundary rule. Following a Simon's two-stage design, 11 patients were included in stage I of the trial. If two or more responders were observed, further exploration is warranted in stage II. Results Between January 2021 and April 2022, eleven women of which ten are currently evaluable were enrolled in the trial. Patients received a median of two lines of prior treatment for MBC, of which 6 out of 11 patients were treated with trastuzumab emtansine (T-DM1). The majority of patients had hormone receptor positive BC (72% of the patients) and had low levels of tumor-infiltrating lymphocytes (TILs) with a median of 1% (ranging from 1% to 20%). Patients received a median of four cycles of trastuzumab and monalizumab. Treatment was well tolerated with no dose-limiting toxicities. No objective responses were observed in the first ten out of eleven evaluable patients. Therefore, MIMOSA stage I did not meet its primary endpoint, leading to discontinuation of the trial. Conclusions The novel combination of trastuzumab and monalizumab did not induce objective responses in heavily pre-treated HER2+ MBC patients.

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TATEN TRIAL (SOLTI-1716) Targeting non-Luminal disease by PAM50 with pembrolizumab + paclitaxel in Hormone Receptor-positive/HER2-negative (HR+/HER2-) metastatic breast cancer (MBC): interim analysis

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Background Within HR+/HER2- disease, patients with non-luminal subtypes of breast cancer (HER2-enriched [HER2-E] and Basal-like) have poorer prognosis than those with luminal subtypes, may be more sensitive to chemotherapy, and have higher expression of immune-related genes and tumor infiltrating lymphocytes (TILs). Here, we report the interim efficacy and safety data of the TATEN trial (NCT04251169), the first study designed to evaluate pembrolizumab and paclitaxel in HR+/HER2-negative, PAM50 non-luminal, metastatic breast cancer (MBC). Methods TATEN is a single-arm, multicenter phase II study evaluating pembrolizumab in combination with paclitaxel in patients with HR+/HER2-, PAM50 non-luminal, MBC. Key inclusion criteria include progression to prior CDK4/6 inhibitors, presence of measurable disease by RECIST V1.1, no prior chemotherapy for MBC, and ECOG 0-1. Patients receive pembrolizumab at 200 mg every 3 weeks (on D1 of each 21-day cycle, beginning at cycle 1) in combination with weekly paclitaxel at 80 mg/m², beginning at cycle 2. The primary endpoint is to evaluate overall response rate (ORR), defined as the rate of complete (CR) and partial response (PR) according to RECIST V1.1. Secondary endpoints include clinical benefit rate (CBR; CR + PR + stable disease >24 weeks), progression free survival, overall survival, safety, and predictive biomarkers. Tumor samples collected during advanced/metastatic disease are mandatory to assess PAM50 and other translational endpoints. This study had a planned interim analysis after 15 patients were evaluable for ORR based on a Simon's two stage design with 80% power and a type I error rate of 0.05. Stage I of the trial would be considered successful if at least 6 patients achieved a PR and/or CR. In that case, the trial would recruit up to 46 evaluable patients for a target ORR \geq 41. Here we report results from the patients who received at least one dose of combination treatment and had a first, post-baseline, tumor assessment according to RECIST v1.1 (evaluable population). Results From July 2020 to December 2021, 119 patients were screened, and 25 PAM50 non-luminal tumors were identified (21%). From these, 17 (68%) patients were recruited, and 15 were evaluable for primary endpoint. Two patients discontinued the trial before the first dose of pembrolizumab and paclitaxel, because of clinical progressive disease (PD). Baseline patient characteristics were as follows: median age 53 years (range: 40-77), ECOG 0 52.9%, de novo MBC at diagnosis 29.4%, and visceral disease 64.7% (including 53.3% with liver metastasis). Ten patients had received paclitaxel treatment in the adjuvant setting. Regarding PAM50 intrinsic subtype, two patients had basal-like and 13 HER2-E tumors. At the time of data cut-off (May 17, 2022), 8 patients (53.3%) had stopped their treatment because of PD and 2 (13.3%) due to toxicity. Five patients (33.3%) were still on treatment. The ORR was 53.3% (8 of 15, 95% CI 26.6-78.7), meeting the pre-specified ORR for the first stage of the trial. The CBR was 86.6% (13 of 15, 95% CI 59.5-98.34), and median PFS was 7.5 months (95% CI: 5.6 – 10.2). Overall, all patients experienced treatment-related adverse events (TRAEs) of any grade, while 53.3% of patients experienced grade 3 TRAEs. No grade 4 or 5 TRAEs were reported in the evaluable population. Correlative analysis including gene expression analysis and centralized TILs scoring and PD-L1 IHC will be presented. Conclusions The first stage of TATEN

combining pembrolizumab with paclitaxel after progression to CDK4/6 inhibitors in patients with HR+/HER2-negative, PAM50 non-luminal MBC met its pre-specified endpoint. Completion of the stage II part of the trial with the inclusion of up to 46 patients is warranted to assess the activity of this combination in this group of patients. Correlative studies to find predictive biomarkers of response to this regimen are ongoing and will be presented at the meeting. This study was funded by MSD.

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P3-06-03

Trilaciclib induces immune changes within the tumor microenvironment in early-stage triple-negative breast cancer

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Background: In early-stage triple-negative breast cancer (TNBC), there is accumulating evidence of a correlation between tumor-infiltrating lymphocytes in tumor tissue and favorable clinical outcomes, with a high CD8+/regulatory T-cell (Treg) ratio after neoadjuvant chemotherapy being predictive of overall survival and associated with pathologic complete response (Ladoire S, et al. Br J Cancer. 2011; Park YH, et al. Nat Commun. 2020). Trilaciclib is a transient inhibitor of cyclin-dependent kinase 4/6 that is administered intravenously prior to chemotherapy. In preclinical studies, trilaciclib has been shown to have immune-enhancing effects by differentially arresting CD8+ T-cell and Treg subsets, which is followed by the faster recovery of CD8+ T cells than Tregs in the tumor microenvironment. **Methods:** This phase 2, single-arm, open-label study aims to evaluate neoadjuvant, single-dose trilaciclib followed by trilaciclib plus dose-dense anthracycline/cyclophosphamide and taxane in patients with early-stage TNBC (NCT05112536). Patients with previously untreated, non-metastatic, confirmed TNBC and a primary tumor ≥ 1.5 cm of any nodal status receive a single dose of trilaciclib 240 mg/m² during the lead-in phase, followed by 4 cycles of doxorubicin 60 mg/m² plus cyclophosphamide 600 mg/m², and 12 weekly cycles of paclitaxel 80 mg/m². Trilaciclib 240 mg/m² is administered prior to the first chemotherapy dose of each cycle. Pembrolizumab 400 mg every 6 weeks starting on day 1, cycle 1, and/or carboplatin AUC 1.5 every week starting on day 1, cycle 5, is allowed per investigator discretion. Tumor biopsies and peripheral blood samples are collected prior to any treatment, 7 days \pm 1 day post administration of trilaciclib, and during surgery, with an additional blood sample collection on day 1, cycle 2. The primary objective is to evaluate the immune-based mechanism of action of trilaciclib after a single dose of trilaciclib, as measured by changes in the CD8+/Treg ratio in tumor tissue. Pathologic complete response, safety and tolerability, and additional exploratory immune biomarker endpoints will also be assessed. **Results:** As of June 3, 2022, 9 patients with early-stage TNBC had been enrolled and 8 patients had received the trilaciclib lead-in dose and initiated doxorubicin/cyclophosphamide. Patients had a median age of 53.0 years, and all had stage II tumors at diagnosis, with 7 having ductal carcinoma. The median number of chemotherapy cycles received was 3 (range 1–6), and all 8 patients received pembrolizumab. Seven patients continue study treatment; 1 patient discontinued due to disease progression. Five patients had an adverse event (AE) related to any study treatment, including 4 patients with ≥ 1 trilaciclib-related AE. There were no grade ≥ 3 treatment-related AEs or serious AEs. On-treatment, post-trilaciclib monotherapy biopsies were available for 4 patients. Following neoadjuvant trilaciclib treatment, the median density of stromal CD8+ T cells increased from 103.1/mm² at baseline to 229.8 /mm² at day 7. The median CD8+/Treg ratio increased in 2 patients from 1.85 at baseline to 1.90 at day 7. **Conclusions:** Preliminary analysis of on-treatment tumor biopsies from 4 patients suggests that a single dose of trilaciclib may modulate the immune cell composition in the tumor microenvironment to support antitumor immune responses. The increase in CD8+ T cells following 7-day neoadjuvant treatment with trilaciclib supports previous data suggesting a role in T-cell infiltration. The complete dataset from all patients (estimated enrollment: N \approx 24) and additional biomarker analyses will be presented.

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5:00 PM - 6:15 PM

P3-06-04

Treatment of Metastatic Breast Cancer with Multipotent Oncolytic/Helper Adenovirus CAAdVEC

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Background: Metastatic breast cancer (MBC) which causes significant morbidity and mortality worldwide is in need of more effective treatment regimens. In combination with chemotherapy, anti-PD1 antibody pembrolizumab has been shown to prolong progression-free survival (PFS) of patients with triple-negative subtype MBC (TN-MBC), however, its efficacy remains low for the other 80% of patients with MBC. MBC's heterogenous pattern of immune infiltration and expression make it challenging to treat with single immunotherapeutic agents such as pembrolizumab and successful immunotherapy must therefore target multiple pathways. To augment antitumor host immune responses during treatment, studies have examined adjunct agents such as "oncolytic" adenovirus (OAd), which are vectors that preferentially replicate in and lyse tumor cells leading to the activation of host immunity. OAd have been tested in a myriad of clinical trials with the hope to enhance host immune activation but those trials have shown limited successes. Methods: To overcome the multiple immunogenic barriers in solid tumors, our group developed a binary oncolytic/helper-dependent adeno-immunotherapy (CAAdVEC). The first generation CAAdVEC (CAAdTrio) contains an OAd and a "helper-dependent" adenovirus (HAd) that produces immunostimulant molecules including interleukin (IL)-12p70 and anti-PD-L1 antibody. Based on successful results using animal models, a first-in-human Phase 1 study with CAAdTrio was conducted among patients with all solid tumors (NCT03740256). Four patients with MBC were enrolled in the virus dose-escalation phase of the trial and received an intra-tumor injection of CAAdTrio. Given the novelty of this binary agent, starting dose of CAAdTrio was more than 2-logs lower than that used in other OAd trials. Three patients received dose level (DL) 1 and one patient received DL2. All patients also received pembrolizumab 6 weeks after the virus injection. The primary endpoint for this phase I dose escalation was dose-limiting toxicities (DLT). Secondary outcomes included overall response rates (ORR), disease control rate (DCR), PFS, overall survival (OS), and treatment-related adverse events. Results: No patients developed DLT. The most common toxicities were fever, fatigue and pain around the injection site, but none were greater than grade 2. No significant elevation in liver enzymes were observed. Three of the four patients had partial response (PR). One patient progressed after ten weeks of stable disease and passed away. The three patients with PR received pembrolizumab within 7 weeks of CAAdVEC injection. Analysis of injected tissues prior to pembrolizumab treatment showed that CAAdTrio repolarized the tumor microenvironment toward immune activity by increasing the number of infiltrating Th1 immune cells, leading to responses in some treated tumors and even in one distant metastasis,

demonstrating the potent systemic immune response to local CAdTrio treatment in patients with MBC. Conclusions: Our study demonstrated that intra-tumor injection with CAdTrio was safe and effective in patients with MBC but the significance of the results was limited by the small sample size. An MBC dedicated phase II trial is planned to be conducted to fully evaluate the efficacy and safety of CAdVEC treatment and to further elucidate mechanisms of resistance/sensitivity among patients with MBC.

Disclosure(s):

Natalie Chen, M.D., Ph.D.: No financial relationships to disclose

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P3-06-05

Effects of isoflavone genistein, combined with anti-estrogen fulvestrant, on anti-PD1 therapy response against E0771 mammary tumors in mice

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Although immune checkpoint blockers (ICBs) have revolutionized the treatment of many cancers, only less than 30% of patients respond to any ICB as a monotherapy. Estrogens, produced by the adipose tissue in the mammary glands, are immunomodulators in the tumor microenvironment (TME). Estrogens suppress anti-tumor immunity and activate immunosuppression through the estrogen receptor α (ER α) in the immune cells but activate anti-tumor immunity through ER β . Genistein (GEN) is a biologically active isoflavone and is structurally similar to estradiol (E2). However, in contrast to E2, GEN binds preferentially to ER β . Here we studied if GEN combined with ER α inhibitor fulvestrant (Fulv) alters response to anti-PD1 therapy in ER α negative, ER β positive E0771 mouse mammary tumors. Syngeneic C57BL/6 mice were fed either a control (CON) diet or GEN supplemented diet for 5 weeks and then allografted E0771 mammary tumor cell into the 4th mammary fat pad. When tumors reached an average size of 16mm², mice in both diet groups were further divided into 4 sub-groups treated with: 1) anti-PD1 (150 μ g or 100 μ g every 3 days for a total of 3 doses), 2) Fulv (1mg) once weekly, 3) anti-PD1+Fulv or 4) IgG control group. We found that three doses of 150 μ g of anti-PD1 alone effectively reduced tumor growth in the CON ($p=0.0005$) group and its efficacy was notably weakened in the GEN group ($p=0.04$). Combination with Fulv did not improve PD1 response. These findings suggest that when using a highly effective anti-PD1 dose, GEN may reduce rather than improve the response, and anti-ER α does not add to anti-PD1's effect in control of GEN group. A suboptimal dose (100 μ g) of anti-PD1 alone did not inhibit E0771 tumor growth in mice fed CON diet, but in the GEN group the tumor inhibition by anti-PD1 alone almost reached statistical significance ($p=0.057$). The combination of suboptimal PD1+Fulv significantly reduced tumor growth compared with IgG ($p=0.04$) or Fulv ($p=0.02$). During GEN feeding, anti-PD1+Fulv was even more potent in inhibiting tumor growth when compared with IgG group ($p=0.02$) and Fulv group ($p=0.007$). Thus, when anti-PD1 alone is not effective, either Fulv or GEN will improve responsiveness to anti-PD1. In the suboptimal anti-PD1 dose experiment, GEN feeding increased CD8+ T cells ($P=0.04$) and decreased

CD4⁺Foxp3⁺ cells ($p=0.01$) in the TME. Further, GEN reduced the proportion of immunosuppressive MDSC cells (CD3⁺CD11B⁺Ly6G^{high}6C^{low}) in the PD1⁺ Fulv group ($p=0.01$) in the Peyer's patches. In vitro experiments showed that both GEN and Fulv, and especially their combination, inhibited the E0771 cells proliferation, indicating that these two treatments can also directly suppress the growth of ER α negative but ER β positive breast cancer cells. Taken together, the data show that anti-estrogens and GEN in the diet may improve response to anti-PD1 therapy, possibly both through activation of tumor immune response and inhibition of tumor cell proliferation and induction of tumor cell death.

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Fabia de Oliveira Andrade, n/a: No financial relationships to disclose

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Ester Molina Hoyo, n/a: No financial relationships to disclose

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P3-06-06

Real-world analysis of adverse events of patients with triple negative breast cancer receiving therapy per KEYNOTE-522

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Background: KEYNOTE-522 was a randomized, double-blind, placebo-controlled phase 3 trial which resulted in the FDA approval of pembrolizumab with neoadjuvant chemotherapy for patients (pts) with newly diagnosed, high-risk, early-stage triple negative breast cancer (TNBC). Given the improvement in pathological complete response (pCR) and event-free survival rates, this regimen has emerged as standard-of-care (SOC) therapy. Adverse events in pts on this treatment regimen in clinical practice is unknown and understanding the real-world toxicity of this regimen is critical.

Methods: In this IRB approved retrospective, single-center study we examined pts with early-stage TNBC who received planned treatment per KEYNOTE-522 per SOC from 2021-present. This regimen includes a year of pembrolizumab combined with 4 cycles of neoadjuvant carboplatin/paclitaxel followed by 4 cycles of doxorubicin/cyclophosphamide. Number and length of treatment delays, treatment related toxicities of all grades, and pCR rate were collected from the electronic medical record.

Results: Of the 87 identified pts, 2 were excluded due to locally recurrent or metastatic disease and 6 did not receive immunotherapy due to concerns for toxicity or patient preference. Of the 79 pts who initiated treatment with chemotherapy and immunotherapy, median age of the cohort was 52 (27-77). 9 pts had a BRCA1 mutation and 1 pt had a BRCA2 mutation. 41 (51.9%) had T1-2 disease and 38 (48.1%) had T3-4 disease. 37 (46.8%) pts had N0 disease and 42 (53.2%) had N1-3 disease. 15 pts had baseline comorbidities, including heart disease, kidney disease, type II DM, and/or peripheral neuropathy. 68 pts (86.1%) had baseline ECOG 0, 9 (11.4%) had ECOG 1, and 2 (2.5%) had ECOG 2. At the time of analysis, 70 pts (88.6%) were receiving active treatment, of which 47 (67.1%) had completed $\geq 50\%$ of the planned neoadjuvant therapy. Of pts completing $\geq 50\%$ of planned neoadjuvant therapy and pts off therapy (N=56), 31 (55.4%) had 1 or more hospitalizations and 23 (41.1%) had 1 or more emergency room visits. 30 pts had treatment delays (53.6%) and 21 pts (37.5%) had dose reductions. Rates of adverse events are presented in Table 1. Of the 79 analyzed pts, 35 have undergone surgery. pCR rate was 45.7% (N=16). 8 (22.9%) pts had RCB-I, 4 (11.4%) pts had RCB-II, 3 (8.6%) pts had RCB-III, and 4 (11.4%) pts had residual disease without RCB calculation. Updated analysis will be included at time of presentation.

Conclusions: In this single-center retrospective study of pts receiving chemoimmunotherapy for TNBC, we found higher rates of grade 3 toxicity, including nausea, fatigue, neutropenia, diarrhea, peripheral neuropathy, and hypothyroidism, and lower pCR rate than was reported in the KEYNOTE-522 trial. This may reflect a more heterogeneous population of pts treated in routine clinical practice who are typically less fit than pts on clinical trials. Additionally, pts in this study had higher T stages (48.1% with T3-4 disease vs 26.0% in trial) and node positive disease (53.7% with N1-3 disease vs 48.8% in trial). Limitations include immaturity of data and small sample size; however, these data warrant validation through longer-term follow-up and multicenter validation.

Adverse Events

Adverse Event	Standard of Care (N=56) Any Reported	Grade 3 or higher	Keynote-522 Pembrolizumab-Chemotherapy (N=781) Any reported	Keynote-522 Grade 3 or Higher
Nausea	38 (67.9%)	9 (16.1%)	490 (62.7%)	26 (3.3%)
Neutropenia	41 (73.2%)	31 (55.4%)	365 (46.7%)	370 (34.6%)
Fatigue	37 (66.1%)	15 (26.8%)	321 (41.1%)	27 (3.5%)
Diarrhea	25 (44.6%)	8 (14.3%)	230 (29.4%)	17 (2.2%)
Peripheral Neuropathy	25 (44.6%)	6 (10.7%)	154 (19.7%)	15 (1.9%)
Rash	5 (8.9%)	2 (3.6%)	170 (21.8%)	7 (0.9%)
Immune-related adverse events				
Hypothyroidism	7 (12.5%)	3 (5.4%)	107 (13.7%)	3 (0.4%)
Hyperthyroidism	1 (1.8%)	1 (1.8%)	36 (4.6%)	2 (0.3%)
Type I Diabetes	1 (1.8%)	1 (1.8%)		
Primary Adrenal Insufficiency	4 (7.1%)	1 (1.8%)	18 (2.3%)	10 (1.3%)
Colitis	3 (5.4%)	3 (5.4%)	13 (1.7%)	7 (0.9%)
Pancreatitis	2 (3.6%)	1 (1.8%)	4 (0.5%)	4 (0.5%)
Hepatitis	1 (1.8%)	1 (1.8%)	11 (1.4%)	9 (1.2%)
Pneumonitis	1 (1.8%)	0 (0%)	10 (1.3%)	3 (0.4%)

Adverse Events in pts receiving Keynote-522 regimen as SOC and on clinical trial

Disclosure(s):

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P3-06-07

Phase Ib/II study to evaluate safety and tolerability of cabiralizumab in combination with nivolumab and neoadjuvant chemotherapy in patients with localized triple-negative breast cancer

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Background: Neoadjuvant immune checkpoint inhibition (ICI) in combination with chemotherapy is approved for patients with high-risk, early-stage triple-negative breast cancer (TNBC) based on improved outcomes in the KEYNOTE-522 trial. However, some patients have primary resistant disease and do not achieve a pathological complete response (pCR), while others experience significant toxicity. Tumor-associated macrophages (TAMs) are a potential resistance mechanism for ICIs and are dependent on colony-stimulating factor 1 receptor (CSF1R). Therefore, we examined the addition of cabiralizumab, a CSF1R inhibitor, to neoadjuvant paclitaxel, carboplatin, and nivolumab to assess the safety, tolerability, and changes in the tumor microenvironment (TME) in patients with early-stage TNBC. Methods: This is a phase Ib/II, single-institution, randomized controlled clinical trial (NCT04331067) in patients with newly diagnosed Stage II-III TNBC. The primary endpoints include: (1) to determine the safety of a 12-week neoadjuvant regimen of paclitaxel (80 mg/m² IV q week) + carboplatin (AUC5 IV q3 weeks) + nivolumab (240 mg IV q2 weeks) with or without cabiralizumab (4 mg/kg IV q2 weeks) and (2) to evaluate the effect of cabiralizumab on TAMs and changes in tumor infiltrating lymphocytes (TILs) in the TME between baseline and an on-treatment biopsy after 4 weeks of therapy. Adjuvant treatment is per investigator's choice. Secondary objectives include evaluation of pCR rate and recurrence-free survival. Paired tissue and bone marrow biopsies are collected for evaluation of the TME and disseminated tumor cells, respectively. The study was designed to enroll 50 patients, including a 12-patient safety lead-in cohort. Here, we report the planned interim analysis of the safety lead-in cohort. Results: Between December 2020 and May 2022, we enrolled 12 patients to the safety lead-in, including 6 patients in each arm. 5 of 12 patients (41.7%) enrolled are underrepresented minorities, including 4 Black patients and 1 Hispanic patient. 2 of 6 patients in the nivolumab arm experienced grade 3 severe toxicity, including 1 patient who developed sepsis and 1 who developed peripheral neuropathy. 3 of 6 patients in the nivolumab + cabiralizumab arm developed grade 3 severe toxicity including 2 patients who experienced myositis and 1 patient who developed periorbital edema. Of the first 10 patients enrolled, 5 had a pCR (2 pCR in cabiralizumab arm, 3 pCR in non-cabiralizumab arm) and 3 had non-pCR (1 RCB-1 and 1 RCB-3 in cabiralizumab arm, 1 RCB-1 in non-cabiralizumab arm). 2 patients came off study prior to surgery (1 due to toxicity and 1 due to missing study visits). Data from the final 2 patients still on treatment will be available at the time of presentation. Discussion: Full safety, pathologic, and clinical response data in the safety lead-in cohort for patients with early-stage TNBC receiving neoadjuvant chemotherapy + nivolumab with or without cabiralizumab, will be presented.

Disclosure(s):

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Katherine Weilbaecher, MD: No financial relationships to disclose

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5:00 PM - 6:15 PM

P3-06-08

Turning tumor cells into antigen-presenting cells for cancer immunotherapy

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Miguel Lopez-Lago¹, Sagarika pachhal¹, Charles L. Wiseman¹, William V. Williams¹. ¹BriaCell Therapeutics Corporation, Philadelphia, PA Turning tumor cells into antigen-presenting cells for cancer immunotherapy Background: Therapeutic cancer vaccines are based on specific stimulation of the immune system using tumor antigens to elicit an antitumor response. We have been conducting clinical trials using the breast cancer cell line SV-BR-1-GM as a therapeutic vaccine. SV-BR-1-GM is a GM-CSF expressing breast cancer cell line with features of an antigen presenting cell (APC) owing to the expression of several immunomodulatory molecules, including MHC-I (HLA-A, B & C) and MHC-II (HLA-DRB3 & -DRA). Initial results in patients treated with irradiated SV-BR-1-GM cells, low dose cyclophosphamide and local IFN α suggest that patients that match SV-BR-1-GM at least at 1 HLA allele are more likely to derive clinical benefit. This clinical observation, together with the fact that SV-BR-1-GM cells can directly activate CD4+ T-cells in an antigen-specific HLA-restricted manner, as demonstrated by an in vitro antigen presentation assay (1), lead us to hypothesize that SV-BR-1 (the parent cell line) can function as APC. To further enhance direct antigen presentation to T-cells, SV-BR-1 cells have been genetically modified to express co-stimulatory molecules, immunomodulatory cytokines, and an extended repertoire of HLA alleles. Methods: To generate an off-the-shelf semi-allogeneic cell therapy covering most of the population, SV-BR-1 was genetically modified to express an extended repertoire of HLA alleles. Based on population analysis, four cell lines, each carrying two (2) HLA-A and two (2) HLA-DRB3/4/5 alleles, should produce at least a single match in 99% of the population, with a 92% match at Class I HLA-A alleles and a 98% match at Class II HLA-DRB3/4/5 alleles. SV-BR-1 was genetically modified using CRISPR/cas9 deletion of the endogenous HLA-A and HLA-DRB3 alleles and subsequent lentiviral mediated expression of alternative HLA-A and DRB3 alleles. To generate tumor cell lines with enhanced direct antigen presentation to T-cells, SV-BR-1 cells were genetically modified to express co-stimulatory molecules and immunomodulatory cytokines by using a lentiviral mediated expression system. Results: Following sequential CRISPR/Cas9 editing, the SV-BR-1 cells were cloned, and one clone selected (clone 17) for further engineering. Lack of expression of HLA-A and HLA-DRB3 was confirmed using flow cytometry and DNA sequencing. Clone 17 was subsequently transduced with 6 lentiviral vectors each expressing 2 genes under the control of separate promoters: CD86-IL12, CD80-HLA-DRA, 4-1BBL-IL7, GM-CSF-IFN α , HLA-allele-1-HLA-allele-2 and HLA-DR-allele-1-HLA-DR-allele-2. Four cell lines were generated with different combinations of HLA alleles. Following selection, cells were evaluated by ELISA, flow

cytometry and RT-PCR to confirm gene expression. Cell lines that secreted GM-CSF, IFN γ , IL12, IL7 and expressed CD80, CD86, 4-1BBL, and both Class I and Class II HLA alleles are then transferred to GMP manufacturing. These modified breast cancer cell lines will be used in clinical studies designed to first evaluate the safety of intradermal inoculation with the irradiated cells and later combined with other agents to augment the immune response. Each patient will be treated with the cell line(s) that match them at least at one HLA allele. 1. Lacher M. D. et al, Front Immunol. 2018 May 15;9:776

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Charles Wiseman, n/a: Wiseman Research Initiatives: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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5:00 PM - 6:15 PM

P3-06-09

Real-world toxicity of pembrolizumab-based neoadjuvant regimen in patients with early triple negative breast cancer

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Background Pembrolizumab (pembro, anti-PD-1 antibody) combined to chemotherapy (CT) in neoadjuvant/adjuvant setting has demonstrated its efficacy for early triple negative breast cancer (eTNBC). Pembro obtained FDA marketing authorization on July 26, 2021 and is available in France through the French Early Access Program. Methods We built an ambispective cohort that aimed to evaluate the efficacy and safety of the pembro-CT combination in the real world setting in patients with eTNBC. This study included patients treated from September 2021 to May 2022, at Institut Curie, France. Patients provided written authorization to report their clinical data. We report here the safety results. Results Between September 2021 and May 2022, 51 patients were included. Median age was 49 years [29; 68].

Germline mutations were recorded in 8 patients (22.2% of 36 tested patients). All pts were ECOG PS 0 or 1. Baseline clinical TNM stage were T1 (8 pts, 15.7%), T2 (30 pts, 58.9%), T3 (7 pts, 13.7%) and T4 (6 pts, 11.7%). Out of 37 pts (72.5%) with radiological axillary lymph node involvement, 19 pts (51.4%) had positive node involvement confirmed by guided fine needle aspiration. SBR grade 2 and 3 were observed in 9 (17.6%) and 42 (82.4%) pts, respectively. HER2 score was 0 or 1+/2+(FISH neg) for 31 (60.8 %) and 20 pts (39.2 %), respectively. A CPS score ≥ 10 was observed in 19 pts (50% of 38 tested patients). The CT backbone was a combination of carboplatin (Cb) plus weekly paclitaxel (wP) 4 courses (with Cb regimen AUC 5 q3W (81.1%), AUC4 q3w (5.4%) and AUC1,5 q1w (13.5%), and wP 80 mg/m²), followed by standard AC60/600 q3w for 4 courses. Out of the 37 pts (72.5%) who completed the Cb + wP 4 courses, all experienced adverse events (AEs), including 21 pts (56.8%) with at least 1 grade ≥ 3 AE (anemia 5.4%, thrombopenia 5.4%, neutropenia 51.5%, neuropathy 2.7%). Transfusion support was needed for 8 pts (21.6%). Grade ≥ 2 neuropathy occurred in 3 pts (8.1 %). Dose reduction and drug discontinuation were performed in 9 (24.3%) and 5 pts (13.5%), respectively. On the entire cohort, 15 pts (29.4%) had IrAE all grades: dysthyroidism (6 pts, 11.7%), skin toxicity (2 pts, 3.9%), adrenal insufficiency (1 pt, 2%), hypophysitis (1 pt, 2%), immune-allergic nephropathy (1 pt, 2%), suspicion of myocarditis (1 pt, 2%), hepatitis (1 pt, 2%) and ophthalmologic AE (1 pt, 2%). Consequently, after a median follow up of 5 months, pembro postponement and permanent discontinuation were performed in 7 (13,7%) and 5 pts (9,8%), respectively. At abstract submission 6 pts had breast surgery (pCR in 5 pts = 83.3%).

Conclusions Our real-world data are consistent with the results of the KEYNOTE-522 trial in terms of patients characteristics. We observed a very high rate of hematological and immune related adverse events, frequently leading to dose reduction or discontinuation, underlying the need for a very close clinical management of those patients. Updated data including toxicity during the whole neoadjuvant sequence and pCR rate will be presented at the meeting.

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12/7/2022

5:00 PM - 6:15 PM

P3-06-10

Immune-related adverse events (irAEs) and pathological complete response (pCR) rates in patients receiving neoadjuvant chemotherapy (CHT) and pembrolizumab (PEM) for early triple-negative breast cancer (eTNBC)

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Background and Significance: Recently, the addition of the immune checkpoint-inhibitor PEM to CHT was shown to increase pCR rates and invasive event-free survival in the Keynote-522 (KN522) trial. Several irAEs are known to occur during use of PEM in various cancer entities. In our multicenter analysis we aimed to identify real-world occurrence rates of irAEs and pCR rates in women receiving PEM and CHT, analogously to KN522, for eTNBC treatment.

Methods: All patients receiving CHT + PEM for eTNBC treatment at participating centers were followed prospectively and monitored for occurrence of irAEs and neoadjuvant treatment outcome as defined by pCR from October 2020 until data cut-off on September 15th 2022. Only patients who underwent surgery for their primary tumor before data cut-off were included.

Results: A total number of 22 patients with available pCR outcomes were included. All patients were female. Median age was 51 years (range 25-72). Mean tumor size at baseline was 29mm (range 10-75). 41% (9/22) of patients exhibited nodal involvement according to baseline radiological findings. Median MIB-1/Ki67 expression at biopsy was 70%. Patients received a median of 8 (range 1-8) neoadjuvant cycles of PEM and exhibited a median duration of CHT of 24 weeks (range 4-24). Neoadjuvant PEM was discontinued in 32% (7/22) of patients. Discontinuation of neoadjuvant treatment before week 18 occurred in 22,7% (5/22) of patients. We report irAE rates of any kind and all grades of 50% (11/22) and of grade 3-4 in 9% of patients (2/22). Steroids were administered in 7/11 patients experiencing irAEs (64%). 8 irAEs

occurred during the neoadjuvant treatment phase, 3 during postneoadjuvant treatment with PEM. No grade 5 toxicity was observed. irAEs observed were hypothyroidism (n=3, all grade 2), arthritis (n=3, all grade 2), myocarditis (n=2, one grade 3/one grade 4), and single cases of hepatitis (grade 2), nephritis (grade 3) and pneumonitis (grade 1). 18% (4/22) of patients underwent mastectomy and 36% (8/22) of patients underwent axillary dissection. Lastly, upon definitive surgery of the primary tumor, we observed pCR in 50% (11/22) of cases. Patients who completed >18 weeks of neoadjuvant therapy exhibited a pCR rate of 59% (10/17), whilst patients who completed ≤18 weeks of neoadjuvant therapy reached pCR in 20% of cases (1/5). Conclusion: We report real-world prospective data about irAE as well as pCR rates during eTNBC treatment with PEM and CHT. irAEs occurred in similar rates as observed in KN522, although numerically higher for irAEs of all grades. The pCR rate within our cohort was numerically lower than reported for KN522, most probably due to a low pCR rate observed for 5 of 22 patients included in this analysis who completed ≤18 weeks of neoadjuvant treatment. Looking at our data, we hypothesize that clinical benefit from combination therapy of PEM and CHT depends on reaching an adequate duration of >18 weeks of neoadjuvant treatment.

Disclosure(s):

Maximilian Marhold, Department of Medicine 1, Division of Oncology: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing)

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Kathrin Strasser-Weippl, n/a: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Travel / Accommodation / Expenses (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Travel / Accommodation / Expenses (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Travel / Accommodation / Expenses (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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12/7/2022

5:00 PM - 6:15 PM

P3-07-01

Mebendazole displays selective anti-breast cancer cytotoxicity via the induction of mitotic catastrophe

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Metastatic breast cancer (mBC) is still an incurable disease and is responsible for the majority of breast cancer-related death, despite tremendous efforts spent on developing better regimens for mBC. Microtubule-targeting chemotherapy agents (MTAs) have been on the front lines of treating mBC. However, many of these drugs become ineffective following treatment, as a consequence of either primary or acquired resistance, which leads to refractory disease. Furthermore, failures of the first-line MTA treatment will negatively affect the effectiveness of the second- and third-line agents in the patients, as the overall response rates of the subsequent treatments are in a range of only ~12% to 35%. Thus, there is an urgent need for alternative MTAs that are significantly different in biological characteristics from those currently used MTAs for mBC therapy. For this purpose, we investigated Mebendazole (methyl 5-benzoyl-2-benzimidazole-carbamate (MEB), which binds different sites on the α/β -tubulin remote from the binding sites of other MTAs, for its potential against mBC cells. MEB has much lower in vivo toxicity than the other MTAs used to treat mBC and it can be orally administrated. We explored MEB for its effectiveness in anti-mBC cells with a panel of human breast normal and mBC cell lines. The data from clonogenic survival studies indicate that MEB delivers < 10-fold greater cytotoxicity toward mBC cells compared to normal mammary epithelial (HME) or benign breast tumor cells. Furthermore, the cytotoxicity in detected in mBC cells was attributed to the induction of mitotic catastrophe, as demonstrated by the increased mitotic cell population (cells with 4N-DNA content and Histon-H3-Ser10 phosphorylation) and concurrent nuclear fragmentation. In contrast, under the same dose range, MEB did not cause mitotic catastrophe in HME cells. In addition, our data also show that MEB is much more efficient in killing p53-deficient mBC cells than p53-proficient mBC cells for the same reason, induction of mitotic catastrophe, which suggest the protective function of p53 against MEB-induced mitotic catastrophe. Collectively, our data support a great potential for MEB as an innovative regimen for improving mBC treatment.

Disclosure(s):

Ying Yan, Ph.D.: No financial relationships to disclose

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P3-07-02

Anti-tumor efficacy of GMF-1A3, an MMAE-based antibody drug conjugate targeting cell surface cleaved Amphiregulin in breast cancer

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The Epidermal Growth Factor Receptor ligand, Amphiregulin, is a key proliferative effector of estrogen receptor signaling in breast cancer and also plays a role in other malignancies. Amphiregulin is a single-pass transmembrane protein proteolytically processed by TACE/ADAM17 to release the soluble EGFR ligand, leaving a residual transmembrane stalk that is subsequently internalized. Here, we describe the development of an antibody drug conjugate, GMF-1A3-MMAE, targeting an AREG neo-epitope revealed following ADAM17-mediated cleavage. The antibody does not interact with uncleaved Amphiregulin, providing a novel means of targeting cells with high rates of Amphiregulin shedding. Using fluorescent dye conjugation, we demonstrated that the antibody is internalized by cancer cells in a manner dependent on the presence of cell surface cleaved Amphiregulin. Antibodies conjugated with monomethyl auristatin E (MMAE) were cytotoxic in vitro and induced rapid regression of established breast tumor xenografts in immunocompromised mice. We further demonstrate that these antibodies recognize the Amphiregulin neo-epitope in formalin fixed paraffin embedded tumor tissue, suggesting their utility as a companion diagnostic for patient selection. A pan-cancer tissue microarray analysis indicates that the target is commonly detected (> 50% of cases) in breast, prostate, liver and lung cancer.

Disclosure(s):

Kristopher Lofgren, Ph.D.: Gundersen Medical Foundation: Receipt of Intellectual Property Rights / Patent Holder (Ongoing); Sema4: Salary (Ongoing)

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P3-07-03

Anti-tumor activity of a liposomal formulation of Eribulin compared with the same dose of Eribulin in patient-derived breast cancer xenografts

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Backgrounds:

A liposomal formulation of Eribulin, E7389-LF may allow increased access to tumor tissues and has been under development for breast cancer. In a phase 1, expansion cohort as a late line treatment, objective response rate was observed to be 35.7% (Her2-negative breast cancer), and 42.9% for hormone receptor-positive (HR+ve) patients (Masuda, *European Journal of Cancer*, 2022). However, survival benefit and its mode of action of E7389-LF remains unclear, although E7389-LF seems more effective than Eribulin in clinic.

Methods:

PDX#1 is a breast cancer patient-derived xenograft (PDX) from a patient with triple negative breast cancer who later received Eribulin for 7 cycles until progression in lung metastases. PDX#2 is also a breast cancer PDX from paclitaxel-resistant HR+ve/ HER2-ve breast cancer, respectively. These two PDXs were provided by the National Cancer Center J-PDX library, Japan, and were bred in NOD/Shi-scid, IL-2R γ null (NOG) mice and observed until the onset of a mammary tumor approximately 180 and 240 mm³ in volume (Day 0). PDX tumors were randomized and monitored with tumor growth measurements. Each group received either saline, 0.34mg/kg, or 0.67 mg/kg (clinically relevant dose of E7389-LF, estimated) of Eribulin or E7389-LF at Day 0 and 7 (Experiment 1). For short-term experiments, 9 PDX#1 or 12 PDX#2 tumors were removed one week after an injection of saline, 0.67 mg/kg of Eribulin, or 0.67 mg/kg of E7389-LF (n=3/group for PDX#1, n=4/group for PDX#2), and tumors were immunohistochemically stained with anti-CD31 antibody, an endothelial cell marker, to investigate microvessel density and RNA sequencing was additionally performed (Experiment 2).

Results:

Table 1 summarizes the results. In Experiment 1, both E7389-LF and Eribulin showed significant antitumor activity compared with saline in a dose-dependent manner with respect to tumor growth inhibition and survival benefit, extension of tumor doubling time (earlier day with relative tumor volume >200%), in PDX#1 and #2. Tumor shrinkage was seen in PDX#1, and E7389-LF at 0.34 mg/kg, or 0.67 mg/kg were more potent than the same doses of Eribulin at Day 21 in both PDXs (p < 0.05). E7389-LF at 0.67 mg/kg also showed relative tumor growth

inhibition compared with the same dose of Eribulin in PDX#2 ($p < 0.05$). As for survival, PDX#1 with E7389-LF at 0.67 mg/kg demonstrated significantly longer survival ($p=0.03$) than Eribulin at 0.67 mg/kg, while PDX#2 with E7389-LF at 0.67 mg/kg did not ($p=0.10$). In Experiment 2, microvessel density increased in PDX#1 after receiving eribulin and E7389-LF compared with untreated ones, with a significant difference for E7389-LF ($p=0.006$), and showed an increasing tendency over Eribulin ($p=0.06$), while microvessel density in PDX#2 did not differ between groups.

Conclusions:

Pre-clinical data demonstrates that E7389-LF is more potent than the same dose of Eribulin in patient-derived breast cancer xenografts. Survival benefit was observed in a PDX with a tumor shrinkage and an increase in microvessel density.

Table 1. Summary of the findings

	PDX#1					PDX#2				
	Experiment 1			Experiment 2		Experiment 1			Experiment 2	
	n	Mean Tumor volume at Day21 (mm ³ , %)	Median survival (days)	n	Microvessel density (count/mm ²)	n	Mean Tumor volume at Day10 (mm ³ , %)	Median survival (days)	n	Microvessel density (count/mm ²)
Saline	5	773 (426)	7	3	114	5	1741 (690)	7	4	75
E7389-LF at 0.34 mg/kg	5	68 (36) ^{##}	49 [#]			5	532 (223) [#]	14 [#]		
Eribulin at 0.34 mg/kg	5	136 (75) [#]	42 [#]			5	227 (110) [#]	10 [#]		
E7389-LF at 0.68 mg/kg	5	27 (14) ^{##}	77 ^{##}	3	195 [#]	5	639 (287) ^{##}	21 [#]	4	75
Eribulin at 0.68 mg/kg	5	55 (30) [#]	83 [#]	3	149	5	421 (190) [#]	14 [#]	4	83

#: $p < 0.05$ vs Saline (at the indicated time point for tumor volume), *: $p < 0.05$ E7389-LF vs Eribulin (at Day 21 for tumor volume)

Disclosure(s):

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P3-07-04

A multicenter, single-arm, open-label Phase I study of AN1004 (Pelareorep) oncolytic virus plus paclitaxel in Chinese patients with Hormone receptor-positive and HER2-negative advanced/metastatic breast cancer (REO 026-1)

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A multicenter, single-arm, open-label Phase I study of AN1004 (Pelareorep) oncolytic virus plus paclitaxel in Chinese patients with Hormone receptor-positive and HER2-negative advanced/metastatic breast cancer (REO 026-1) Background: AN1004, also known as Pelareorep is an intravenously delivered immuno-oncolytic unmodified reovirus being evaluated to treat multiple malignancies. AN1004 was shown to be safe and well-tolerated in both monotherapy and combination therapy in multiple clinical trials in North American and European populations, including two completed and two ongoing breast cancer studies. The completed phase 2 study (NCT01656538) in advanced/metastatic breast cancer demonstrated improved median overall survival (OS) in Canadian patients treated with AN1004 plus paclitaxel (PTX) versus PTX alone, and the greatest benefit in OS was observed in patients with hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) subtype. Since there has been no clinical trial assessing AN1004 in Chinese population, a bridging study (REO 026-1) was initiated to evaluate its safety and tolerability in combination with PTX in Chinese patients with HR+/HER2- advanced/metastatic breast cancer. Methods: Eligible

Chinese patients must be female with good performance status (ECOG PS: 0 or 1), have had histopathological diagnosis with HR+/HER2- advanced/metastatic breast cancer, and were previously treated with at least one endocrine therapy with no more than one line of chemotherapy regimen for recurrent/metastatic disease. Patients are intravenously infused with AN1004 at escalating dose levels of 1.5×10^{10} (Dose Level 1, DL1 group), 3×10^{10} (DL2 group) and 4.5×10^{10} TCID50 (DL3 group) on days 1, 2, 8, 9, 15, and 16 every 28 days plus PTX 80 mg/m² intravenously on days 1, 8, and 15 every 28 days. Three to six patients will be enrolled in the DL1 group, and 6 patients will be enrolled in each of the DL2 and DL3 groups. The primary objective is to assess the safety and tolerability of AN1004 in combination with PTX. A secondary objective is to evaluate the preliminary activity of AN1004 and PTX combination therapy. Results: By the data cutoff date of June 2nd, 2022, a total of 10 female patients were enrolled, with a median age of 58 years (range 36-67). Two (20%) patients had failed more than one prior line of endocrine therapy for advanced/metastatic disease, and 3 (30%) patients were previously treated with a CDK4/6 inhibitor. Three patients were treated with AN1004 and PTX in DL1 group; six patients were treated in DL2 group; one patient was treated in DL3 group. The most common (>50%, and/or liver function related) treatment emergent adverse events (TEAEs) included neutrophil count decreased and white blood cell count decreased (90% each), hypertriglyceridemia (70%), pyrexia, ALT increased and anemia (60% each), and AST increased (40%). Three (30%) patients had Grade 3 or above TEAEs, including neutrophil count decreased (30%), white blood cell count decreased (20%), hypertriglyceridemia, ALT increased and GGT increased (10% each). No serious AE or AE leading to treatment discontinuation was reported to date. One patient was not evaluable for dose-limiting toxicity (DLT) due to early withdrawal, and there were no DLTs observed in the 9 evaluable patients. Among the 10 treated patients, 2 (20%) patients achieved confirmed partial response (PR), 2 (20%) patients achieved unconfirmed PR, and 5 (50%) patients showed stable disease (SD). One patient in DL1 group achieved a confirmed PR and later progressed, and the other 8 patients who had PR or SD continue to receive treatment as of the data cut. Conclusion: To date, intravenous administration of AN1004 plus PTX is safe and well-tolerated in Chinese patients with advanced/metastatic breast cancer, and demonstrates anti-tumor activity.

Disclosure(s):

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P3-07-06

Comedications at Breast Cancer diagnosis impact overall survival: results from the ADRENALINE (Atlas for DRug and brEast caNcer survivAL INtEraction) study (n=235,368)

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Background: More than half of Breast Cancer (BC) patients take chronically used non-cancer treatments (denoted as comedications) at BC diagnosis. Epidemiological evidence has reported that several non-cancer treatments may modify BC risk, BC recurrence, and overall survival (OS). The ADRENALINE project (Atlas for DRug and brEast caNcer survivAL INtEraction) analyses the impact of the use of each commonly prescribed non-cancer treatment at BC diagnosis on OS using the French social security system data on a comprehensive cohort of French BC patients. Methods: We identified all women diagnosed with an incident BC treated with surgery in France from 2011 to 2017 and affiliated to the general health insurance scheme. Women with concomitant cancer or metastases at diagnosis were discarded from the analyses. Comedication intake was defined as the delivery in pharmacy of at least 3 months of full treatment (e.g. 90 pills) the 6 months preceding BC diagnosis. A Cox proportional hazard model was used to estimate the hazard ratio (HR) for each molecule. The model was adjusted on more than 100 confounding variables: social factors, comorbidities and other comedications by Inverse Probability of Treatment Weighting (IPTW). We assumed that the adjustment was sufficient to control for confounding if the standardized mean difference of each confounder after adjustment did not exceed 0.1. Molecules which did not pass the adjustment quality test were discarded. Results: Overall, 235,368 patients were included in the study. Among 219 selected drugs, 91 passed the adjustment quality test. The full set of results is available on a web application (<https://adrenaline.curie.fr>). Several drugs or drug classes were associated with an improved survival: statins (e.g. rosuvastatin, HR=0.65, p< 0.001); proton-pump inhibitors (HR=0.93; p=0.002); or beta-blocking agents (atenolol, HR=0.78, p=0.003). Conversely, anti-anemic preparations (folic acid and ferrous sulfate) had a significant deleterious effect (HR = 1.63; p< 0.001). Drugs from the same therapeutic class, could have different effects: within benzodiazepines, bromazepam was protective (HR = 0.91; p = 0.038) while oxazepam was deleterious (HR = 1.37; p < 0.001). Conclusion: ADRENALINE reports the impact on BC survival of 219 widely prescribed drugs. It can be used to identify molecules with a potential protective or deleterious effect relative to BC. Some of them are currently under mechanistical investigation within a drug screening program. This atlas highlights candidates to drug-

repurposing trials or pharmacovigilance warnings, and will be extended to cancers of other localizations in a near future.

Disclosure(s):

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P3-07-07

The use of ribociclib/letrozole combination as an alternative for neoadjuvant chemotherapy in selected patients with early luminal breast cancer

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Introduction In hormone receptor-positive, HER2-negative early-stage breast cancer (BC), cyclin-dependent kinases 4 and 6 inhibition (CDK4/6i) in combination with endocrine therapy (ET) could represent an alternative to neoadjuvant chemotherapy (NAC). Methods NEOLBC is a randomized phase II trial that tailored neoadjuvant therapy in postmenopausal patients with

early, luminal (ER >50%, PR any), HER2-negative, stage II/III BC based on the percentage of Ki67 positive cancer cells after a window of opportunity of two weeks letrozole. Patients with a Ki67 \geq 1% after 2 weeks were randomized between ribociclib plus letrozole (RL) and chemotherapy (CT; AC-T regimen). The primary objective was to determine if RL gives a doubling in complete cell cycle arrest (CCCA; Ki67 < 1% on IHC) as compared to CT in the surgical specimen (70% vs. 35% of patients, respectively). Secondary endpoints included pathological response, toxicity and ER pathway activity (measured by the OncoSIGNaI qPCR test). Results Out of 161 registered patients, 70 patients were randomized and 66 patients started treatment; 34 RL and 32 CT. Patient characteristics were equally distributed between the two groups, except for the PR status (RL 23.5% negative vs. 50.0% negative in the CT group). In the intention to treat analysis, the CCCA in the surgical specimen was similar for both groups: 35.3% in the RL vs. 31.3% in the CT group ($p = 0.73$). The pathological complete response (pCR) in the breast was not significantly different between the two groups (11.8% vs. 3.1%, $p = 0.36$) nor was the pCR rate in breast plus lymph nodes (8.8% vs. 3.1%, $p = 0.61$) for the RL vs. CT group, respectively. An explorative analysis on the difference in Ki67% (decline, no change, increase) from baseline to surgery showed a decline in 73.5% vs. 50.0%, no change in 17.6% vs. 31.3% and an increase in 8.8% vs. 18.8% of patients ($p = 0.06$) for the RL vs. CT group, respectively. In the RL group eight patients (23.5%) discontinued ribociclib early due to toxicity (two SAE's were observed) vs. 10 patients (31.3%) discontinuing treatment in the CT group (one SAE was observed). Secondary endpoints, including the ER pathway activity analysis, will be presented in-depth during the meeting. Conclusion Although the primary endpoint was not met, the NEOLBC trial showed a similar CCCA and pathological response at surgery for RL vs. CT. Therefore, RL as an alternative for NAC merits further investigation in follow-up studies. ClinicalTrials.gov: NCT03283384

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Exposure-adjusted incidence rates (EAIRs) of adverse events (AEs) from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) vs treatment of physician's choice (TPC) in HR+/HER2- metastatic breast cancer (MBC)

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Background: SG is a Trop-2-directed antibody-drug conjugate approved by the FDA for patients (pts) with metastatic triple-negative breast cancer who received ≥ 2 prior chemotherapies (≥ 1 for MBC). In the phase 3 TROPiCS-02 study, SG demonstrated a 34% reduction in risk of progression or death vs TPC in heavily pretreated, endocrine-resistant HR+/HER2- MBC (Rugo H, et al. ASCO 2022. LBA1001). The safety profile was manageable, with neutropenia and diarrhea as the key AEs. Absolute incidence rate is the most used metric to summarize AEs in routine clinical safety analyses. However, when the treatment duration differs

significantly between treatment arms, these rates may need adjustment to account for longer treatment exposure, which may incur a higher incidence of AEs. Given that the median treatment duration was longer for SG in TROPiCS-02, EAIRs were assessed in post hoc safety analyses.

Methods: Pts with HR+/HER2– unresectable locally advanced or MBC and 2-4 prior chemotherapy regimens for MBC were randomized 1:1 to receive SG or TPC (capecitabine, eribulin, vinorelbine, or gemcitabine) until unacceptable toxicity or disease progression. The primary endpoint was progression-free survival per RECIST 1.1 by central review. Safety was a secondary endpoint. Time-at-risk EAIR considers pts' exposure of a specific AE in quantifying the risk of AE, defined as the number of pts who experienced at least 1 specific AE, divided by the total exposure time (pt-year of exposure [PYE]) in each arm. For pts who experienced specific AEs, exposure time was calculated from first dose date up to the first AE onset, and for pts who did not, from first dose up to data cutoff (if still on study treatment) or up to last dose (if discontinued study treatment). The 95% CI of the EAIR difference is a standard method to assess the statistical significance of AE incidence rate differences between arms.

Results: Of 543 pts enrolled (median age, 56 y; visceral metastases, 95%; prior CDK4/6 inhibitor for MBC, 99%; median lines of chemotherapy for MBC, 3), 517 pts (SG, n=268; TPC, n=249) received ≥ 1 dose of study treatment. At data cutoff (Jan 3, 2022), 18 pts (7%) vs 4 pts (2%) remained on treatment in the SG vs TPC arms; median treatment duration was 4.1 months and 2.3 months, respectively. The absolute incidence, EAIRs (incidence per 1 PYE), and EAIR differences for the overall safety summary and most common grade ≥ 3 TEAEs are provided (Table). Overall, SG had higher absolute incidence rates vs TPC for grade ≥ 3 treatment-emergent AEs (TEAEs), serious AEs, and TEAEs leading to death, but the EAIRs were similar between arms, suggesting an association with duration of treatment exposure. When adjusted for exposure, the incidence of grade ≥ 3 diarrhea remained higher for SG vs TPC; however, the incidence of grade ≥ 3 neutropenia was similar between arms.

Conclusions: The safety profile of SG was manageable in pts with heavily pretreated HR+/HER2– endocrine-resistant, unresectable locally advanced or MBC. Though there was a higher absolute incidence of TEAEs leading to death and grade ≥ 3 neutropenia with SG vs TPC, the EAIRs were similar. Taken together with the efficacy benefit with SG, this supports a favorable risk/benefit profile for SG compared with standard chemotherapy in this pt population with limited therapeutic options.

Table. Overall Safety Summary and Summary of Common (Absolute Incidence $\geq 5\%$) Grade ≥ 3 TEAEs With Absolute Incidence, Exposure-Adjusted Incidence Rates (EAIRs),^a and EAIR Differences^{b, c}

	SG (n=268)	TPC (n=249)
Overall Safety Summary		
No statistically significant EAIR difference^b		
Grade ≥ 3 TEAEs		
n (%)	198 (74)	149 (60)
Patient years of exposure	49.2	38.5
EAIR (95% CI)	4.02 (3.48-4.62)	3.87 (3.28-4.55)
EAIR difference vs TPC (95% CI)	0.15 (-0.72-0.99)	
Serious AEs		
n (%)	74 (28)	47 (19)
Patient years of exposure	103.6	63.0
EAIR (95% CI)	0.71 (0.56-0.90)	0.75 (0.55-0.99)
EAIR difference vs TPC (95% CI)	-0.03 (-0.32-0.24)	
TEAEs leading to treatment discontinuation		
n (%)	17 (6)	11 (4)
Patient years of exposure	123.8	72.0
EAIR (95% CI)	0.14 (0.08-0.22)	0.15 (0.08-0.27)
EAIR difference vs TPC (95% CI)	-0.02 (-0.15-0.10)	
TEAEs leading to death		
n (%)	6 (2) ^d	0
Patient years of exposure	123.9	72.0
EAIR (95% CI)	0.05 (0.02-0.11)	0 (0-0.05)
EAIR difference vs TPC (95% CI)	0.05 (-0.01-0.11)	
Most Common Grade ≥ 3 TEAEs		
Statistically significant EAIR difference^c		
Grade ≥ 3 Diarrhea		
n (%)	27 (10)	3 (1)
Patient years of exposure	116.2	71.8
EAIR (95% CI)	0.23 (0.15-0.34)	0.04 (0.01-0.12)
EAIR difference vs TPC (95% CI)	0.19 (0.08-0.30)	
No statistically significant EAIR difference^b		
Grade ≥ 3 Neutropenia		
n (%)	138 (51.5)	96 (38.6)
Patient years of exposure	67.3	47.5
EAIR (95% CI)	2.05 (1.72-2.42)	2.02 (1.64-2.47)
EAIR difference vs TPC (95% CI)	0.03 (-0.53-0.56)	
Grade ≥ 3 Leukopenia		
n (%)	23 (8.6)	15 (6.0)
Patient years of exposure	118.6	68.3
EAIR (95% CI)	0.19 (0.12-0.29)	0.22 (0.12-0.36)
EAIR difference vs TPC (95% CI)	-0.03 (-0.18-0.11)	
Grade ≥ 3 Anemia		
n (%)	20 (7.5)	9 (3.6)
Patient years of exposure	118.5	71.3
EAIR (95% CI)	0.17 (0.10-0.26)	0.13 (0.06-0.24)
EAIR difference vs TPC (95% CI)	0.04 (-0.09-0.16)	
Grade ≥ 3 Febrile neutropenia		
n (%)	16 (6.0)	11 (4.4)
Patient years of exposure	119.7	69.8
EAIR (95% CI)	0.13 (0.08-0.22)	0.16 (0.08-0.28)
EAIR difference vs TPC (95% CI)	-0.02 (-0.16-0.09)	
Grade ≥ 3 Fatigue		
n (%)	16 (6.0)	8 (3.2)
Patient years of exposure	115.3	71.1
EAIR (95% CI)	0.14 (0.08-0.23)	0.11 (0.05-0.22)
EAIR difference vs TPC (95% CI)	0.03 (-0.10-0.13)	

^aReported as events per 1 patient year. ^bSG and TPC EAIRs were similar if the 95% CI covers 0, nominally not statistically significant based on informal testing. ^cPositive upper and lower bound for EAIR difference 95% CI favors the TPC arm. Nominally statistically significant based on informal testing. ^dOne patient experienced a treatment-related AE leading to death (septic shock due to neutropenic colitis). The AEs leading to death in the remaining 5 patients included (n=1 each) arrhythmia, COVID-19 pneumonia, pulmonary embolism, pneumonia, and nervous system disorder; these events were not considered to be treatment-related.

AE, adverse event; EAIR, exposure-adjusted incidence rate; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event; TPC, treatment of physician's choice.

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Pan-NOS Inhibitor L-NMMA in combination with Docetaxel Enhances Antitumor Effect in Obesity-associated Triple Negative Breast Cancer

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Background: Obesity is associated with increased risk of triple negative breast cancer (TNBC). Obese patients with TNBC have worse outcomes compared to patients with normal weight. Both obesity and TNBC are associated with chronic inflammation including elevated nitric oxide (NO). In a recently completed Phase I/II clinical trial using a pan-NOS inhibitor L-NMMA in combination with chemotherapy docetaxel in chemorefractory and metastatic TNBC, a higher response rate was observed in obese patients. Furthermore, tumor microenvironment analysis from responders revealed a neutrophil phenotype shift from protumor N2 to antitumor N1. We thus hypothesize that combining pan-NOS inhibitor L-NMMA with docetaxel can modulate neutrophil mediated pathways, and further enhance antitumor effect in obese mice with TNBC. Methods: Three-week old syngeneic female C57/black mice were randomized to high fat diet (HFD, 18% protein, 21% carbohydrates, and 61% fat, n=50) and normal diet (ND, 20% protein, 70% carbohydrates, and 10% fat, n=50) for 10 weeks. Mouse weights were measured weekly. After 10 weeks on their respective diets, glucose tolerance test, serum cytokine and leptin analysis were performed. At week 13, TNBC E0771 tumor cells (1×10^5) were injected into the right mammary fat pads. Tumor progression was monitored twice weekly and tumor volume $[0.5 \times (\text{long dimension}) \times (\text{short dimension})^2]$ was calculated. Once the tumor reached 80-100 mm³, mice in both HFD and ND groups were randomized to vehicle [saline, intraperitoneal (IP), n=10], docetaxel (20 mg/kg, IP, n=10), L-NMMA (400 mg/kg on day 1, 200 mg/kg on days 2-5, n=10), docetaxel and L-NMMA combination (same doses and schedule as in single agent groups, n=10). Tumor volume was measured throughout the experiment and tumor growth was calculated (tumor volume on day X/tumor volume at baseline). RNA sequencing of tumors from vehicle and combination groups in HFD and ND (n=6 in each arm) was performed

(Azenta/Genewiz, NJ) and BioJupies was utilized for pathway analysis. GraphPad Software (La Jolla, CA, USA) was used to perform two-tailed Student's t test and ANOVA statistical analysis. A p-value < 0.05 was considered statistically significant. Results: Compared to ND group, HFD group mice had significantly higher weight gain (64.8% vs 83.2%, $p < 0.0001$); they also demonstrated significant glucose intolerance, and higher serum leptin level consistent with metabolic changes observed in diet-induced obesity. After tumor injection, tumor growth rate was much higher in HFD mice compared to that in ND mice. At end-of-treatment, compared with vehicle, a significantly slower tumor growth in HFD mice ($p = .015$), and a trend of slower tumor growth was observed in ND mice ($p = .92$) in docetaxel and L-NMMA combination treatment. The reduction of tumor growth was significantly higher in HFD mice than that in ND mice (median of differences -2.0, $p = .031$). Differential gene expressions from RNA sequencing showed that HFD mice displayed higher expression of genes related to neutrophil degranulation and neutrophil mediated immunity compared to ND mice at baseline; while treatment with L-NMMA and docetaxel combination downregulated these genes. Conclusion: HFD mice had significantly faster tumor growth and higher expression of genes related to neutrophil mediated pathways, while treatment with pan-NOS inhibitor L-NMMA and docetaxel combination downregulated these genes. The combination treatment resulted in a more significant anti-tumor effect in HFD mice, likely through remodeling neutrophils. Future spatial analysis including CODEX and immunophenotyping are planned to further explore the role neutrophils play in the pathogenesis of obesity associated TNBC and its response to combination treatment.

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CCTG IND.236: A Phase 1b trial of combined CFI-402257 and weekly paclitaxel in patients with HER2-negative (HER2-) advanced breast cancer (aBC)

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CCTG IND.236: A Phase 1b trial of combined CFI-402257 and weekly paclitaxel in patients with HER2-negative (HER2-) advanced breast cancer (aBC) Philippe L. Bedard, Mihaela Mates, John Hilton, Nathalie Levasseur, Arif Awan, Amirrtha Srikanthan, David Cescon, Karen Gelmon, Andrew Robinson, Nancy Drummond-Ivars, Irene Li, Laleh Rastgou, Jackie Edwards, Linda Hagerman, Siwei Zhang, Mark Bray, Lesley Seymour, Moira Rushton-Marovac, Pierre-Olivier Gaudreau Background: CFI-402257 is a selective oral inhibitor of TTK protein kinase, a critical regulator of the mitotic spindle assembly checkpoint overexpressed in breast cancer (BC). CFI-402257 monotherapy has anti-proliferative and cytotoxic activity and enhances antitumor activity of paclitaxel in BC xenograft models. Material and methods: Primary objectives were to establish safety and Recommended Phase 2 dose (RP2D) of CFI-402257 combined with weekly paclitaxel (Phase 1b) and Overall Response Rate (ORR) as per RECIST 1.1 (Phase 2). Patients with HER2- aBC with adequate organ function, PS 0-1, previously treated with >1 non-taxane chemotherapy, were eligible. A 3+3 design was used for Phase 1b, with dose limiting toxicities (DLTs) assessed during cycle 1 (28 days). Starting dose CFI-402257 was 84mg (DL1 = 84mg, DL2 = 112mg, DL3 = 168mg, DL4 = 210mg and DL5 = 252mg) on a 2-day on, 5-day off schedule with paclitaxel 80mg/m² day 1, 8, 15. Safety assessments were performed weekly (CTCAE v5.0) and response every 2 cycles. A Simon 2-stage design was used for Phase 2 (stage 2 required ≥4 responses in 17 evaluable patients from stage 1). Results: 37 patients received a total of 260 cycles including all 5 dose levels. Median age was 59; 92% ER+/HER2-; 49% PS1; 22% ≤3 prior chemotherapy lines; 41% ≤4 sites of metastatic disease, and 81% had received prior CDK4/6 inhibitors. Grade ≤3 hematological adverse events (AEs, all dose levels) were neutropenia (70%), lymphopenia (41%) and anemia (14%). Six DLTs occurred: 5 dose-related grade 4 neutropenia and 1 febrile neutropenia. Three DLTs occurred at DL3, two at DL4, and one at DL5. Three serious AEs (two at DL3, and one at DL4) at least possibly related to treatment were seen: 2 febrile neutropenia and 1 skin infection (all grade 3). Frequent AEs (>5%; all dose levels) considered at least possibly related to treatment were: diarrhea (38%), nausea (30%), fatigue (27%), vomiting (16%), anorexia (14%), maculo-papular rash (14%), oral mucositis (11%), alopecia (11%) and pruritus (8%). DL3 (168mg) was selected as RP2D. ORR was 3/36=8% and 1/17=5.9% in all vs Phase 2 evaluable patients, respectively. Clinical Benefit Rate (CBR; defined as complete response, partial response or stable disease >16 weeks in duration) was 18/33=54.6% and 10/17=58.8% in all vs Phase 2 evaluable patients, respectively. During Phase 2, the 17 evaluable patients from stage 1 did not meet pre-specified threshold for anti-tumor activity to proceed to stage 2. Conclusions: CFI-402257 and paclitaxel was well tolerated, with neutropenia as the main toxicity. DL3 (168mg) was selected as RP2D. Phase 2 ORR and CBR was 5.9% and 58.8%, respectively; during Phase 2, the 17 evaluable patients from stage 1 did not meet the pre-specified threshold for anti-tumor activity to proceed to stage 2 and the trial was closed to accrual on April 7, 2022. Final analysis and correlative analyses are ongoing. Acknowledgements: Coordinated by the CCTG. Funding supported by SU2C Canada - Canadian Cancer Society Breast Cancer Dream Team Research Funding (SU2C-AACR-DT-18-15) and OICR. CFI-402257 provided by Treadwell Therapeutics.

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5:00 PM - 6:15 PM

P3-07-12

Allogeneic, Antigen-Presenting, GM-CSF-secreting, SV-BR-1-GM Whole Cell Therapeutic Vaccine in Advanced Metastatic Breast Cancer

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Background: SV-BR-1-GM is an irradiated allogeneic cell line derived from a hormone receptor-negative (HR-) HER2-positive (HER2+) breast cancer (BC), now engineered to express HLA class I and II antigens, secrete GM-CSF and function as an antigen-presenting cell. Here we report post-hoc exploratory data for metastatic BC (MBC) patients treated with the SV-BR-1-GM regimen (SV) alone (NCT03066947) and in combination (CO) with immune checkpoint inhibitors (ICIs) (NCT03328026).

Methods: SV includes cyclophosphamide 300 mg/m² i.v. 48-72 hours prior to SV-BR-1-GM (20 x 10⁶ cells) intradermally followed by interferon-alpha-2b at the SV-BR-1-GM inoculation sites on days 2 and 4. SV was given every 2 weeks for 3 cycles and then monthly in NCT03066947, and every 3 weeks in combination with PD-1 inhibitors in NCT03328026. Treatment was continued until disease progression or unacceptable toxicities.

Results: A total of 34 refractory MBC patients (pts) were treated, including 24 with SV, and 14 with CO, including 4 who crossed over from SV to CO plus one who restarted the SV after a protocol specified administrative interruption in treatment. Median prior regimens were 5; 55% of pts had hormone receptor-positive (HR+) BC, 42% had HER2+ BC, and 16% were triple-negative BC (TNBC). Objective response rates (ORR) were 4% for monotherapy and 7% for combination. Clinical benefit rate (CBR) was 21% for monotherapy and 29% for combination. Responses and clinical benefits were seen across most BC subtypes (see table). Notably, CBR among 10 pts with HR+ BC (any HER2) who received the combination was 50% (5/10). The duration of response (DOR) among 4 patients treated with monotherapy was 49-223 days and DOR among 6 patients treated with combination was 72-292 days. Median PFS was 2.8 months for monotherapy and 4.2 months for combination. Median OS was 7.0 months for monotherapy, and 12.0 months for combination. Of 28 pts with available prior treatment data, 12 (43%) had PFS on study treatment exceeded PFS on prior treatment, of these 8/12 had >1 HLA match and 5/8 had ≥ 2 loci HLA-matched with SV-BR-1-GM. PFS ratio improvement was independent of the prior number of lines of therapy or BC subtypes. The SV-BR-1GM regimen was well tolerated with the most common treatment-related adverse events (AEs) being injection site reaction in 67%. There was no dose-limiting toxicity, special interest AEs such as cytokine storm, and no grade 5 observed. There were 2 non-treatment-related grade 4 AEs: worsening pleural effusion and altered mental status. Significant improvement in PFS was observed in patients with matched HLA and in association with the delayed-type hypersensitivity skin test, peripheral blood circulating tumor cells, and cancer-associated macrophages.

Conclusions: SV-BR-1-GM demonstrated promising activity in patients with MBC. Treatment was well tolerated with no concerning AEs. The PFS ratio compares favorably with prior penultimate standards of care, more notably in patients with matched HLA. Clinical benefits were observed across multiple subtypes of BC, particularly in patients with HR+ disease receiving combination therapy. Phase II clinical trial is currently ongoing to evaluate the efficacy of SV-BR-1-GM in combination with ICIs.

Clinical benefit and PFS on SV-BR-1-GM

	SV (n=24)						CO (n=10)					
	HER2- HR+	HER2- HR+ matched	HER2+	HER2+ matched	TNBC	unknown	HER2- HR+	HER2- HR+ matched	HER2+	HER2+ matched	TNBC	unknown
# of subject	9	8	8	5	5	2	2	1	6	5	1	1
ORR (CR+PR)	11%	13%	0	0	0	0	0	0	17%	20%	0	0
CR[SD+PR+CR]	11%	13%	25%	20%	0	50%	50%	100%	50%	60%	0	0
FFS(m) median+/-SD	2.7 +/- 2.3	2.6 +/- 2.4	3.1 +/- 2.0	1.6 +/- 1.6	2.4 +/- 0.8	6.2 +/- 1.1	3.4 +/- 0.9	4.2 +/- 1.1	2.4 +/- 3.2	2.4 +/- 3.4	3.4	1.2

SV-BR-1-GM Whole Cell Therapeutic Vaccine in Heavily Pre-Treated Metastatic Breast Cancer Results Stratified by HER2 and HLA Matching

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P3-07-13

The next generation oral selective estrogen receptor degrader (SERD) camizestrant (AZD9833) is active against wild type and mutant estrogen receptor α

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Endocrine therapy forms the backbone treatment for patients with estrogen receptor (ER) positive tumors in both the adjuvant and metastatic setting. Aromatase inhibitors (AI) are the most common endocrine treatment option. Mutation of ESR1, the gene encoding ER α , is a common mechanism of resistance to AIs which leads to ligand independent activity of ER α . Camizestrant (AZD9833) is a next generation SERD and pure ER antagonist that is in Phase 3 trials (SERENA-4: NCT04711252; SERENA-6: NCT04964934). Here we report the preclinical and clinical activity of camizestrant in patients with ESR1 wild-type (ESR1wt) and mutant (ESR1m) tumors. The binding affinities of camizestrant, fulvestrant, and estradiol to wt ER α and ER α variants with mutations in the ligand binding domain were assessed. All three compounds exhibited reduced binding to mutant forms of ER α compared with wt ER α ; the Y537S mutation had the greatest impact on binding. This was reflected in requirement for greater concentrations of camizestrant and fulvestrant to degrade and antagonize mutated ER α and to impact cellular proliferation in MCF-7 cells that expressed Y537S ESR1m compared to ESR1wt MCF-7 cells. Furthermore, while a 3 mg/kg dose of camizestrant achieved a maximal anti-tumor effect in a ESR1wt patient derived xenograft model, a 10 mg/kg was required for maximal effect in a D538G ESR1m model. Considering this difference between ESR1m and ESR1wt, pharmacokinetic/pharmacodynamic modelling of preclinical data predicted that a camizestrant dose of 75 mg would be maximally efficacious in patients with ESR1m tumors. Indeed, analysis of ESR1m circulating tumor DNA levels in patients from the SERENA-1 (NCT03616587) Phase

1 trial showed a clear effect of 14 days treatment with 75 mg camizestrant resulting in a >2-fold reduction in ESR1m variant allele frequency in 12/13 (92%) cases with complete clearance of ESR1m ctDNA in 7/13 (54%) cases. Interestingly, the clinical activity of camizestrant was higher in heavily pretreated patients with metastatic breast cancer with ESR1m tumors compared to those with no detectable mutation (ESR1m not detected). At a camizestrant dose of 75 mg, median progression-free survival was 8.3 months (maturity 12/15) in patients with ESR1m tumors compared to 5.6 months (8/9) in those with ESR1m not detected (data cut-off 6 October 2021). Camizestrant-induced ER α degradation was seen in both groups (mean reduction in H-score 42% in ESR1m tumors (n= 12 evaluable pairs) and 46% in tumors with ESR1m not detected (n=7)). Whole transcriptome analysis revealed a trend towards higher ER α activity at baseline in ESR1m tumors compared to ESR1m not detected; ER α activity reduced on treatment in both groups. Consistent with the clinical activity data, camizestrant induced more profound reductions in cell proliferation in ESR1m tumors compared to ESR1m not detected tumors (as seen by greater reductions in Ki67-positive tumor cells). These data demonstrate the activity of camizestrant in patients with ESR1m tumors. Clinical activity along with degradation and antagonism of the ER α is also seen in patients with tumors in which ESR1 mutations are not detected. In this heavily pre-treated Phase 1 patient population from SERENA-1, ESR1m may be a predictive biomarker to enrich for patients with maintained endocrine sensitivity. The SERENA-6 trial is investigating the efficacy and safety of camizestrant plus a CDK4/6 inhibitor in patients with metastatic breast cancer and detectable ESR1m. We acknowledge Helen Heffron, PhD, from InterComm International who provided medical writing support funded by AstraZeneca.

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A phase II study of CFI-400945 in patients with advanced/metastatic cancer: Canadian Cancer Trials Group (CCTG) IND.237

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A phase II study of CFI-400945 in patients with advanced/metastatic cancer: Canadian Cancer Trials Group (CCTG) IND.237

Authors:

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Background:

CFI-400945 is a selective oral inhibitor of Polo-like Kinase 4 (PLK4), a controller of centriole duplication and mitotic progression identified by functional screening of genomically unstable breast cancer (BC). IND.237 (NCT01954316) is an open label, multicentre, phase 2 study in HER2 negative metastatic breast cancer (MBC) with 3 cohorts, 1 enriched for PTEN loss of function. Enrollment started in 2018 at 64mg based on a previously established recommended phase 2 dose (RP2D). The initial patients had higher than expected grade 3/4 neutropenia which led to a voluntary hold and dose de-escalation; the new RP2D was declared at 32mg as previously reported Here we report the results of the phase 2 study of CFI-400945 in advanced BC patients.

Materials and Methods:

49 patients were enrolled across 3 cohorts: 1: triple negative; 2: ER+/HER2- PTEN low (by IHC); 3: ER+/HER2-, PTEN intact. The primary outcome is objective response rate (ORR); secondary outcomes included disease control rate (DCR) >16w, and safety. A Simon 2-stage design was used (9 – 25 pts planned for each cohort). CFI-400945 would be considered active if ≥3 responses were observed in any given cohort. Eligibility included ECOG 0-1, adequate organ function and receipt of at ≥1 prior line of cytotoxic chemotherapy in any setting including anthracycline taxane (unless contraindicated). Treatment was 32mg 7d on 7d off in cycle 1 (cycle length=28d), then continuously starting cycle 2. Safety assessments were performed each cycle and response (RECIST 1.1) every 2 cycles.

Results:

60 patients have been screened, 49 enrolled: 10 were in initial dose ranging and were excluded from phase 2 response assessment. 10 patients were enrolled in cohort 1, 4 in cohort 2, and 25 in cohort 3. Table 1 presents patient characteristics and response results. 1 patient in cohort 3 has not had disease re-assessed at time of abstract submission. The most common adverse events have been cytopenias, nausea, fatigue, headache, constipation and vomiting. Less than 5% of patients experienced a non-hematologic AE > grade 3; 33% experienced ≥ grade 3

neutropenia.

Patient Characteristics Cohort 1 Cohort 2 Cohort 3 Overall
 (n=10) (n=4) (n=25) (n=39)
 Age median (range) 58 (47-77) 63 (40-71) 57 (41-73) 58 (40-77)
 Performance Status (0/1) 60%/40% 25%/75% 56%/44% 54%/46%
 Liver metastases 3 (30%) 4 (100%) 21 (84%) 28 (72%)
 ≥ 3 prior chemotherapy regimens 4 (40%) 2 (50%) 14 (56%) 20 (51%)
 Best overall response Cohort 1 Cohort 2 Cohort 3
 (n=10) (n=4) (n=25)
 Partial Response 0 0 2
 Stable Disease 3 2 5
 SD > 16wks 1 0 1
 Progressive Disease 6 0 16
 Inevaluable 1 1 2
 ORR (evaluable pts) 0% 0% 8.7%
 DCR (evaluable pts) 11.1% 0% 13.0%

Table 1: Patient characteristics and response rates in each cohort treated with CFI-400945

Conclusions:

CFI-400945 32mg is well tolerated in this MBC population with moderate incidence of uncomplicated neutropenia. The TNBC cohort so this arm has been closed to further accrual for lack of responses. The PTEN loss group has been slow to accrue and remains open. Responses in the ER+/HER2- arm are encouraging – results from patients remaining on study are awaited and correlative studies to identify features associated with responses are underway.

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Table 1: Patient characteristics and response rates in each cohort treated with CFI-400945

Patient Characteristics	Cohort 1 (n=10)	Cohort 2 (n=4)	Cohort 3 (n=25)	Overall (n=39)
Age median (range)	58 (47-77)	63 (40-71)	57 (41-73)	58 (40-77)
Performance Status (0/1)	60%/40%	25%/75%	56%/44%	54%/46%
Liver metastases	3 (30%)	4 (100%)	21 (84%)	28 (72%)
≥ 3 prior chemotherapy regimens	4 (40%)	2 (50%)	14 (56%)	20 (51%)
Best overall response	Cohort 1 (n=10)	Cohort 2 (n=4)	Cohort 3 (n=25)	
Partial Response	0	0	2	
Stable Disease	3	2	5	
SD > 16wks	1	0	1	
Progressive Disease	6	0	16	
Inevaluable	1	1	2	
ORR (evaluable pts)	0%	0%	8.7%	
DCR (evaluable pts)	11.1%	0%	13.0%	

Table 1: Patient characteristics and response rates in each cohort treated with CFI-400945

Disclosure(s):

David W. Cescon, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Research funding to institution (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Ongoing); Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), Research funding to institution (Ongoing); GlaxoSmithKline: Consulting Fees (e.g., advisory boards) (Ongoing), Research funding to institution (Ongoing); Inivata: Research funding to institution (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing), Research funding to institution (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Research funding to institution (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Research funding to institution (Ongoing)

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12/7/2022

5:00 PM - 6:15 PM

P3-07-15

Preliminary data from a Phase 1b dose escalation study of OP-1250, an oral CERAN, in combination with palbociclib in patients with advanced and/or metastatic estrogen receptor (ER)-positive, HER2-negative breast cancer

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Background: OP-1250 is a small molecule oral complete estrogen receptor antagonist (CERAN) that binds the ligand binding domain of the ER and completely blocks ER-driven transcriptional activity. CDK4/6 inhibitors in combination with endocrine therapy have improved progression free survival and overall survival for patients (pts) with metastatic breast cancer (MBC) in the first- and second-line settings. However, most patients will progress and newer combinations such as with OP-1250 may provide improved clinical outcome. OP-1250 potentially inactivates both wild-type ER and mutant forms of ER. The latter confers ligand independent activity and is a mechanism of resistance to standard of care endocrine therapies. In preclinical studies, OP-1250 in combination with palbociclib demonstrated synergistic activity in models of wild-type ER and those containing ESR1 activating mutations, and in models of brain metastasis. A Phase 1/2 monotherapy study of OP-1250 is ongoing in MBC subjects who have received 1 or more prior endocrine therapies (NCT04505826). Monotherapy is well tolerated and the recommended phase 2 dose is 120 mg QD. The aim of this combination trial is to define the maximum tolerated dose (MTD), safety, tolerability, and pharmacokinetics (PK) of

OP-1250 in combination with palbociclib. Methods: Eligibility criteria include pts with MBC or locally advanced breast cancer who have received no more than 1 prior line of endocrine therapy (prior CDK4/6 inhibitors and one line of chemotherapy are permitted) and measurable or non-measurable disease. Using a 3+3 design, cohorts are sequentially enrolled, and pts receive escalating doses of OP-1250 orally QD continuously in combination with 125 mg of palbociclib orally for 21 of 28 days. Pts are evaluable for dose limiting toxicities (DLTs) if >75% of both treatments were administered within the first 28-day treatment cycle. Blood is collected for PK on cycle 1 days 1, 2 and cycle 2 days 15, 16 for OP-1250 and cycle 1 day 15 for palbociclib. PK profiles, exposure parameters, and drug-drug interactions (DDIs) are assessed. Pts are monitored for adverse events (AE) and tumor assessments (RECIST 1.1) are conducted every two cycles. Results: As of July 7, 2022, 9 pts were evaluable for DLTs after 28 days of treatment in dose levels 30 mg, 60 mg, and 90 mg of OP-1250 in combination with palbociclib. No DLTs occurred at any of the dose levels. As of May 13, 2022, of the 7 pt safety data set, the most common Grade 1/2 treatment emergent adverse events (TEAE), which occurred in 2 patients, were nausea, gastroesophageal reflux, vomiting, and fatigue. Grade 3 neutropenia occurred in 4 pts and all were attributed to palbociclib by the investigator. No Grade 4 events were observed. OP-1250 was highly bioavailable and showed dose proportional exposure in combination with palbociclib. The single and multiple dose exposure of OP-1250 was consistent with that observed in the monotherapy study, indicating an absence of effect of palbociclib on OP-1250 PK. 90 mg steady-state evaluation is ongoing. Palbociclib concentrations at steady state did not demonstrate a meaningful difference from published exposure parameters for the three dose levels evaluated, indicating an absence of DDI. Conclusions: In the first three cohorts of OP-1250 and palbociclib, the combination was well tolerated and no DLTs occurred. There were no clinically significant DDIs observed between OP-1250 and palbociclib at the doses evaluated and exposure of each drug was consistent with observed monotherapy exposure levels. Dose escalation of OP-1250 continues to 120 mg, to be followed by dose expansion. Updated data will be presented. (NCT05266105)

Disclosure(s):

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12/7/2022

5:00 PM - 6:15 PM

P3-07-16

Pre-clinical study of amcenestrant and HER2-targeted therapies in HER2+/ER+ breast cancer cell line models

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12/7/2022

5:00 PM - 6:15 PM

P3-07-17

Nanosecond Electric Pulses Modify Breast Tumor Microenvironment to Promote Antitumor Immunity

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Cancer immunotherapy has had a significant impact on the management of many types of solid tumors. While some patients respond favorably to it, a significant number of patients do not respond or initially respond but develop resistance later, highlighting an unmet need to improve the effectiveness of this treatment. Cancers with intrinsic resistance include breast cancer, not only respond poorly to single agent immunotherapy, but also often show no durable response. Tumor microenvironment (TME) plays a critical role in both pre-existing and acquired immune resistance which is responsible for the low immunogenicity of cancers. We previously reported that an electrical engineering technology generating nanosecond length electric pulses (nsEP) can greatly enhance the immunogenicity of poorly immunogenic cancers including 4T1 breast and Pan02 pancreatic in animal models. To understand how nsEPs overcome predominant immunosuppression in the TME to induce a strong immune response, we further investigated the effects of nsEPs on the breast TME by performing transcriptomic and immune profiling of 4T1 breast cancer cells treated with nsEP. RNAseq data and cell death signaling results demonstrated that nsEPs induced regulated necrotic cell death rather than apoptosis. nsEPs-treated cancer cells greatly decreased angiogenic factors and multiple chemoattracts for myeloid-derived suppressor cells (MDSCs) and macrophages. On the other hand, nsEP-treated cancer cells significantly upregulated chemoattracts for T lymphocytes and a number of proinflammatory/immunostimulatory cytokines. Flow cytometry analysis showed that the dynamic changes of TME following nsEP treatment included: (1) the significant reduction of immunosuppressive cells (MDSCs, Tregs and TAMs); (2) the preservation of cytotoxic CD8+ T cells and conventional CD4+ T cells; and (3) a persistent elevation in cytotoxic cells vs Treg ratio and tissue resident memory CD8+ T cells. Taken together, our results suggest nsEP is a TME modifier that can potentially overturn the immunosuppressive hurdle in the TME to promote antitumor immunity.

Disclosure(s):

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12/7/2022

5:00 PM - 6:15 PM

P3-07-18

CCTG IND.239: A phase 2 study of combined CFI-400945 and durvalumab in patients with advanced triple negative breast cancer (aTNBC)

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CCTG IND.239: A phase 2 study of combined CFI-400945 and durvalumab in patients with advanced triple negative breast cancer (aTNBC) John Hilton, David W. Cescon, Andrew Robinson, Sukhbinder Dhesy-Thind, Sara Kristina Taylor, Arif Awan, Terry Ng, Moira Rushton, Marie-France Savard, Lindsay Muyot, Marie Claude Reeves, Linda Hagerman, Hongbo Lui, Mark Bray, Dongsheng Tu, Lesley Seymour, Pierre-Olivier Gaudreau Background: CFI-400945 is a selective oral inhibitor of Polo-like Kinase 4 (PLK4), which controls centriole duplication and mitotic progression, and was identified as a drug target based on functional screening of genomically unstable breast cancers. CFI-400945 monotherapy has anti-proliferative activity and enhances antitumor activity when combined with anti-PD-1 immune checkpoint blockade in transplantable murine cancer models. Material and methods: In this multi-centre phase II trial of CFI-400945 and durvalumab combination therapy, the primary objective was overall response rate (ORR) per RECIST 1.1. Patients with aTNBC with adequate organ function, PS 0-1, previously treated with >1 line of chemotherapy including anthracycline and/or taxane, were eligible. CFI-400945 32mg monotherapy was administered on a 7-day on, 7-day off schedule for cycle 1 (which reduced the likelihood of significant hematologic toxicity). From cycle 2 onwards, CFI-400945 32mg daily was administered in combination with durvalumab 1500mg IV every 28 days; responses were assessed every 8 weeks. Following trial activation, 3 patients received a CFI-400945 dose of 40mg (same schedule) for a total of 9 cycles before 32mg was declared as the new recommended phase 2 dose (based on other ongoing trials using CFI-400945). A Simon 2-stage design was used; $\geq 3/15$ responses in stage 1 were required to expand to stage 2. Exploratory PD-L1 expression was measured on immune and tumor cells using the SP263 assay. Results: 15 patients received a total of 45 cycles (1-12 cycles per patient). Median age was 56 (31-76); 53% PS1; 20% ≥ 3 prior chemotherapy lines and; 27% ≥ 4 sites of metastatic disease. Immune vs tumor cell PD-L1 expression was $\leq 1\%$ in 50% and 23% of patients, respectively (immune and tumor cell expression was mutually exclusive). Immune vs tumor cell PD-L1 expression was $\leq 10\%$ in 17% and 15% of patients, respectively. Grade ≥ 3 hematological adverse events (AEs) were lymphopenia (40%), neutropenia (20%), anemia and thrombocytopenia (7% for both). One serious AE at least possibly related to treatment was seen: grade 3 febrile neutropenia. Frequent AEs (>5%) considered at least possibly related to CFI-400945 were: nausea and anorexia (both 20%), fatigue and dysgeusia (both 13%), headache, dizziness, maculo-papular rash, back pain and gastroesophageal reflux disease (all 7%), Frequent AEs (>5%) considered at least possibly related to durvalumab were: anorexia (13%), arthritis, fatigue, back pain, pain in extremity and hot flashes (all 7%). No responses were observed in 14 evaluable patients during stage 1, therefore the pre-specified threshold for anti-tumor activity to proceed to stage 2 was not met. Disease control rate (complete response, partial response or stable disease >16 weeks in duration) was 7% (1/14). Conclusions: CFI-400945 and durvalumab was well tolerated, with no unexpected toxicities of the combination. However, in this heavily pretreated and PD-L1 unselected TNBC population, no responses were observed and the pre-specified threshold for anti-tumor activity for stage 2 was not met. The trial was closed to accrual on April 26, 2022. Final analysis and correlative analyses are ongoing. Acknowledgements: Coordinated by the CCTG. Funding supported by Astra Zeneca. CFI-400945 provided by Treadwell Therapeutics and durvalumab provided by Astra Zeneca.

Disclosure(s):

John Hilton, MD, FRCPC: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); BMS: Consulting Fees (e.g., advisory boards) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing)

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5:00 PM - 6:15 PM

P3-07-19

Anti-depressant Amitriptyline Augments the Efficacy of Tamoxifen in ER positive breast cancer

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Anti-depressant Amitriptyline Augments the Efficacy of Tamoxifen in ER positive breast cancer
Pitta Venkata Prabhakar¹, Arhan D Rao¹, Timilsina Santosh¹, Deepika Singh¹, Ratna Vadlamudi^{1,2}, Virginia Kaklamani³, Manjeet Rao^{1,2}. ¹Greehey Children's Cancer Research Institute, University of Texas Health San Antonio, San Antonio, TX, USA. ²Mays Cancer Center, University of Texas Health San Antonio, San Antonio, TX, USA. ³Department of Medicine, UT Health, San Antonio, USA. Background: Breast cancer (BC) is the most common cancer in women and the leading cause of cancer-related deaths in women worldwide, with 1 out of 8 women being diagnosed with invasive breast cancer during their lifetime. The majority of breast cancer patients (80%) are diagnosed with Estrogen Receptor positive (ER+) breast cancer. The most commonly used treatment option for ER+ Breast cancer is endocrine therapy, such as Tamoxifen(TAM). Although survival of breast cancer patients has dramatically improved with the use of endocrine therapy, acquired resistance and debilitating side effects of treatment became major concerns. Therefore, safer treatment options that effectively suppress cancer progression, reduce treatment associated side effects, and improve efficacy of standard of care therapies are much needed. Repurposing of clinically approved or investigational drugs has become promising alternative approach for treating cancer. Therefore, we tested the repurposing potential of anti-depressant Amitriptyline for the treatment of ER+ breast cancer. Methods: The anti-cancer effect of Amitriptyline was determined in vitro using short and long-term viability, migration, and apoptosis assays. To substantiate the in vitro data, the effect of

Amitriptyline on tumor growth was assessed using orthotopic xenograft model. RNA-seq analysis was performed in Vehicle and Amitriptyline treated breast cancer cells to understand the mechanism of action. Finally, to test whether amitriptyline can sensitize ER+ breast cancer cells to endocrine therapy, we performed cell viability assays after treatment with Amitriptyline and Tamoxifen. Results: Amitriptyline treatment resulted in significant reduction of short term and long term viability, as well as, migration of ER+ BC cells. Furthermore, Amitriptyline treatment significantly increased apoptosis in BC cells. Our RNA-seq analysis revealed that Amitriptyline treatment inhibited important genes involved in cancer growth and survival including E2F signaling, G2/M pathway, and DNA repair pathways. Confirming our in vitro findings, Amitriptyline treatment blocked the growth of ER+ BC growth in pre-clinical orthotopic xenograft model of breast cancer. Importantly, Amitriptyline treatment sensitized ER+ BC to TAM, showing highly synergistic effects. Amitriptyline treatment significantly improved the effects of TAM on cell viability, survival, migration, and apoptosis. Furthermore, Amitriptyline augmented the efficacy of Tamoxifen in TAM resistant BC cells. Conclusion: Our study establishes potential of Amitriptyline as a repurposable drug as safe and robust treatment option for ER+ patients, either as a monotherapy or in combination. We are poised to begin a clinical trial and test the therapeutic efficacy of Amitriptyline for treating breast cancer patients.

Disclosure(s):

Prabhakar Pitta Venkata, PhD: No financial relationships to disclose

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12/7/2022

5:00 PM - 6:15 PM

P3-07-20

Treatment of 4T1 Breast Cancer with Liposome-Encapsulated AdAPT-001, a TGF-beta Trap Encoded Oncolytic Adenovirus Currently in a Phase 1/2 Anticancer Trial

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Adenoviral vectors have been used extensively for gene therapy. However, efficient infection of cells requires expression of the coxsackie-adenoviral receptor (CAR). Many tumor cells lack adequate expression of CAR and, hence, are not good targets for adenoviral based vectors. We have developed a unique nanoparticle (Epi-039) that can be used to efficiently introduce adenoviral vectors into tumor cells that have low or no CAR expression. We used the CAR-negative 4T1 mammary carcinoma model system, which represents a typical triple-negative breast cancer cell line (ER-, PR-, HER2-) and which is refractory to adenoviral infection to demonstrate effective transduction of an encapsulated oncolytic adenovirus. The adenovirus that was used is called AdAPT-001. This armed oncolytic virus, which is currently in a phase I/II clinical trial called BETA PRIME for the treatment of refractory cancers, expresses a TGFb receptor trap to neutralize the immunosuppressive cytokine, TGF beta. Overexpression of TGF-beta positively correlates with metastasis in breast carcinoma and thus confers a poorer prognosis. In this study, the unique Epi-039 nanoparticle carrying AdAPT-001 not only significantly enhanced the transduction efficiency of AdAPT-001 but also protected it from neutralization by natural antibodies in human whole blood. Accordingly, we demonstrate a significant increase (P value= 0.0029) in the expression of green fluorescent protein (GFP) in CAR-negative 4T1 cells infected with the encapsulated AdAPT-001 adenovirus but not the unencapsulated AdAPT-001 adenovirus. Additional in vivo studies using nanoparticle encapsulated adenoviral vectors including AdAPT-001 to treat breast cancer are underway for rapid translation to the clinic.

Disclosure(s):

Tony Reid, MD, PhD: EpicentRx: Employed at EpicentRx (Ongoing), Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Salary (Ongoing)

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Scott Caroan, MBA: No financial relationships to disclose

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P3-07-21

Therapeutic efficacy of NGY-091 against triple negative breast cancer is mediated by direct cell killing and activation of antitumor immunity

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Aberrant metabolic reprogramming is known to drive triple negative breast cancer progression and metastasis. The increase in glycolytic flux in cancer cells creates a lactate-rich tumor microenvironment (TME) that is exploited by tumors to their advantage by activating

immunosuppressive cell populations, such as Tregs and MDSCs, that thrive on lactate as a fuel source. Therefore, blockade of lactate export from glycolytic cancer cells while inhibiting lactate entry into suppressive immune cells is a novel therapeutic strategy to treat cancer. Lactate transport in cells is predominantly mediated by MCT1 and MCT4 transporters. We have developed a compound, NGY-091, that is a first-in-class small molecule dual inhibitor of the MCT1 and MCT4 lactate transporters. NGY-091 treatment exhibited a potent in vitro cytotoxicity against breast cancer cells with various levels of MCT1 and MCT4 expressions. The on-target activity of NGY-091 was validated by measuring intracellular and extracellular lactate levels. NGY-091 strongly blocked MCT1 mediated lactate import and lactate export through MCT4 in vitro. Furthermore, a direct in vivo tumor cell killing was evident in human TNBC CDX (MDA MB 231) and PDX models with the treatment of NGY-091. In a syngeneic model of 4T1, we observed a significant reduction in tumor growth and synergistic tumor regression when combined with immune checkpoint blockade therapy. Profiling of lymphoid and myeloid cells in NGY-091 treated tumors by flow cytometry revealed a significant alteration in immune architecture suggesting activation of antitumor immunity. NGY-091 treated tumors induced a profound increase in effector T cell populations, CD8/Treg ratio and tumor-suppressive M1 macrophages while significantly downregulating M2 macrophages. To further investigate if NGY-091 directly alters immune cell activation and functionality in vitro, we treated CD4 T, CD8 T, Tregs and MDSCs in a lactate-rich culture condition mimicking lactate level in the TME. NGY-091 treatment strongly increased effector CD4 and CD8 T cells while significantly reducing suppressive function of Treg and MDSCs in vitro. These findings indicate the direct effect of NGY-091 on immune cell and validate the in vivo observations in 4T1 tumors. Therefore, NGY-091 intervenes two key hallmarks of cancer – metabolism and immunity and provides a novel avenue to therapeutically target aggressive breast cancer.

Disclosure(s):

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5:00 PM - 6:15 PM

P3-07-22

Presurgical Trial of Metformin plus Atorvastatin in Women with Operable Breast Cancer

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Introduction:

Metformin is an oral anti-diabetic agent that exhibits direct anti-proliferative effects on pre-clinical models through activation of the AMPK pathway. However, pre-surgical studies of metformin alone among women with operable breast cancer have not consistently shown reductions in tumor proliferation, and adjuvant metformin in women with high-risk operable breast cancer did not improve invasive disease-free survival compared with placebo. Dysregulation of the mevalonate pathway of cholesterol synthesis can also lead to cell proliferation, and inhibition of HMG-CoA reductase by statins can decrease tumor proliferation. There is close interaction between the AMPK and mevalonate pathways, and dual therapy with a statin and metformin might be synergistic to decrease cell proliferation. We evaluated the effect of combination therapy with metformin plus atorvastatin on markers of proliferation (i.e. Ki67 proliferation index) in women with operable breast cancer.

Methods:

We conducted an open-label, single-arm presurgical “window of opportunity” study of metformin plus atorvastatin in non-diabetic women age 21+ years with newly-diagnosed stage 0-III operable breast cancer at Columbia University Irving Medical Center (CUIMC). Enrolled patients received metformin 1500mg oral [p.o.] daily (500mg in the morning/1000mg in the afternoon) and atorvastatin 80mg p.o. nightly for up to 4 weeks before breast surgery. The primary endpoint was change in Ki67 proliferation index from baseline (diagnostic biopsy) to post-treatment (surgical specimen). Secondary endpoints included change in body mass index (BMI), waist and hip circumferences, tumor assessment of AMPK/mTOR signaling and apoptosis, and reduction of fasting markers of the insulin growth factor pathway. Paired t-tests were conducted to assess difference in ln(Ki67) pre- and post-therapy, as well as differences in absolute Ki67, BMI, and waist/hip circumferences pre- and post-therapy, at a level of significance of 0.05.

Results:

Between Nov. 2013 and Jan. 2018, 22 women were enrolled, and two withdrew consent prior to study treatment. Among evaluable participants (n=20), 45% were Hispanic with median age 56 years (range, 33-73) and median baseline BMI 28.4 kg/m² (range, 22.5-45.8). All had hormone receptor-positive (HR+), HER2-negative breast cancer, and 16 (80%) had invasive cancer. Median time on study treatment was 11 days (range, 5-29). Changes in Ki67 and anthropomorphic measures are shown in Table 1. There was no significant change in BMI, waist or hip circumference with study treatment. Among women with available Ki67 measurements (n=11), there was no significant difference in pre- and post-treatment ln(Ki67) (p=0.25). There was a numeric decrease in absolute Ki67, though statistical significance was not reached (p=0.09).

Discussion:

There was a numeric reduction in absolute Ki-67 with presurgical metformin plus atorvastatin in patients with newly diagnosed HR+/HER2- breast cancer, although our analysis was limited by small sample size and statistical significance was not achieved. There was no difference in ln(Ki67) or anthropometric measurements. Analyses of additional tissue and serum biomarkers, including markers of insulin resistance, are ongoing to identify associations with absolute Ki67

Table 1

Variable	Median Pre-Treatment (Range)	Median Post-Treatment (Range)	Mean Change (SD)	p-value
Absolute Ki67 (n=11)	20.6 (0, 80.3)	14.0 (2.6, 60.2)	-6.5 (11.3)	0.09
ln(Ki67) (n=11)	3.0 (1.0, 4.4)	2.4 (4.1, 2.6)	-0.4 (1.0)	0.25
BMI, kg/m ²	28.4 (22.5, 45.8)	29.0 (22.3, 46.6)	-0.1 (0.6)	0.39
Waist circumference (cm)	91.4 (66.0, 123.0)	91.4 (66.0, 123.0)	-0.1 (0.9)	0.62
Hip circumference (cm)	106.3 (90.0, 147.0)	105.4 (90.0, 147.0)	-0.1 (0.6)	0.53

Disclosure(s):

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12/7/2022

5:00 PM - 6:15 PM

P3-07-23

Defendor Special: Primary empegfilgrastim prophylaxis (prolonged G-CSF) for optimal treatment outcomes in high risk early breast cancer cohort. The interim analysis.

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BACKGROUND Relative dose intensity (RDI) of chemotherapy (CT) < 85% significantly decrease therapy efficiency (including overall survival) in early breast cancer (BC) patients (pts). Pathological complete response (pCR) reflects better outcomes and correlates with the RDI of neoadjuvant CT (NAC). Neutropenia is the most common AE leading to RDI drop. Recent studies demonstrate that G-CSF could switch immunosuppressive tumor microenvironment via neutrophils plasticity. In early BC neutrophils, can mediated antitumor responses by direct killing of tumor cells and by participating in cellular networks that mediate antitumor resistance. Primary G-CSF prophylaxis (PP) with prolonged G-CSF may be an option for optimal therapy results. This multicenter prospective study was designed to evaluate the RDI and treatment outcomes of cytotoxic therapy under PP by empegfilgrastim (E) in pts with high-risk early BC. **METHODS** High-risk BC pts (n=195) with II-III stages are getting NAC of the following regimens: 4 dose dense doxorubicin/cyclophosphamide with E followed by 12 weekly paclitaxel/carboplatin (4ddAC+E/12P+carbo) for triple negative (TN) pts or 4 dose dense doxorubicin/cyclophosphamide with E followed by 4 dose dense paclitaxel with E (4ddAC+E/4ddP+E) for HR+HER2- pts and 6 docetaxel/carboplatin trastuzumab/pertuzumab (TCHP+E) for HER2+ pts. RDI of therapy course was primary endpoint and presented here for pts who completed the planned regimen. For each agent, the planned and actual dose intensity were calculated by dividing the total cumulative dose by treatment duration in days. RDI was calculated for each single agent in CT regimen and for CT regimen in total. These descriptive analyses were performed for the whole CT regimen. The secondary endpoint: pCR (ypT0/is, ypN0) is also presented here. ClinicalTrials.gov No NCT04905329. **RESULTS** At the data cut-off (April'2022) 111 pts with BC (HER2+ (n=56); HR+ HER2- (n=17); TN (n=38)) underwent ≥ 1 cycle of NAC with E. The planned CT course completed in 67 (60%) BC pts. RDI≥85% were fixed in 56 (84%) pts: 93% RDI for 4ddAC+E/4ddP+E regimen; 90,3% RDI for 6TCHP+E; 94,1% RDI for 4ddAC+E/12P+carbo. Preliminary, in HER2+ BC pts pCR rate exceeds KRISTINE trial data despite a more enriched pts' population with poor prognosis (36% pts with IIIB - III C and 65% pts with IIA-III A stages per TNM v.8): 93,3% (15 pts HR-) and 70,4% (34 pts

HR+). In TNBC pts pCR rate is 56% (9 pts) according to historical control. In HR+ HER2- BC – pCR rate is 20% (10/17 pts under surgery). Neutropenia as a reason of RDI drop was in 1 (0,9%) case in HER2+BC pt. The mature data are awaited. CONCLUSION PP with E allows to maintain RDI efficiently and safely in high-risk recurrence pts populations. High pCR rate under E in HER2+ BC pts focused on further confirmation with translational research. KEY WORDS: empegfilgrastim, neutropenia, pCR, dose intensity, G-CSF, breast carcinoma, neoadjuvant therapy

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Irina Sorokina, n/a: Biocad: Salary (Ongoing)

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5:00 PM - 6:15 PM

P3-07-24

Role of tumor cell-derived lactic acid in the PD-1/PD-L1 blockade resistant tumor

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Immune checkpoint blockade therapy targeting the PD-1/PD-L1 axis (PD-1/PD-L1 blockade therapy) has shown remarkable clinical impact in multiple cancer types. Despite the recent success of PD-1/PD-L1 blockade therapy, acquired resistance, emerging as late relapses or recurrences, has been reported in the long-term follow-up of clinical trials. The altered metabolic activity of cancer cells shapes the anti-tumor immune response by affecting the activity of immune cells. In particular, glycolytic metabolites, such as glucose and lactate, regulate T cell proliferation and function. However, it remains mostly unknown how the altered metabolic activity of cancer cells impacts the therapeutic efficacy of, and resistance to, PD-1/PD-L1 blockade therapy. Here, we found that increased lactic acid functionally contributes to an immunosuppressive tumor microenvironment in the PD-1/PD-L1 blockade therapy resistant tumors through decreasing PD-L1 and PD-L1 antibody interaction. Furthermore, combining PD-L1 targeting with our PD-L1-antibody-drug conjugate (ADC) and reducing lactic acid by an MCT-1 inhibitor, AZD3965, within the tumor microenvironment effectively eradicated the resistant tumor cells. Together, our results suggest a new combination treatment strategy to improve the therapeutic efficacy of immune checkpoint blockade therapies

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Efficacy and safety of neoadjuvant pertuzumab biosimilar TQB2440, trastuzumab and docetaxel in HR negative, HER2 positive breast cancer: a single-arm trial

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Background: Despite that dual anti-HER2 therapy (Trastuzumab and Pertuzumab, TP) is one of the commonly used regimens for neoadjuvant treatment of HER2-positive breast cancer, previous studies showed that its pCR rate rarely exceeds 63%. Additionally, it is associated with higher risk of cardiac adverse events. TQB2440, a biosimilar of pertuzumab, with strong affinity and specificity, can effectively bind with HER2 epitope. In the PDX mouse model, TQB2440 showed promising biological activity and minimal cardiotoxicity. In this study, we designed a single-arm trial of dual anti-HER2 therapy (TQB2440 and trastuzumab, TT) plus docetaxel in neoadjuvant therapy of HER2 positive breast cancer. We aimed to examine the

efficacy and safety of TQB2440 and study whether new dual anti-HER2 therapy (TT) can boost pCR rate in the neoadjuvant treatment. The cardiotoxicity and other adverse reactions were closely monitored. Methods: Upon approval by the Medical Ethics Committee of Xijing Hospital, patients with HR negative HER2-positive breast cancer (cT2-3/N0-1/M0) receiving neoadjuvant therapy were enrolled. The patients were treated with docetaxel 75 mg/m², trastuzumab 8 mg/kg loading, then 6 mg/kg, TQB2440 840 mg loading, then 420 mg, iv, q3w for 4 cycles, with strict monitoring of cardiotoxicity. The primary endpoint was pCR rate, and secondary endpoint was cardiotoxicity. Results: From April 2021 to February 2022, a total of 28 patients were recruited. Among the 28 patients with a median age of 52 (28-74), 12 patients had positive lymph node status. Overall, the pCR rate was 67.9% (19/28). The pCR rate was higher than that in the NeoSphere trial (pCR 63.2%) and the PEONY study (pCR 52.5%). The lymph-positive tumor achieved a higher pCR rate than lymph-negative tumor (70.8% vs 52.3%, p = .019). Multivariate regression analysis showed that for participants aged 50 or above, HER2 3+ (IHC) showed a statistically significant positive influence on pCR rate. The common adverse reactions of grade \geq 3 were leukopenia (46.4%), neutropenia (35.7%), asthenia (3.6%), and peripheral sensory neuropathy (2.3%). Left ventricular insufficiency was detected in 1 patient, and no cardiotoxic events higher than grade 2 occurred during the neoadjuvant therapy. There was no treatment-related death. Conclusion: TQB2440 and trastuzumab plus docetaxel is a feasible and effective neoadjuvant therapy for early-stage HR negative HER2-positive breast cancer, showing high pCR rate and acceptable cardiotoxicity. These results support a further random controlled trial testing for dual anti-HER2 therapy using TQB2440 in neoadjuvant or adjuvant therapy of HER2 positive breast cancer.

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Anti-cancer activity of naturally formulated *Trigonella foenum graecum* (Fenugreek) PLGA hyaluronic acid-coated nanoparticles for treatment of breast cancer cell lines

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There are several growing evidences of anticancer complementary and alternative medicines worldwide. *Trigonella foenum graecum* (Fenugreek) is traditionally applied to treat several disorders such as diabetes, inflammation, and gastrointestinal ailments. Previously, we reported that Fenugreek has anticancer properties against liver cancer due to its active beneficial chemical constituents. Herein, Fenugreek-loaded poly (l-lactic-co-glycolic acid) (PLGA) hyaluronic acid (HA)-coated nanoparticles have been formulated to improve and enhance the anticancer potential of Fenugreek against human breast cancer cell lines. The cytotoxic effects, physicochemical characterization in vitro and pharmacodynamic study of optimized formulation of the FCE-loaded (PLGA)-(HA)-coated nanoparticles in vivo were investigated in (ER-positive) and (triple-negative), breast cancer cell lines, ZR-75-1 and MDA-MB-231, respectively. The particle size, PDI, zeta potential, entrapment efficiency, and loading capacity of FCE-loaded nanoparticles were 188.5 ± 3.1 d.nm, 0.198 ± 0.114 , -0.118 mV, $38.41 \pm 1.4\%$, and $6.37 \pm 1.08\%$, respectively. The in vitro cytotoxicity study of FCE-loaded NPs by Wst-1 proliferation assay on both tested breast cancer cell lines showed an anti-cancer activity after 48 h of treatment in a dose-dependent manner. Furthermore, the anticancer effect of FCE-loaded nanoparticles was examined by the morphological cell changes, histone release, caspase-3 activity, and modulation of the oncogenic signal pathways of m-tor, β -catenin, cyclin D-1 and STAT3 that are constitutively active in wide variety of breast cancer cell lines which in turn could be important as therapeutic targets in breast cancer. 66 μ g/mL FCE-loaded PLGA nanoparticles induced 67.3% apoptosis in both tested cell lines after 48 h that was associated with increased expression of caspase 3, Bax, Bak, p53, and cell cycle arrest at G0/G1 in a time-and dose-dependent manner compared to unloaded-nanoparticles or untreated cells. Moreover, there were significant inhibition in m-tor, β -catenin, cyclin-D1, and STAT3 expression levels in both tested cell lines compared to un-loaded-nanoparticles or untreated cells. All in all, our results showed that the formulated FCE-loaded (PLGA)-(HA)-coated nanoparticles induced apoptosis in both ER-positive and triple-negative breast cancer cell lines respectively by increase the expression of pro-apoptotic genes and inhibited several oncogenic genes that might hold a promise for the complementary therapy for human breast cancer.

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P3-07-27

In vitro antitumoral activity of endophytic fungi isolated from *Lophocereus marginatus* against the human breast cancer cell line MCF-7

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Breast cancer is the most frequent malignant tumor among women and is the leading cause of death from cancer worldwide. In 2020, 90,222 deaths from breast cancer were reported in México. However, cancer cells resistant to antineoplastic drugs are frequent, which compromises the patient's survival. For this reason, in oncology, it is essential to search for new sources of anticancer compounds. Endophytic fungi are currently considered potential reservoirs for compounds with antitumor activity. More than 100 different classes of secondary metabolites have been reported with activity against different types of cancer, including breast cancer. Therefore, the objective of this study was to evaluate the activity of methanol extracts of endophytic fungi isolated from *Lophocereus marginatus* against the MCF-7 breast cancer cell line, using as controls the MA-104 cell line human peripheral blood mononuclear cells. Fungal strains were isolated from stems of *L. marginatus* and molecularly identified from ribosomal DNA internal transcript spacer region sequencing. Extraction of the secondary metabolites was performed from the maceration of mycelium fungus in methanol. The solvent was removed with a rotary evaporator and the extract was reconstituted with dimethyl sulfoxide (DMSO). Next, cells were incubated with the extract at concentrations ranging from 31.25 µg/mL to 250 µg/mL for 48 h at 37 °C and 5% CO₂. Growth inhibition was assessed by the 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide reduction assay, using 1% DMSO was used as a negative control. IC₅₀ values and selectivity indexes (SI) were then calculated. It was found that tumor

cells growth inhibition by the extracts increased in a concentration-dependent manner. *A. versicolor* PME-H005 strain extract showed the highest antitumor activity, with up to 58.9% growth inhibition at 250 µg/mL and IC50 value of 95.21 ± 1 µg/mL against MCF-7 cells. The highest SI was obtained with MCF-7 cells with 2.77, as compared with normal PBMC with an IC50 of 264 ± 1.5 µg/mL. In addition, the *M. anisopliae* PME-H007 strain presented a high SI value of 2.1 and an IC50 of 245.9 ± 1.9 µg/mL, using the MCF-7 cell line. This study shows the potential of the endophytic fungus *A. versicolor* PME-H005 isolated from *L. marginatus* for production of secondary metabolites with antitumor activity against MCF-7 cells.

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SERENA-1: Updated analyses from a Phase 1 study of the next generation oral selective estrogen receptor degrader camizestrant (AZD9833) combined with abemaciclib, in women with ER-positive, HER2-negative advanced breast cancer

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Background: SERENA-1 (NCT03616587) is a Phase 1, multi-part, open-label study of camizestrant in women with ER+/HER2- advanced breast cancer. Parts A/B and C/D (escalation/expansion) examined camizestrant as monotherapy and in combination with palbociclib respectively and have been presented previously.^{1,2} Here we present data from parts G/H which examined camizestrant in combination with abemaciclib. Methods: The primary objective was to determine the safety and tolerability of camizestrant 75 mg once daily (QD) in combination with abemaciclib 150 mg twice daily (BID). Secondary objectives included investigation of anti-tumor response and pharmacokinetics (PK). Participants were previously treated women of any menopausal status (pre-menopausal women received this combination alongside ongoing ovarian function suppressors). Prior treatment with ≤ 2 lines of chemotherapy in the advanced setting was permitted. There was no limit on the number of lines of prior endocrine treatment in the advanced setting; previous treatment with CDK4/6 inhibitors

(CDK4/6i) and fulvestrant was permitted. Results: As of 1st June 2022, 24 patients had received camizestrant in combination with abemaciclib with a median 7.7 month follow up. Tolerability of the combination of camizestrant and abemaciclib was consistent with that of each drug individually. No patient required camizestrant dose reduction. All camizestrant-related heart rate decreases were Grade 1 (asymptomatic). PK data for camizestrant in combination with abemaciclib were consistent with camizestrant as monotherapy and published abemaciclib steady-state PK data, indicating no clinically relevant drug-drug interaction. In these heavily pre-treated patients (46% prior chemotherapy, 75% prior CDK4/6i, 54% prior fulvestrant; all in the advanced disease setting) and of whom 67% had visceral metastases, the objective response rate was 5/19 (26.3%), the clinical benefit rate at 24 weeks was 16/24 (66.7%) and the median progression-free survival had not been reached, with 8/24 patients experiencing a progression event. These data support the use of camizestrant 75 mg QD combined with the approved abemaciclib dose. Conclusions: Camizestrant 75 mg QD in combination with abemaciclib 150 mg BID was well tolerated with encouraging clinical activity. The inclusion of this regimen in the ongoing Phase 3, SERENA-6 trial 3, of camizestrant combined with CDK4/6i versus an aromatase inhibitor, will further clarify the role of this combination in the treatment of patients with ER+/HER2- advanced breast cancer with tumors expressing ESR1 mutations. References 1. Baird R, Oliveira M, Ciruelos Gil EM, et al. SABCS 2020 Virtual Meeting. Abstract PS11-05. 2. Oliveira M, Hamilton EP, Incorvati J, et al. J Clin Oncol 40, 2022 (suppl 16; abstr 1032). 3. SERENA-6 trial. Available at <https://clinicaltrials.gov/ct2/show/NCT04964934> We acknowledge Helen Heffron, PhD, from InterComm International who provided medical writing support funded by AstraZeneca.

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Nicholas Turner, PhD, FRCP: Arvinas: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); BioRad: Contracted Research (Ongoing), Contracted Research (Ongoing); Bristol Myers Squibb: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing); GlaxoSmithKline: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing); Guardant Health: Contracted Research (Ongoing), Contracted Research (Ongoing); Inivata: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Invitae: Contracted Research (Ongoing), Contracted Research (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing); Merck Sharpe and Dohme: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Natera: Contracted Research (Ongoing), Contracted Research (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing); Personalis: Contracted Research (Ongoing), Contracted Research (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Repare therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing); Roche/Genentech: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Zentalis pharmaceuticals: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing)
Christos Vaklavas, n/a: AstraZeneca: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Research Funding

(Ongoing); CytomX: Research Funding (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Flaitron: Salary (Ongoing); Gilead: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Guidepoint: Consulting Fees (e.g., advisory boards) (Ongoing); H3 Biomedicine: Research Funding (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Research Funding (Ongoing); SeaGen: Consulting Fees (e.g., advisory boards) (Ongoing), Research Funding (Ongoing)

Emiliano Calvo, n/a: Adcendo: Consulting Fees (e.g., advisory boards) (Ongoing); Amunix: Consulting Fees (e.g., advisory boards) (Ongoing); Anaveon: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Beigene: leadership (Ongoing); Bristol-Myers Squibb: Consulting Fees (e.g., advisory boards) (Ongoing); Chugai Pharma: Consulting Fees (e.g., advisory boards) (Ongoing); Elevation Oncology: Consulting Fees (e.g., advisory boards) (Ongoing); Ellipses Pharma: Consulting Fees (e.g., advisory boards) (Ongoing); EORTIC: leadership (Ongoing); HM Hospitales Group: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Salary (Ongoing); Janssen/Cilag: Consulting Fees (e.g., advisory boards) (Ongoing); MonTa: Consulting Fees (e.g., advisory boards) (Ongoing); MSD Oncology: Consulting Fees (e.g., advisory boards) (Ongoing); Nanbiotix: Consulting Fees (e.g., advisory boards) (Ongoing); Nouscom: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), leadership (Ongoing); Oncoart Associated: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); OncoDNA: Consulting Fees (e.g., advisory boards) (Ongoing); PharmaMar: Consulting Fees (e.g., advisory boards) (Ongoing), Salary (Ongoing); Roche/Genentech: Consulting Fees (e.g., advisory boards) (Ongoing); Sanofi: leadership (Ongoing); Servier: Consulting Fees (e.g., advisory boards) (Ongoing); START Madrid: leadership (Ongoing), Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing); TargImmune Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); T-knife: Consulting Fees (e.g., advisory boards) (Ongoing)

Javier Garcia-Corbacho, n/a: Alkermes: Research Funding (Ongoing); Amgen: Research Funding (Ongoing); Astellas Pharma: Research Funding (Ongoing); AstraZeneca: Research Funding (Ongoing); Bayer: Research Funding (Ongoing); Black Diamond Therapeutics: Research Funding (Ongoing); Boehringer Ingelheim: Research Funding (Ongoing); Bristol-Myers Squibb: Research Funding (Ongoing); CytomX Therapeutics: Research Funding (Ongoing); GalaxoSmithKline: Research Funding (Ongoing); Incyte: Research Funding (Ongoing); Janssen: Research Funding (Ongoing); Menarini: Research Funding (Ongoing); MSD: Research Funding (Ongoing); Novartis: Research Funding (Ongoing); Puma Biotechnology: Research Funding (Ongoing)

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Chris Twelves, MD: No financial relationships to disclose

Anne Armstrong, n/a: AstraZeneca: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Research Funding (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing)

Begoña Bermejo, MD, PhD: No financial relationships to disclose

Erika Hamilton, MD: Abbvie: Research Funding - Paid to Institution (Ongoing); Accutar Biotechnology: Research Funding - Paid to Institution (Ongoing); Acerta Pharma: Research Funding - Paid to Institution (Ongoing); ADC Therapeutics: Research Funding - Paid to Institution (Ongoing); AKESOBIO Australia: Research Funding - Paid to Institution (Ongoing); Amgen: Research Funding - Paid to Institution (Ongoing); Aravive: Research Funding - Paid to Institution (Ongoing); Arcus: Consulting Fees to Institution (Ongoing); ArQule: Research

Funding - Paid to Institution (Ongoing); Artios: Research Funding - Paid to Institution (Ongoing); Arvinas: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); AstraZeneca: Study sponsor, consulting fees and research grant paid to institution (Ongoing); AtlasMedx: Research Funding - Paid to Institution (Ongoing); Black Diamond: Consulting and Research Funding - Paid to Institution (Ongoing); Bliss BioPharmaceuticals: Research Funding - Paid to Institution (Ongoing); Boehringer Ingelheim: Consulting and Research Funding - Paid to Institution (Ongoing); Cascadian Therapeutics: Research Funding to Institution (Ongoing); Clovis: Research Funding to Institution (Ongoing); Compugen: Research Funding to Institution (Ongoing); Cullen-Florentine: Research Funding to Institution (Ongoing); Curis: Research Funding to Institution (Ongoing); CytomX: Consulting Fees and Research Funding to Institution (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Dana Farber Cancer Inst: Research Funding to Institution (Ongoing); Dantari: Consulting Fees and Research Funding to Institution (Ongoing); Deciphera: Consulting Fees and Research Funding to Institution (Ongoing); Duality Biologics: Research Funding to Institution (Ongoing); eFFECTOR Therapeutics: Research Funding to Institution (Ongoing); Eisai: Consulting Fees to Institution (Ongoing); Ellipses Pharma: Research Funding to Institution (Ongoing); Elucida Oncology: Research Funding to Institution (Ongoing); EMD Serono: Research Funding to Institution (Ongoing); Fochon: Research Funding to Institution (Ongoing); FujiFilm: Research Funding to Institution (Ongoing); G1 Therapeutics: Research Funding to Institution (Ongoing); Greenwich Lifesciences: Consulting Fees to Institution (Ongoing); H3 Biomedicine: Consulting Fees and Research Funding to Institution (Ongoing); Harpoon: Research Funding to Institution (Ongoing); Hutchinson MediPharma: Research Funding to Institution (Ongoing); Immunogen: Research Funding to Institution (Ongoing); Immunomedics: Research Funding to Institution (Ongoing); Incyte: Research Funding to Institution (Ongoing); Infinity Pharmaceuticals: Research Funding to Institution (Ongoing); InvestisBio: Research Funding to Institution (Ongoing); iTeos: Consulting Fees to Institution (Ongoing); Jacobio: Research Funding to Institution (Ongoing); Janssen: Consulting Fees to Institution (Ongoing); Karyopharm: Research Funding to Institution (Ongoing); Leap Therapeutics: Research Funding to Institution (Ongoing); Lilly: Consulting Fees and Research Funding to Institution (Ongoing); Loxo: Consulting Fees to Institution (Ongoing); Lycera: Research Funding to Institution (Ongoing); Mabspace Biosciences: Research Funding to Institution (Ongoing); MacroGenics: Research Funding to Institution (Ongoing); MedImmune: Research Funding to Institution (Ongoing); Merck: Consulting Fees and Research Funding to Institution (Ongoing); Mersana: Consulting Fees and Research Funding to Institution (Ongoing); Merus: Research Funding to Institution (Ongoing); Millennium: Research Funding to Institution (Ongoing); Molecular Templates: Research Funding to Institution (Ongoing); Myraid Genetic Laboratories: Research Funding to Institution (Ongoing); Novartis: Consulting Fees and Research Funding to Institution (Ongoing); Nucana: Research Funding to Institution (Ongoing); Olema: Research Funding to Institution (Ongoing); OncoMed: Research Funding to Institution (Ongoing); Onconova Therapeutics: Research Funding to Institution (Ongoing); ORIC Pharmaceuticals: Research Funding to Institution (Ongoing); Orinove: Research Funding to Institution (Ongoing); Orum Therapeutics: Consulting Fees to Institution (Ongoing); Pfizer: Consulting Fees and Research Funding to Institution (Ongoing); PharmaMar: Research Funding to Institution (Ongoing); Pieris Pharmaceuticals: Research Funding to Institution (Ongoing); Pionyr Immunotherapeutics: Research Funding to Institution (Ongoing); Plexxikon: Research Funding to Institution (Ongoing); Propella Therapeutics: Consulting Fees to Institution (Ongoing); Puma Biotechnology: Consulting Fees to Institution (Ongoing); Radius Health: Research Funding to Institution (Ongoing); Regeneron: Research Funding to Institution (Ongoing); Relay Therapeutics: Consulting Fees and Research Funding to Institution (Ongoing); Repertoire Immune Medicine: Research Funding to Institution (Ongoing); Rgenix: Research Funding to Institution (Ongoing); Roche/Genentech: Consulting Fees and Research Funding to Institution (Ongoing); SeaGen: Consulting Fees and Research Funding to Institution

(Ongoing); Sermonix Pharmaceuticals: Research Funding to Institution (Ongoing); Shattuck Labs: Research Funding to Institution (Ongoing); Silverback: Consulting Fees and Research Funding to Institution (Ongoing); StemCentRx: Research Funding to Institution (Ongoing); Sutro: Research Funding to Institution (Ongoing); Syndax: Research Funding to Institution (Ongoing); Syros: Research Funding to Institution (Ongoing); Taiho: Research Funding to Institution (Ongoing); TapImmune: Research Funding to Institution (Ongoing); Tesaro: Research Funding to Institution (Ongoing); Tolmar: Research Funding to Institution (Ongoing); Torque Therapeutics: Research Funding to Institution (Ongoing); Treadwell Therapeutics: Research Funding to Institution (Ongoing); Verastem: Research Funding to Institution (Ongoing); Vincerx Pharma: Research Funding to Institution (Ongoing); Zenith Epigenetics: Research Funding to Institution (Ongoing); Zymeworks: Research Funding to Institution (Ongoing)

Mafalda Oliveira, MD, PhD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Terminated, September 21, 2022), Other financial benefit (Terminated, September 21, 2022); Eisai: Contracted Research (Terminated, September 21, 2022), Travel grant (Terminated, September 21, 2022); Gilead: Consulting Fees (e.g., advisory boards) (Terminated, September 21, 2022), Contracted Research (Terminated, September 21, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, September 21, 2022), Travel grant (Terminated, September 21, 2022); Guardant Health: Consulting Fees (e.g., advisory boards) (Terminated, December 31, 2020); iTEOS: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Terminated, September 21, 2022), Contracted Research (Terminated, September 21, 2022); Novartis: Contracted Research (Terminated, September 21, 2022), Other financial benefit (Terminated, September 21, 2022); Pfizer: Consulting Fees (e.g., advisory boards) (Terminated, September 21, 2022); Relay Therapeutics: Consulting Fees (e.g., advisory boards) (Terminated, September 21, 2022); Roche: Consulting Fees (e.g., advisory boards) (Terminated, September 21, 2022), Contracted Research (Terminated, September 21, 2022), Other financial benefit (Terminated, September 21, 2022); SeaGen: Consulting Fees (e.g., advisory boards) (Terminated, September 21, 2022), Contracted Research (Terminated, September 21, 2022)

Eva Ciruelos, MD, PhD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer,: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Travel, accommodations, expenses (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Travel, accommodations, expenses (Ongoing)

Peter Kabos, MD: AstraZeneca: Contracted Research (Ongoing); Genentech: Contracted Research (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Pfizer: Contracted Research (Ongoing); Radius Health: Contracted Research (Ongoing); Sanofi: Contracted Research (Ongoing)

Manish R Patel, MD: Accutar Biotech: Research Funding (Ongoing); Acerta Pharma: Research Funding (Ongoing); Adagene: Research Funding (Ongoing); Adaptive Biotechnologies: Honoraria (Ongoing); ADC Therapeutics: Research Funding (Ongoing); Agenus: Research Funding (Ongoing); Aileron Therapeutics: Research Funding (Ongoing); Artios: Research Funding (Ongoing), Research Funding (Ongoing); Astellas: Research Funding (Ongoing);

AstraZeneca: Research Funding (Ongoing); Bayer: Honoraria (Ongoing); BioNTech AG: Research Funding (Ongoing); BioTheryX: Research Funding (Ongoing); Black Diamond Therapeutics: Research Funding (Ongoing); Blueprint Medicines Corporation: Research Funding (Ongoing); Boehringer Ingelheim: Research Funding (Ongoing); Celgene: Research Funding (Ongoing), Speakers Bureau (Ongoing); Checkpoint Therapeutics: Research Funding (Ongoing); CicloMed: Research Funding (Ongoing); Clovis Oncology: Research Funding (Ongoing); Cytair Therapeutics: Research Funding (Ongoing); Daiichi Sankyo: Research Funding (Ongoing); EMD Serono: Research Funding (Ongoing); Evelo Therapeutics: Research Funding (Ongoing); Exelixis: Speakers Bureau (Ongoing); FORMA Therapeutics: Research Funding (Ongoing); Genentech: Honoraria (Ongoing); Genentech/Roche: Research Funding (Ongoing), Speakers Bureau (Ongoing); Gilead Sciences: Research Funding (Ongoing); GlaxoSmithKline: Research Funding (Ongoing); H3 Biomedicine: Research Funding (Ongoing); Hengrui Therapeutics: Research Funding (Ongoing); Hutchison MediPharma: Research Funding (Ongoing); IgM Biosciences: Research Funding (Ongoing); Ignyta: Research Funding (Ongoing); Immunogen: Research Funding (Ongoing); Incyte: Research Funding (Ongoing); ION Pharma: Leadership Role (Ongoing); Jacobio: Research Funding (Ongoing); Janssen: Research Funding (Ongoing); Janssen Oncology: Honoraria (Ongoing); Klus Pharma: Research Funding (Ongoing); Kymab: Research Funding (Ongoing); Lilly: Research Funding (Ongoing); Loxo: Research Funding (Ongoing); LSK Biopartners: Research Funding (Ongoing); Lycera: Research Funding (Ongoing); Mabspace: Research Funding (Ongoing); MabSpace Biosciences: Research Funding (Ongoing); MacroGenics: Research Funding (Ongoing); Merck: Research Funding (Ongoing); Millennium: Research Funding (Ongoing); Mirati Therapeutics: Research Funding (Ongoing); Moderna Therapeutics: Research Funding (Ongoing); NGM Biopharmaceuticals: Research Funding (Ongoing); Novartis: Research Funding (Ongoing); Nurix: Research Funding (Ongoing), Research Funding (Ongoing); Olema: Research Funding (Ongoing); ORIC: Research Funding (Ongoing); Pfizer: Honoraria (Ongoing), Research Funding (Ongoing); Pfizer/EMD Serono: Consulting Fees (e.g., advisory boards) (Ongoing); Pharmacyclics: Honoraria (Ongoing); Pharmacyclics/Janssen: Consulting Fees (e.g., advisory boards) (Ongoing); Placon: Research Funding (Ongoing); Portola Pharmaceuticals: Research Funding (Ongoing); Prelude Therapeutics: Research Funding (Ongoing); PureTech: Research Funding (Ongoing), Research Funding (Ongoing); Relay Therapeutics: Research Funding (Ongoing); Ribon Therapeutics: Research Funding (Ongoing); Samumed: Research Funding (Ongoing); Seven and Eight Biopharmaceuticals: Research Funding (Ongoing); Silicon Therapeutics: Research Funding (Ongoing); Syndax: Research Funding (Ongoing); Taiho Pharmaceutical: Research Funding (Ongoing), Speakers Bureau (Ongoing); Takeda: Research Funding (Ongoing); TeneoBio: Research Funding (Ongoing), Research Funding (Ongoing); Tesaro: Research Funding (Ongoing); TopAlliance BioSciences Inc: Research Funding (Ongoing); Treadwell: Research Funding (Ongoing); Treadwell Therapeutics: Research Funding (Ongoing); Vigeo: Research Funding (Ongoing); Zymeworks: Research Funding (Ongoing)

Maria Borrell, n/a: No financial relationships to disclose

Howard Burris, n/a: AbbVie: Research Funding (Ongoing); Agios: Research Funding (Ongoing); Arch Oncology: Research Funding (Ongoing); ARMO Biosciences: Research Funding (Ongoing); Array Biopharma: Research Funding (Ongoing); Arvinas: Research Funding (Ongoing); AstraZeneca: Research Funding (Ongoing); Bayer: Research Funding (Ongoing); BeiGene: Research Funding (Ongoing); BioAtla: Research Funding (Ongoing); BioMed Valley Discoveries: Research Funding (Ongoing); BioTheryx: Research Funding (Ongoing); Boehringer Ingelheim: Research Funding (Ongoing); Bristol-Myers Squibb: Research Funding (Ongoing); CALGB: Research Funding (Ongoing); CicloMed: Research Funding (Ongoing); Coordination Pharmaceuticals: Research Funding (Ongoing); eFFECTOR Therapeutics: Research Funding (Ongoing); EMD: Research Funding (Ongoing); EMD Serono: Research Funding (Ongoing); Foundation Medicine: Research Funding (Ongoing);

GalaxoSmithKline: Research Funding (Ongoing); Gossamer Bio: Research Funding (Ongoing); Harpoon therapeutics: Research Funding (Ongoing); Hengrui Therapeutics: Research Funding (Ongoing); InCyte: Research Funding (Ongoing); Janssen: Research Funding (Ongoing); Jounce Therapeutics: Research Funding (Ongoing); Kymab: Research Funding (Ongoing); Lilly: Research Funding (Ongoing); MacroGenics: Research Funding (Ongoing); MedImmune: Research Funding (Ongoing); Merck: Research Funding (Ongoing); Millenium: Research Funding (Ongoing); Moderna: Research Funding (Ongoing); NGM Biopharmaceuticals: Research Funding (Ongoing); Pfizer: Research Funding (Ongoing); Revolution Medicines: Research Funding (Ongoing); Roche: Research Funding (Ongoing); Ryvu Therapeutics: Research Funding (Ongoing); SeaGen: Research Funding (Ongoing); Tesaro: Research Funding (Ongoing); TG Therapeutics: Research Funding (Ongoing); Verastem: Research Funding (Ongoing); Vertex Pharmaceuticals: Research Funding (Ongoing); XBiotech: Research Funding (Ongoing); Zymeworks: Research Funding (Ongoing)

Bruno de Paula, n/a: AstraZeneca: Salary (Ongoing)

Alejandro Falcon, Oncologist: Grunenthal: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing)

Cristina Hernando, MD, PhD: No financial relationships to disclose

Irene Moreno, MD: No financial relationships to disclose

Ciara S. O'Brien, MD, PhD: Astra Zeneca: Conference attendance (Terminated, December 1, 2021); Lilly Oncology: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing)

Elena Shagisultanova, MD, PhD: Novartis: Funding for investigator initiated clinical trials (Ongoing); Pfizer: Funding for investigator initiated clinical trials (Ongoing); Seagen: Funding for investigator initiated clinical trials (Ongoing)

Ivan Victoria Ruiz, n/a: No financial relationships to disclose

Judy S. Wang, MD: No financial relationships to disclose

Mei Wei, MD: Gilead Science: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022); IntrinsiQ Specialty Solution: Royalty (Terminated, May 12, 2022); OncLive.com: Royalty (Terminated, February 28, 2022); Targetedonc.com: Royalty (Terminated, April 11, 2022)

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Danielle Carroll, n/a: AstraZeneca: Salary (Ongoing)

Carmela Ciardullo, n/a: AstraZeneca: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Research Funding (Ongoing), Salary (Ongoing)

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Christopher Morrow, PhD: AstraZeneca: Employee (Ongoing), Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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Richard D. Baird, MD, PhD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Boehringer-Ingelheim: Contracted Research (Ongoing); Carrick Therapeutics: Contracted Research (Ongoing); Daiichi-Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Genentech: Contracted Research (Ongoing); Molecular Partners: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Shionogi: Contracted Research (Ongoing)

12/7/2022

5:00 PM - 6:15 PM

P3-08-01

Loss of NF1 drives hormone dependent mammary carcinogenesis in a rat model with intact immune system

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Loss of NF1 plays a major role as an oncogenic driver in many cancer types and can be found in up to 33% of all breast cancers (BC). Loss of NF1 is also a prognostic indicator for increased cancer risk at an earlier age, poorer outcomes, and therapeutic resistance. In addition, certain NF1 genotypes may increase cancer risks, while others do not. NF1 is largely perceived as a classic Ras-opathy syndrome due to inactivating mutations in neurofibromin affecting RAS-MAPK signaling. However, recently it has been shown that NF1 binds estrogen receptor alpha (ER) and acts as a transcriptional corepressor. This helps explain some BC findings specifically in ER+ BC. In this model, specific changes to NF1 that abrogate ER signaling lead to Ras driven tumor resistance to endocrine therapy as cells are able to grow in low levels of E2 (and tamoxifen). Hence, NF1-mutant tumors represent a distinct molecular class in need of new therapeutics. A preclinical mammalian model of NF1 loss and BC would be helpful in both evaluating the role of NF1/ER transcriptional signaling in BC, evaluating the role of immune cells in BC, and testing therapeutics. Novel Nf1 rat models have a very robust ER+ BC phenotype, therefore more closely recapitulating clinical tumors compared to other preclinical models. Our models include a pathogenic patient missense allele c.3827G>A, p.R1276Q (knockin or KI), associated in humans with familial spinal NF1 and malignancy, as well as a 14 base pair deletion c.3661_3674del, p.P1220fs*1223 (knockout or KO) model. Heterozygous (het) Nf1 females develop mammary gland adenocarcinoma spontaneously, but het KO rats develop multiple tumors with earlier onset while het KI rats tend to develop fewer tumors with later onset. Tumors are generally Grade 2 and do not differ by genotype. By 16 weeks, 70% of

KO females have developed at least one tumor whereas only 20% of KI rats and 2% of WT rats have developed tumors. This impacts survival as by 1 year 76% of KI females survive yet only 58% of KO females survive. However, by 2 years, both alleles have 54% survival. The divergence in phenotype between patient and null alleles may be due to residual function of R1276Q missense NF1 protein. A more in-depth analysis indicates that mammary tumor formation likely begins relatively early, as we find evidence of aberrant morphology and hyperplasia prior to the formation of palpable tumors. Interestingly, we find histological evidence of lung metastases and expression of breast markers GCDFP15, MGA, and CEA in the lung. Again, we see allele-specific effects in that KO rats develop lung tumors earlier than KI rats. While het male rats also develop mammary tumors at low rates, they experience longer survival times (76% of KO males survive 1 year and 98% of KI males survive 1 year) and males also develop tumors in other locations. Using single nuclei RNASeq to characterize the transcriptional profile of the mammary tumors, we find allele-specific effects beyond repression of Ras activity that drive aggressive tumor development. We identified different tumor cell populations (2 epithelial cell populations, Myeloid cells, B cells, T cells, Basal mammary cells, and WT specific cells) and identified different pathways altered due to the loss of Nf1 including Ephrin B signaling, Cyclin and Cell Cycle signaling, and Glycolysis signaling. Our overall goal is to characterize the phenotype of these rat models in terms of histopathology, Ras signaling, hormone signaling, immune components, and targeted drug response and compare/contrast them with what is known regarding patients with somatic or germline inactivation of NF1 and breast cancer. Ultimately, this will provide better prognostic predictions for patients and better therapeutic options for treatment.

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P3-08-02

Prospective Use of Feline Mammary Carcinomas to Study MiR-10b and Metastasis

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Despite many advances in cancer treatment, metastatic disease is estimated to be responsible for 90% of all cancer-related deaths. Current treatments for metastatic disease target various aspects of carcinogenesis but not specifically the metastatic process, representing a major unmet clinical need. MicroRNA-10b, a small non-coding RNA, offers tremendous potential as a treatment target for metastatic disease. It is implicated in invasion, migration, and viability of metastatic cells across a variety of cancer types, and it is upregulated in metastases compared to their matched primary tumor, establishing miR-10b as a potential treatment target unique to metastatic niche. We have previously developed a therapeutic targeting miR-10b in metastases and tested it in murine models of metastatic breast cancer. This therapeutic, consisting of an anti-miR-10b antisense oligonucleotide conjugated to iron oxide-based nanoparticles, prevents metastasis and eradicates pre-existing metastases in murine breast cancer models. With an outlook to clinical translation of our approach, we seek to test our therapeutic strategy in larger animal models. Feline mammary carcinomas are considered by most to be the best large animal model for human breast cancer due to similarities such as relative age of onset, histopathology, metastatic patterns, and treatment response. To support the use of this model with our therapeutic, we investigated the characteristics of miR-10b expression in spontaneous metastatic breast cancer in companion cats. Archival blocks of matched primary tumors and metastatic lymph nodes from companion cats diagnosed with mammary carcinoma (n=9, 44%TNBC, 56%HER2+) were obtained from the tissue bank of the Michigan State University (MSU) Veterinary Diagnostic Laboratory (VDL). Tissues were analyzed for miR-10b and its target HOXD10 expression using qRT-PCR and in situ hybridization. qRT-PCR revealed that miR-10b expression was significantly upregulated in 55.5% of lymph node metastases compared to their matched primary tumor, mirroring findings in human metastatic cancer. This was validated by qRT-PCR for HOXD10 gene expression (a direct target of miR-10b), which was significantly downregulated in these metastases compared to their matched primary tumor. In situ hybridization demonstrated that miR-10b expression was increased at the invasive edge of tumors and in actively invading cells, suggesting miR-10b plays a similar role in invasion in

feline breast cancer as it does in human breast cancer. Altogether, these findings support the use of feline mammary carcinomas as a model of human breast cancer and as an excellent candidate for treatment with our therapeutic.

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P3-08-03

Establishment of patient-derived xenograft tumor models from breast cancer patients for quantitative elemental profiles and testing candidate therapies

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Breast cancer (BC) is a heterogeneous disease comprising different clinical, histopathological, and molecular subtypes. Triple negative breast cancer (TNBC) is among the most aggressive clinical manifestations of breast cancer (BC), and represents a significant clinical challenge to the effective treatment of early metastatic and treatment-refractory disease because of its poor outcomes. Therefore, there exists a need to develop pre-clinical models that retain the characteristics of the original TNBC tumor—e.g., PDX tumor models—to better understand the mechanisms of drug resistance in metastatic TNBC and to effectively evaluate the effects of anti-cancer drugs on patients with this disease. Furthermore, quantitative changes in cellular element signatures, which indicate levels of enzymatic activity, are emerging new biomarkers for cancer in the clinic, but are of yet systematically understudied in tumor samples from breast cancer patients or/and PDX models of these tumors. Due to limitations in current cellular element signature quantitation profiles, there also exists a need to investigate further. Seven samples of advanced BC patient pleural effusion were obtained from Northwestern Memorial Hospital to establish a PDX tumor model in immunodeficient NSG female mice using breast fat pad xenografting and to develop derived 3D spheroid cultures for anti-cancer drug evaluation. To authenticate, STR profiling against with original patient tumor DNA was conducted. Five developed BC PDX tumor models were shown by pathology to have highly heterogeneous characteristics and the metastatic features of the origin patient tumor. Liver and lung metastases were observed in breast fat pad xenografted PDX tumor mice. 3D tumor spheroid cultures were successfully established from original BC pleural effusion or/and PDX tumor

cultures. Using the newly developed, highly sensitive, and reliable Wash-Free Inductively Coupled Plasma Mass Spectrometry (WF ICP-MS) method, we evaluated the inorganic phenotypes from samples of breast cancer patient tumor tissue and of the established PDX tumor to quantify the mobile elements (Na, K, and Ca) and less mobile elements (P, Mg, Mn, Fe, Cu, and Zn) simultaneously within the same sample. The data was collected for further analysis of breast cancer inorganic signatures from normal and tumor cells. Our results suggested that BC 3D spheroid cultures and PDX tumor models could serve as models to further study the mechanisms of MBC and serve as promising tools for in vivo and in vitro quick testing and mechanistic studies of novel antitumor drugs respectively. Identifying quantitative elemental profiles is fundamental to understanding the pathologies of various metal-related cancers and thus opens up new opportunities for disease management and therapeutic intervention

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Discovery of cancer genes and pathways operative in PI3K-activated mammary cancer reveals clinically relevant genotype-phenotype correlations.

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Human breast cancer (BRCA) shows tremendous genomic, gene expression, clinical, and phenotypic heterogeneity. Known driver gene alterations can only explain a portion of this heterogeneity, some of which likely arise from variation in the target cell for transformation, in addition to incompletely understood gene copy number and epigenetic alterations. These factors are difficult to identify with certainty using human patient samples due to widely varying germline genetic backgrounds, thousands of gene copy and epigenetic changes per sample, and, unknown target cell transformation. Activating mutations in the p110 α catalytic subunit of PI3K are one of the most common genetic alterations in human BRCA. Here, we report results from two Sleeping Beauty (SB) transposon-accelerated mouse models of Pik3ca-mutant

mammary cancer showing how genotype-phenotype correlations can be drawn providing strong candidates for mediating tumor phenotypes, including estrogen-receptor (ER)-dependent gene expression, high cell cycle activity, and immune cell exclusion. We used SB transposon mutagenesis in mice on a Pik3caH1047R activated mutant background to model mammary cancer development in two different mammary epithelial compartments. Both the target cell for mutagenesis and the specific transposon-induced mutations correlated with specific tumor phenotypes, including whether the tumors were ER positive or negative. RNA sequencing of tumors revealed novel genotype-phenotype correlations implicating specific transposon-altered gene drivers of high cell cycle activity, ER-dependent gene expression, and white blood cell exclusion from the tumor. Many transposon-implicated genes are altered at the gene copy number or epigenetic/methylation level in human BRCA, and several were functionally validated. These models provide a source of genetically heterogeneous mouse mammary tumors with a uniform initiating mutation, Pik3caH1047R, useful for identifying cooperating pathways and drivers of specific tumor phenotypes.

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Correlation of Trop2 expression with in vivo sensitivity to sacituzumab govitecan in a panel of breast XPDX models

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Background: Sacituzumab govitecan (SG) is an antibody-drug conjugate targeting Trop2 with an SN-38 payload recently approved for pretreated patients with locally advanced or metastatic triple-negative breast cancer (TNBC). The XenoSTART Patient-Derived Xenograft (XPDX) breast cancer platform includes over 180 models spanning all subtypes characterized with immunohistochemistry (IHC) including ER α , PR, and HER2 protein levels, genomic and transcriptomic sequencing, and in vivo drug sensitivity. To better understand potential benefit of SG in breast cancers other than TNBC and further annotate our platform, Trop2 protein levels were determined in all breast models by IHC. We evaluated tumor growth inhibition by SG in 125 of our XPDX breast models and compared protein expression with agent activity. Methods: 180 breast XPDX models were evaluated for Trop2 expression (AF650, R&D Systems) and 125 were evaluated in vivo against SG; responses were grouped by ER and Trop2 status (+/-). Models were grown subcutaneously in female athymic nude mice and ER+ models supplemented with estradiol. Models were also characterized for PR, HER2, and AR protein expression by IHC and profiled using WES and RNAseq. For in vivo studies, SG was administered by intravenous injection biweekly for two cycles at 1 mg, flat; endpoints included tumor volume and time from treatment initiation with %T/C values and tumor regression reported at study completion; a T/C of $\leq 20\%$ versus control was considered sensitive. Tumor regression (%T/C < 0%) versus Day 0 tumor volume was also reported. Results: 180 breast models were examined by IHC with 75/180 (42%) classified as ER+ and 105/180 (58%) ER-. In ER+ models 38/75 (51%) were Trop2+ and 37/75 (49%) Trop2-, and in ER- models 41/105 (39%) were Trop2+ and 64/105 (61%) Trop2-. In vivo, 20% of ER+/Trop2+ models reported sensitivity to SG, most notably models from patients with acquired resistance to CDK4/6 inhibitors, including STM001 and ST4316B. Interestingly, >70% of ER+/HER2+/Trop2+ models were insensitive to SG, including ST225 and ST340. Of 41 ER-/Trop2+ models, approximately 40% reported some response to SG with 50% of these sensitive to therapy, including ST5954 established from a patient who began treatment with SG following sample collection and is currently in remission. >75% of Trop2- models were insensitive to SG regardless of ER status. Conclusion: We screened 180 models in our XPDX breast cancer platform for Trop2 expression and compared expression with in vivo SG efficacy in 125 models. Analysis is underway to correlate receptor and molecular profiles with SG sensitivity in breast models and we are expanding expression and in vivo testing to additional indications.

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Monitoring Lymphovascular Invasion and Tumor Growth of Inflammatory Breast Cancer in a Murine Lymphatic Reporter Window Chamber Model

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Background: Lymphovascular invasion (LVI) is a major route of metastatic dissemination and recent studies indicate its value as an independent prognostic indicator for advanced breast, colorectal, squamous cell, prostate, brain cancers. LVI is a clinicopathological hallmark of inflammatory breast cancer (IBC), an understudied and most lethal breast cancer. IBC is often misdiagnosed due to an absence of a solid mass and its unique presentation of diffuse tumor cell clusters/emboli in the dermal lymphatics. Widely used mammary tumor implantation models coupled with bioluminescence or fluorescence imaging to monitor tumor growth kinetics are ineffective for evaluating spatial and temporal changes in growth and migration patterns of individual tumor cells and clusters within their microenvironmental context. The goal of this study was to develop a murine model to simulate the unique clinicopathological features of IBC patients and to assess both qualitatively and quantitatively local tumor growth, motility, and LVI.

Methods: To specifically facilitate visualization of lymphatic and endothelial vessels along with tumor-vessel interactions, we generated a transgenic nude mice model (ProxTom RFP Nu/Nu) wherein, the mice exhibit red, fluorescent lymphatics [tdTomato fluorophore under control of a Prox1 promoter, which encodes a transcription factor (prospero-related homeobox 1) necessary for the formation and maintenance of lymphatic vessels]. Next, we employed a surgical technique, wherein a window chamber is placed on the dorsal skinfold of mice, which allows for microscopic examination of implanted tumor cells and ability to track dynamic changes of the tumor in its local microenvironment from the time of implantation up to 10 days. Patient-derived IBC or PDX stably transfected to express green, red fluorescent and/or dual tagged with luciferase reporters were transplanted in mice bearing window chambers. Intravital fluorescence microscopy and IVIS imaging were used to serially quantify local tumor growth, motility, length density of lymph and blood vessels, and degree of tumor cell lymphatic invasion over 0-140h. Results: Multichannel optical imaging of the window chamber in the ProxTom RFP Nu/Nu mice demonstrated co-localization of IBC tumor cells and lymphatics. Diffuse tumor cells were observed along regions of lymphatic vessels both proximal and distal to the primary tumor site. However, measurement of blood and lymph vessel density showed no significant change over time. Next, these datasets were used for quantitative analysis by setting the tumor cell channel (GFP) at a threshold to count any clusters greater than 50 pixels² (~0.0013mm²) and with greater than the mean + 2 standard deviations of the background signal while avoiding noise/artifacts from very small regions (<~0.001mm²). This allowed for computation of the total tumor area including average area of each cluster. In addition, the area moment, which describes the basic directional growth pattern of the tumor cells, was quantified by multiplying a cluster distance from the center of mass by its area. Conclusions: A key novel finding from structured illumination imaging data was the observation of LVI occurring early, similar with the clinical presentation in IBC patients. This model was able to effectively track tumor cluster migration. This approach of short-term longitudinal imaging time frame in studying transient or dynamic events of diffuse, collectively migrating tumor cells in the local environment and quantitative analysis of the tumor area, motility and vessel characteristics is an innovation that can be used to investigate other cancer cell types exhibiting LVI. Funding in part by DoD W81XWH-17-1-0297; W81XWH201053 (GRD); ACS Mission Boost grant MBG-20-141-01 (GRD) and NIH grant P30-CA014236 (Imaging Core/GMP)

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Self-renewal signatures of peripheral blood T cells are associated with successful engraftment to establish a humanized mouse model of breast cancer

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Background: Stable humanized immune mice transplanted with peripheral blood mononuclear cells (PBMcs) derived from breast cancer patients are important models for assessing the tumor immune responses and the tumor immune microenvironment in breast cancer, helping to advance both pre-clinical and clinical research. The PBMcs of breast cancer patients exhibit various differences from those of healthy individuals depending on the stage of cancer progression, subtype, and type of treatment. Recent studies indicate an association of the self-

renewal signatures of T cells with successful generation of a humanized mouse model; however, the optimal T cell signature for the successful generation of a humanized mouse model derived from cancer patient cells is poorly understood. Therefore, we examined the relationship between the signature of T cell subsets, focusing on the self-renewal signatures, in PBMCs derived from patients with breast cancer and the successful generation of a humanized immune mouse model. **Materials and Methods:** We collected PBMCs from 12 patients with breast cancer. All samples were stimulated with interleukin-2 and beads coated with CD3 and CD28 agonist antibodies to expand T cells. After washing, 1×10^7 cells/mouse were intraperitoneally injected into NOD/Shi-scid IL2rgamma (null) (NOG) mice. Transplants were performed on three mice per case. Successful engraftment of immune cells into NOG mice was defined by the presence of human CD45+ cells in one or more mice. Self-renewal signatures of in vitro expanded T cells before injection into NOG mice, including the markers T cell factor-1 (TCF-1), CD45RA, CCR7, CD95, and CXCR3, were determined using flow cytometry, mass cytometry and quantitative RT-PCR. Comparisons between groups of data were evaluated by t-test. **Results:** The success rate of engraftment of immune cells derived from breast cancer patients into NOG mice was 66.7% (8 out of 12 patients). After expansion, the magnitude of the CD8+ stem cell memory subset and the TCF-1 expression level on the CD4+ and CD8+ T cells in the engrafted group were significantly higher than those in non-engrafted group. TCF-1 and CCR7 mRNA levels in the engrafted group were upregulated compared with those in non-engrafted group. The success of engraftment was not associated with clinical characteristics such as breast cancer progression, subtype, or prior chemotherapy treatment. **Conclusion:** The self-renewal signatures of T cells from breast cancer patients were associated with successful engraftment of a humanized mouse model. These results suggest that prior identification of the self-renewal signatures of the T-cell population is of direct relevance to the appropriate design of a pre-clinical model for testing immunotherapies and for elucidating the characteristics of the tumor immune microenvironment.

Disclosure(s):

Yukiko Fukui, MD: No financial relationships to disclose

Kosuke Kawaguchi, MD, PhD: Astellas: Contracted Research (Ongoing); Becton Dickinson Japan: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Chugai: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Daiichi Sankyo: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Eisai: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Eli Lilly: Contracted Research (Ongoing); KBCRN (Kyoto Breast Cancer Research Network): Contracted Research (Ongoing); Takeda: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); TERUMO: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Contracted Research (Terminated, June 30, 2022)

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5:00 PM - 6:15 PM

P3-08-08

Establishment of a Breast Cancer Rat Model of Chemotherapy-Induced Cardiotoxicity

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Establishment of a Breast Cancer Rat Model of Chemotherapy-Induced Cardiotoxicity

Katherine Wallis, Marjan Boerma, Antiño Allen, Joseph Su, Sam Makhoul, Ping-Ching Hsu
Background. Doxorubicin (DOX) is a highly effective chemotherapy agent that is commonly used in combination with precision medicine to treat a wide range of cancers, including 32% of breast cancer (BC) cases. Although the treatment has greatly increased the number of long-term cancer survivors, it has also increased the number of patients experiencing DOX-induced cardiotoxicity (DIC). Animal models have played a vital role in the development of basic and translational breast cancer research in humans, and rat is a preferred animal to study breast cancer for the similarity to human neoplasms and metabolism. However, most studies were established using mouse models, male rats and commonly non-cancer bearing animals. Currently no single universal cancer-bearing female rat model is utilized for DOX-induced chronic cardiotoxicity. The number of cancer cells to be injected to mimic human experience is not known. Large numbers of injected cancer cells grow quickly and kill the animal before the investigators have the time to assess for cardiac toxicity. Here we aimed to identify the minimal number of cancer cell injections to mimic tumor growth of BC patients and to achieve chemotherapy-induced toxicities. Methods. Various numbers (5×10^4 – 1×10^6) of MAT B III

adenocarcinoma cancer cells derived from Fischer 344 (F344) rats were injected in the mammary fat pad of female F344 rats, followed by six intraperitoneal (IP) injections of either DOX (1.25mg/kg per dose) or saline post tumor cell injection. The treatments were administered on day 4 from cell injection, and every third day after for a total of six injections. Echocardiography (Vevo 3100, VisualSonics) was conducted before and after the end of chemotherapy. Results. Tumor burden reduced significantly among rats treated with DOX compared with the saline group. In the Kaplan-Meier survival curve, an injection of 5×10^4 cancer cells was associated with tumor growth but the tumor burden was low enough to allow long-term follow-up of both DOX and saline treated rats and assess signs of cardiotoxicity. At 4 days after the final DOX administration, increased left ventricular ejection fraction and fractional shortening in the absence of increased stroke volume were an indication of adverse cardiac effects in the DOX animals but not the saline-treated rats. Plasma was collected from the animals to be subjected to metabolomics testing so that a preliminary assessment of metabolites associated with DIC could be gathered. Conclusion. We have established a breast cancer rat model in which DIC can be studied. Research in this model can aid in identifying mechanisms of DIC and testing novel interventions.

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P3-08-09

Development and molecular characterization of hard-to-treat breast cancer pre-clinical models to enhance precision medicine

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Invasive breast carcinoma is a combination of heterogeneous diseases with distinct molecular and clinical features. Some subsets of breast cancer present major clinical challenges, including triple-negative, metastatic/recurrent disease and rare breast histologies. Previously, we developed a unique resource of 37 hard-to-treat breast cancer patient-derived xenografts (PDX). This set included mainly triple negative breast cancer (TNBC) patients that presented poor response to neoadjuvant chemotherapies (Savage et al. 2020 - PMID: 32546838). PDXs accurately reproduce the molecular heterogeneity of the primary tumors and show that multi-

drug chemoresistance was retained upon xenotransplantation. Here, we present the characterization of PDX 3-dimensional cultures organoids (8) and PDX derived epithelial cell lines (11). Using single-cell RNAseq we showed that an organoid cultured for several passages (P8) maintained the heterogeneity of the matched PDX. Although in different proportions, all cancer cell populations found in the PDX were retained in matched organoids supporting that organoids are suitable models that recapitulates the tumor heterogeneity and are therefore a suitable model for drug screening. Among our new PDXs models (30), we have developed four PDXs from rare metaplastic breast cancers (MpBC), an aggressive subtype of breast cancer that present the poorest response to standard of care chemotherapy. We also developed one male breast cancer PDX with matched organoid. Omic analysis on our pre-clinical models and patient primary tumor and metastasis will inform development of therapeutic opportunities. This molecular information will guide selection of compounds that will be validated using our high throughput organoid drug screening pipeline. This will allow rapid screens of thousands of approved drugs, enhancing drug repurposing with potential for rapid clinical translation. The combined use of 3D tumor organoids and PDXs, is an important opportunity poised to transform identification of new therapeutic options for hard-to-treat lethal breast cancers.

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P3-08-10

Combining multiomics and histological assessment to identify patient derived xenograft models of invasive lobular carcinoma

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Background Most breast cancers (~85%) are of no special histologic subtype (NST), and the most common special subtype is invasive lobular cancer (ILC). ILC accounts for 10-15% of all breast cancers, and there will be ~40,000 new cases in 2022 in the US alone. If considered an "independent" cancer type, ILC is the 6th most common cancer in women. The pathognomonic feature of ILC is loss of E-cadherin (CDH1). The resulting lack of adherens junctions causes the unique single-file growth pattern of discohesive ILC cells, which decreases the ability for detection by mammography, in turn resulting in late detection and hence larger tumors. Although ILCs show better prognostic factors than NST, patients with ILC have worse long-term outcome, which is not well understood. Additionally, ILC has historically been understudied, which is in part due to lack of appropriate research models. For example, the Cancer Cell Line

Encyclopedia (CCLE) contains 54 NST cell lines but only 2 ILC cell lines, and only a limited number of patient-derived xenograft (PDX) models are evident in the published literature. There is a critical need for additional in vitro and in vivo models to study ILC biology, as well as to test targeted therapies. ILC PDX and patient derived xenograft organoids (PDXO) are particularly valuable tools to enable target validation and assess drug treatment response. Methods To identify and validate new ILC PDX models, we used Champions Oncology's Lumin Bioinformatics to screen Champions' collection of breast cancer models (n=126) for PDX harboring CDH1 mutation and/or low E-cadherin expression. We performed histological analysis on selected PDX models including H&E staining, and immunohistochemical assessment of E-cadherin, P120, estrogen receptor, progesterone receptor, HER2 and Ki67. Models with 2+ HER2 staining were assessed by FISH. All staining was interpreted by a certified breast pathologist. PDX tumor tissue was further used to develop PDXO models. Results Using Champions Oncology's Lumin tool, we identified 10 putative ILC PDX models based upon CDH1 mutation, low E-cadherin mRNA expression, or clinical annotation of ILC (Table 1). Of the 10 PDX models analyzed, two cases were clinically annotated as ILC, while the remainder were classified as 'carcinoma' (n=5) or as NST (n=3). Histologic analysis revealed loss of E-cadherin and cytoplasmic P120 (lobular pattern) in 8/10 models assessed, and pathologic assessment confirmed these as having a lobular histology. IHC analysis classified these PDXs as 5 TNBC and 5 ER+ tumors, with none showing amplification of HER2 by FISH. All tumors demonstrated high (35%, n=1) or very high (>55%, n=9) Ki67 proliferation marker levels. We further developed PDXOs from one PDX model as proof of concept, and the resulting organoid demonstrated classic 'grape-like' ILC morphology. Conclusion Our study demonstrates how existing PDX banks with in-depth multi-omic and pathology analyses can be interrogated to identify models of unique histological and molecular subtypes of breast cancer. Of the PDX models selected from Champions Oncology's breast cancer cohort, 7 models were classified as ILC either through re-classification from NST/carcinoma to ILC or confirmation of ILC histology. In addition, 1 PDX was re-classified as mixed type. Some of these models are ER+/HER- and thus have the classic molecular features of ILC. Our collaborative omics guided approach allows for reclassification of PDX models to increase available research models for unique breast cancer subtypes such as ILC which in turn will enhance translational research in unique histological subtypes of breast cancer.

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P3-08-11

Establishing Breast Cancer Patient-derived Xenografts from circulating cancer stem cells in the chorioallantoic membrane (CAM) Model

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Background: Circulating cancer stem cells (cCSCs) are a small aggressive subset of circulating tumor cells with cancer stem cells features: resistance to diverse cancer treatments and the capacity for generating new metastases. Patient-derived xenografts (PDX) are an increasingly accepted tool in oncology, providing biologically meaningful models of many cancer types, and potential platforms for the development of precision oncology approaches. Commonly, mouse models are used for the xenotransplant assessment of potential new therapeutic targets in cancers. However, animal models do not necessarily represent the real world scenario and are costly and time consuming. An attractive alternative to such animal experiments is the chicken chorioallantoic membrane (CAM) assay. CAM assay is increasingly used as a rapid cost-effective in vivo drug-testing platform that recapitulates many aspects of human cancers. Methods: In this study, primary cultures from circulating cancer stem cells were established using sphere-forming assays. Subsequently, tumorspheres were transplanted onto the CAM membrane of fertilized chicken eggs to form secondary microtumors. Histopathological analyses were performed to confirm that the CAM tumor had the original morphological profile of the patient tumor. Results: We have developed an innovative reliable in vitro platform for cultivation of CSCs from peripheral blood of breast cancer patients. The number of tumorspheres increased significantly with tumor progression. Patients with metastatic disease had statistically more tumorspheres as compared to patients without metastasis (30 vs 10/100 μ l blood, $p < 0.05$). Patients with multiple metastases had more tumorspheres compared to patients with single metastases (60 vs 30/100 μ l blood, $p < 0.05$). The number of tumorspheres was positively correlated with Ki-67, Her2 status and grade score in primary breast tumors. Tumorspheres showed self-renewal, growth potential, invasion and differentiation in vivo. Tumorspheres could be successfully grafted onto the CAM and grafting positively correlated with aggressiveness and proliferation capacity of the primary tumor. These tumors growing on the CAM pathologically closely resembled the primary tumor. Conclusion: The number of tumorspheres cultured from peripheral blood of cancer patients and the success rate of establishing PDX directly reflect the aggressiveness and proliferation capacity of the primary tumor. Our results support the CAM model using cCSC as a valuable alternative for xenotransplant models. It allows the establishment of new PDXs and provides a fast, cost-effective, and easy to use preclinical platform for cancer biology research, new drug development, treatment individualization, and biomarker discovery.

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P3-09-01

Characterization of residual disease after neoadjuvant selective estrogen receptor degrader (SERD) therapy using tumor organoids in the I-SPY Endocrine Optimization Protocol (EOP)

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Background: Treatment of estrogen receptor (ER)-positive breast cancer with selective estrogen receptor degraders (SERDs) frequently results in the loss or reduction of ER expression. Whether these changes are due to on-target effects of SERDs degrading ER or arise as a mechanism of tumor resistance with associated changes in cellular phenotypes remains unknown. It is critical to distinguish between these possibilities to accurately assess treatment response and determine the most appropriate subsequent therapy. To this end, we created and conducted molecular analyses on patient-derived organoid cultures from post-treatment tissue in patients receiving neoadjuvant SERD therapy for early-stage ER+ breast cancer in the I-SPY2 Endocrine Optimization Protocol (EOP). Methods: The I-SPY2 EOP study is a prospective, randomized substudy within the I-SPY TRIAL testing the oral SERD amcenestrant alone or in combination with letrozole or abemaciclib in stage 2/3 ER+ Her2-negative breast cancer. Enrollment is ongoing, with patients receiving amcenestrant neoadjuvantly for 6 months until the day before surgery. Tumor tissue is collected at baseline, 3 weeks, and at surgery. Organoids were generated from post-treatment surgical samples. Organoid cultures were optimized based on established methods (Dekkers et al., *Nature Protocols*, 2021) to assess ER levels and activity. Pre- and post-treatment tissue samples were also assessed for ER, PR, Ki67, and GATA3, a luminal marker and transcription factor that is

functionally linked with ER, via immunohistochemistry. Results: In 7 patients with both pre- and post-treatment tissue samples including fresh surgical samples for organoid generation, the ER in baseline tumor tissue was $\geq 90\%$ in all patients, PR ranged from 40-90%, and Ki67 ranged from 5-30%. In post-treatment surgical tissue from these cases, ER ranged from 0-30%, PR from 0-50%, Ki67 from $< 1\%$ -10%, and GATA3 was positive in 5 of 5 cases tested to-date. The creation of organoids from residual disease at surgery was attempted for these 7 patients, with organoids successfully propagated in 5 cases thus far. 3 of 5 organoid cultures were ready for analysis and in all cases strong ER and PR expression in organoids was observed after culture for > 1 month in the absence of amcenestrant. Detailed gene expression profiling (including Mammaprint/Blueprint) and gene set enrichment analyses (GSEA) to assess for intrinsic breast cancer subtype and ER activity in each sample and corresponding organoid culture are in progress and will be reported with the full dataset. Conclusion: Patient-derived organoid culturing of residual disease after neoadjuvant endocrine therapy is feasible. Neoadjuvant treatment with a SERD can render ER and PR low or absent at the time of surgical resection, which does not necessarily imply the presence of endocrine therapy resistant disease. The use of organoids and additional IHC markers (GATA3) demonstrate that receptor negativity may be an indicator of the drug hitting its target, suggesting ER signaling is still intact. In general, patient-derived tumor organoid cultures modeling residual disease states can be a useful adjunct to existing methods used to monitor the effects of neoadjuvant endocrine therapy and is being explored in the I-SPY EOP trial.

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5:00 PM - 6:15 PM

P3-09-02

Patient Derived Breast Cancer Organoids as a Model for Testing Personalized Therapies

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Introduction: Breast cancer is one of the most frequently diagnosed cancer in women with a high mortality rate. More than 20 different subtypes of breast cancer are identified. Advancement in patient-derived organoid technology makes it possible to preserve cellular, structural, and tissue microenvironment which mimics the tissue in vivo. Method: We developed patient derived breast organoids both from normal and cancer biopsies recapitulate the structure of breast tissue. Breast biopsies were enzymatically digested to yield a single cell suspension. About 1×10^5 cells were encapsulated in a specialized hydrogel mixture. Immune enhanced breast tumor organoids (iTOs) included 2×10^5 patient matched PMBCs. Results: Histological analyses of the breast organoids shows the characteristics of the breast tissue with well-defined acini in H&E. In tumor organoids acini were somewhat perturbed compared to normal breast organoids. Immuno-fluorescence staining shows the expression of breast biomarkers including EGF receptor 2 (HER2), Progesterone receptor (PR), Estrogen receptor (ER). Zona occludin 1 and 2 and keratin 19 expression in luminal cells and expression of Keratin 14 and P63 in basal cells suggested correct polarization in the organoids. Immunofluorescence staining of (iTOs), with T cell markers including CD3, CD4, and CD8 indicated that immune cells remained viable in the iTOs. Drug responses to Doxorubicin, Paclitaxel and a combination of Doxorubicin-Paclitaxel showed significant inhibition of cell growth in normal and tumor organoids ($p < 0.04$, $n=11$) except for Paclitaxel failed to inhibit tumor cell growth. However, immunotherapy with nivolumab (anti PD-1) showed no significant effect on cell growth. Conclusions: Patient Derived Breast cancer organoids recapitulate the histological features of breast tissue in culture and response to chemotherapies. In the future, patient-derived tumor organoids can provide a platform for personalized medicine.

Disclosure(s):

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P3-10-01

Deciphering the heterogeneity of cell cycle in breast cancer and relevance to clinical application of CDK inhibitors

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BACKGROUND: Deregulation of cellular proliferation represents a defining hallmark of cancer. The mechanisms driving aberrant cell cycle progression across different breast cancer subtypes is highly diverse and likely contributes to therapeutic resistance in a variety of contexts. The significance of cell cycle heterogeneity is most clear in the context of metastatic HR+/HER2- breast cancer, wherein acquired and intrinsic resistance to CDK4/6 inhibition represents a significant clinical challenge. However, aberrant cell cycle regulatory networks likely further confound the use of targeted therapies in the context of TNBC. **METHODS AND RESULTS:** We employed unbiased analyses of large number of breast cancer models to decipher the genetic requirements for different CDK and Cyclins which drive proliferation and the significance to response to CDK4/6 inhibitors. Breast cancer cells harbor heterogeneity in the requirement for a given G1/S regulatory CDK or Cyclin. These dependencies are conditioned by the expression of the respective CDK or Cyclin, as well as other gene expression or genetic features present within the tumor that could represent putative biomarkers. In general, conventional dependency for CDK4 and Cyclin D1 is strongest in HR+/HER2- breast cancer models, whereas TNBC exhibits dependency on a variety of different CDK or Cyclin genes. Resistance to CDK4/6 inhibitors in HR+/HER2- breast cancer models, while occurring through a number of different primary mechanisms, functionally deregulates the phosphorylation of RB. However, genetically enforcing RB activation is sufficient to block proliferation, underscoring the opportunity to ameliorate resistance to CDK inhibitory strategies. CRISPR screens in HR+/HER2- and TNBC models are identifying new mediators of sensitivity

and resistance to CDK4/6 inhibitors. Inherently, elevated expression of Cyclin E and p16INK4A are associated with resistance to multiple therapeutic approaches, including CDK4/6 inhibitors, but denote a requirement for CDK2. The cell cycle conditions disparately dependent on CDK4/D1 vs. CDK2/E can be visualized by multispectral imaging and used to direct CDK inhibitor based strategies. CONCLUSIONS: Together these studies illustrate the complex nature of breast cancer cell cycles which can confound therapy. However, understanding of this heterogeneity can create new opportunities for precision approaches targeting CDK/Cyclin-dependence therapeutically.

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P3-10-02

Cell cycle dysregulation in breast cancer: why the details matter

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Cell cycle dysregulation is a prerequisite for cancer formation. However, whether the type of cell cycle dysregulation event a cell incurs during transformation to malignancy influences the type of cancer that evolves or clinical outcome is unknown. In a comprehensive analysis of cell cycle dysregulation in breast cancer patient tumors, we associate mutations in each of four cell cycle checkpoint kinase genes, ATM, CHEK2, ATR and CHEK1, with known tumor characteristics and clinical outcome, and test these associations experimentally using transgenic mice, patient-derived xenografts and breast cancer cell line model systems. Results of this work demonstrate that dysregulation of specific cell cycle checkpoint kinases differently impacts the type of breast cancer that evolves in patients and in experimental model systems, and influences treatment responsiveness and disease progression. For instance, CHEK2 mutations associate preferentially with the incidence of metastatic, premenopausal estrogen receptor (ER)+/HER2- breast cancer in patient data ($p=0.001$) that is resistant to standard frontline therapy ($HR=6.15$, $p=0.01$). These associations appear causal when tested in an immune-competent genetically-engineered mouse model of Chk2 loss, in patient-derived xenograft, and in cell line experiments. On the other hand, ATR mutation by itself is not frequent in ER+/HER2- breast cancer, but co-incident mutation of ATR and TP53 is 2-fold enriched ($p=0.002$) and associates with metastatic progression ($HR=2.01$, $p=0.007$). Concordantly, ATR dysregulation induces metastatic phenotypes in ER+/HER- TP53 mutant,

but not in TP53 wildtype, cell lines. Together, these results systematize the impact of individual cell cycle checkpoint kinases on the evolution of cancer subtypes, and on disease progression. **Statement of Significance** These findings reframe the paradigm of breast cancer classification through the lens of early cell cycle dysregulation events by demonstrating that cell cycle decisions during malignant transformation can direct the type of breast cancer that evolves, how it will respond to treatment, and whether it will metastasize. This work provides rationale for streamlined testing of checkpoint kinase dysregulation to improve precision diagnostics for cancer patients.

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P3-11-01

Increasing DAXX Expression in ER+ Breast Cancer Cells to Overcome Endocrine Therapy Resistance

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Background: New treatment paradigms are needed to overcome resistance to endocrine therapy (ET; tamoxifen or aromatase inhibitors, AI) in ER+ breast cancer (BC). ET resistance is due to survival of breast cancer stem cells (BCSCs) that contribute to relapse of ER+ BC. Notch signaling drives BCSCs. In order to identify Notch specific biomarkers for the purpose of patient selection for anti-Notch therapy, we conducted a pre-surgical biomarker window study combining ET plus MK-0752, a γ -secretase inhibitor (GSI). Death Associated Protein 6 (DAXX) was discovered to be a novel Notch1 target gene and necessary for GSI-mediated inhibition of BCSCs. Subsequently, we found that DAXX alone was sufficient to inhibit BCSCs. In this current study, we investigated the mechanism by which high DAXX expression inhibited growth of ET resistant ER+ BC cells in vitro and in vivo. Methods: Isogenic ER+ BC cell lines (parental MCF-7, ET resistant MCF-7/5C, parental T47D, and ET resistant T47D-ED) were used. Cells were cultured in estrogen-deprived medium for more than 1 year to mimic AI use. DAXX was depleted using siRNA or overexpressed using a pCMV-expression vector. Bulk cell proliferation was analyzed in response to estrogen depletion or increasing concentrations of 17 β -estradiol. BCSC survival was measured using the mammosphere-forming assay. Tumor onset and burden were measured by injecting DAXX-expressing or depleted mammospheres into mammary fat pads of female, athymic nude mice. Recurrence of an ER+ PDX tumor (BCM 5097) was measured after withdrawal of estrogen. RNA sequencing identified enriched genes and pathways that required DAXX. Based on these results, cell death was assessed using Annexin V/7-AAD flow cytometry, PARP-1 and Caspase 8 cleavage, phosphorylation of JNK, and expression of apoptotic protein regulators, BIM, BAX, Bcl-2, and Bcl-xL. JNK signaling was inhibited using SB600125. Results: Estradiol stimulated proliferation of parental, ER+ MCF-7 and T47D cells. In contrast, estradiol inhibited proliferation of isogenic ET resistant MCF-7/5C and T47D-ED cells in a concentration and ER-dependent manner. Estradiol induced the DAXX protein in both ET sensitive and resistant cells. DAXX was required for BCSC survival in ET sensitive cells. However, once ER+ cells acquired resistance to ET, DAXX was necessary and sufficient to inhibit both bulk cell proliferation and BCSC survival, suggesting that increasing DAXX might be a novel approach to overcome ET resistance. In mice, high DAXX expression significantly inhibited tumor onset and burden of ET resistant tumors compared to DAXX-depleted tumors. Low DAXX expression was significantly associated with recurrence of an ER+

PDX tumor (BCM 5097) after withdrawal of estrogen. RNA sequencing revealed that DAXX activated an anti-neoplastic gene signature, including transcription factors that regulate cell death genes including the Bcl2-family. DAXX was required for high BIM expression and low levels of Bcl-xL. DAXX was necessary and sufficient to induce apoptosis, PARP-1 cleavage, and phosphorylation of JNK in ET resistant cells. A selective JNK inhibitor, SB600125 rescued DAXX-mediated inhibition of ET resistant bulk cell proliferation and BCSC survival, suggesting that high DAXX expression activates JNK signaling to regulate apoptotic proteins to induce cell death of BCSCs-derived from ET resistant BC. Conclusions: Expressing high DAXX levels is a potent method to inhibit ET-resistant BC cell proliferation and BCSC survival. The mechanism by which DAXX inhibits ET-resistant BC is through activation of JNK signaling, regulation of pro-apoptotic genes, and induction of apoptosis. The translational impact of this research is to identify novel agents that can increase DAXX expression and test them pre-clinically and in clinical trials for patients with ET-resistant breast cancer.

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5:00 PM - 6:15 PM

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CST1 Interaction with RAB1B Modulates Tamoxifen resistance of Breast Cancer by Regulating Autophagy

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Background:

Breast cancer is a prominent cause of cancer-related death among women worldwide. Approximately, 70% of breast cancers (BC) are estrogen and progesterone receptor-positive (HR+) at diagnosis. Adjuvant endocrine therapy is a pivotal component of treatment for this type of patient. Tamoxifen (TAM), a widely recommended drug in endocrine therapy, is confronted with a high risk of recurrence after 5 years of treatment among breast cancer patients, which shows big clinical demands. Therefore, it is urgent to find new targets for tamoxifen resistance therapy. Recently, our team found that enhanced expression of Cystatin SN (CST1) was detected in tissues that had undergone tamoxifen treatment appearing to recurrence and metastasis in ER-positive breast cancer patients. However, the molecular mechanisms of modulating tamoxifen resistance remain unknown. Therefore, our team suspected that there might be a correlation between the abnormal expression of CST1 and tamoxifen resistance. To investigate whether CST1 is involved in tamoxifen resistance and its molecular mechanism, we conducted further research. It is critical to elucidate the molecular mechanisms of tamoxifen resistance and to explore a novel effective therapeutic target.

Method:

Enhanced expression of CST1 was confirmed by immunohistochemistry in breast cancer tissue samples and by quantitative real-time PCR in Tamoxifen-resistant cancer cell lines MCF-7R/T47DR. To further investigate the molecular function of CST1, we knockdown its expression in MCF-7R/T47DR cells by transfecting with the lentiviral particles of shCST1 and corresponding negative control (Shanghai Genechem Co., Ltd.) and overexpressed CST1 in MCF-7/T47D cells using over-expressed GST-CST1, over-expressed HA-RAB1B plasmids. The effects of CST1 on cell viability and proliferation in breast cancer cells were detected by cell counting kit-8 and colony formation assays, respectively. The interaction between CST1 and RAB1B was validated by Co-immunoprecipitation and Western blot. Autophagosomes were found using transmission electron microscopy (TEM) along with Western blotting to detect the transformation of LC3-I to LC3-II protein (i.e., the LC3-II/LC3-I ratio) and P62 protein levels.

Results:

We found that aberrant expression of Cystatin SN (CST1) was identified in ER-positive breast cancer (BC) cells (Figure 1) and which is crucial in contributing to Tamoxifen resistance (Figure 2). The direct promotion of autophagy by RAPA can facilitate cells to endocrine resistance. And knockdown of CST1 not only suppressed autophagy in Tamoxifen-resistant cells but also attenuated the resistance, which determined the correlation of CST1 with autophagy in BC (Figure 3). Rab1b (Ras-related protein Rab-1B), a membrane protein essential for autophagosome formation, was verified to have interaction with CST1 through Coimmunoprecipitation (CO-IP) experiments (Figure 4). Meanwhile, RAB1B expression was

also reduced by CST1 knockdown in the resistant cells. The interaction between CST1 and RAB1B induces autophagy which decreases Tamoxifen's therapeutic efficacy. Furthermore, rescue experiments suggested that CST1 knockdown-induced sensitization in the efficacy of TAM Therapy and decreased autophagy could be restored via RAB1B overexpression. Conclusions: These results indicate that CST1 interacts with RAB1B to facilitate BC resistant to TAM through regulation of autophagy and CST1 might be a potential therapeutic target to overcome endocrine therapy resistance.

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li liu, People's Republic of China Medical practitioner's Qualification Certificate: No financial relationships to disclose

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5:00 PM - 6:15 PM

P3-11-03

Novel Targeting of Semaphorin 7a-Mediated Survival Signaling in ER+ Breast Cancer

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Endocrine receptor-positive (ER+) breast cancers (BC) comprise over 70% of all breast cancers and are the leading cause of BC-related deaths in women. Despite available targeted therapies against ER+ BC, recurrence arises primarily due to the development of endocrine therapy resistance and metastases. Thus, there is an unmet need to identify novel biomarkers for treating ER+ BC patients with metastases. We have identified a neuroimmune molecule, Semaphorin 7a (SEMA7A), as a potential biomarker for endocrine therapy resistance, increased relapse and decreased overall survival in ER+ BC patients. We have also found that SEMA7A promotes tumor growth, angio- and lymphangiogenesis, epithelial-to-mesenchymal transition (EMT), metastasis and endocrine therapy resistance in pre-clinical models. Specifically, we have shown that SEMA7A+ ER+ MCF7 tumors result in lung metastases that are resistant to the endocrine therapy, fulvestrant, in part, via downregulation of ER in vivo -- posing the need to identify novel, druggable targets for SEMA7A+ ER+ BC. SEMA7A is a membrane-bound protein that we have shown can inhibit tumor cell death via integrin-mediated activation of PI3K/Akt pro-survival signaling. Thus, we hypothesized that SEMA7A+ ER+ BC cells may be sensitive to PI3K inhibition in combination with fulvestrant. Our results demonstrate that SEMA7A+ MCF7 cells are sensitive to the combination of fulvestrant and PI3K inhibition by alpelisib, which is FDA approved for ER+ BC patients with activating mutations in PI3K; this combination also inhibited tumor cell growth and decreased tumor sphere formation. In complementary studies, we identified that Single-minded 2s (SIM2s), which is expressed in breast epithelial cells and inhibits EMT, is downregulated SEMA7A+ MCF7 tumors. Additionally, our studies show that while ER-mediated signaling turns on SEMA7A expression prolonged expression of SEMA7A results in downregulation of ER, and the loss of SIM2s causes downregulation of ER expression and upregulation of SEMA7A in MCF7 cells. Further, while SEMA7A-overexpressing (OE) tumor cells exhibit increased tumor-promoting PI3K/Akt survival signaling, we found that SIM2s plays a role in suppression of PI3K/Akt survival signaling. Therefore, we are investigating the interactions between SIM2s, SEMA7A and the survival signaling pathways involved in their crosstalk. Our recent results show that MCF7 SIM2-knockout (KO) cells exhibit increased SEMA7A promoter activity, SEMA7A expression, activation of Akt signaling, EMT phenotypes and decreased ER expression. Also, addition of exogenous SEMA7A protein reduces SIM2s expression and promoter activity. Since SIM2s correlates with inhibition of PI3K/Akt signaling and decreased SEMA7A, and SEMA7A promotes survival signaling, we are investigating additional therapeutic strategies to prevent

endocrine therapy resistance via direct inhibition of SEMA7A and/or restoration of SIM2s, including inhibition of COX-2 and Akt signaling.

Disclosure(s):

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Garhett Wyatt, PhD: No financial relationships to disclose

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Endoxifen Downregulates AKT Phosphorylation Through Protein Kinase C Beta 1 in ER+/HER2- Breast Cancer.

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Background: In phase I/II clinical trials, the tamoxifen metabolite Z-endoxifen (ENDX) demonstrated substantial oral bioavailability and promising antitumor activity in endocrine-refractory estrogen-receptor positive breast cancer (ER+ BC) and other solid tumors, with ENDX plasma concentrations reaching as high as 5 μM , a concentration that far exceeds the ER α -targeting nanomolar concentrations. We previously identified protein kinase C beta 1 (PKC β 1), an oncogenic signaling kinase which regulates cell proliferation and tumorigenic transformation, as a novel ENDX receptor. ENDX-bound PKC β 1 (KD: 100 nM) and inhibited PKC β 1 kinase activity (IC50: 357 nM) in vitro, at concentrations achieved in phase I/II ENDX studies. Given the observations that ENDX induces antitumor activity in breast cancers resistant to endocrine therapies, including AIs, tamoxifen and fulvestrant, we postulated that ENDX may impact additional signaling pathways. Therefore, in this study we performed unbiased mass spectrometry to analyze the effects of ENDX on the phosphoproteome and total proteome. Methods: In estrogen unstimulated aromatase-expressing ER+/human epidermal growth factor 2 receptor negative (HER2-) MCF7AC1 breast cancer cells, the effects of ENDX on the phosphoproteome and total proteome were analyzed using ENDX concentrations achieved in tamoxifen treated patients (0.01 and 0.1 μM) and concentrations observed in the ENDX phase I/II trials (5 μM). NetWorKIN and RoKAI prediction tools were utilized to identify the upstream kinases of ENDX downregulated phosphoproteins. In estrogen unstimulated MCF7AC1 as well as in the ER+/HER2- T47D breast cancer cells, the ability of ENDX, tamoxifen, fulvestrant and PKC kinase inhibitor enzastaurin to block insulin or PKC agonist phorbol 12-myristate 13-acetate (PMA)-stimulated AKTSer473 phosphorylation was analyzed by immunoblot (IB) assay. Additionally, ENDX effects on AKTSer473 phosphorylation in the MCF7AC1 xenograft model in vivo was analyzed by IB assay. Further, the effects of PKC β 1 silencing in MCF7AC1 cells and the effects of AKT inhibitor MK-2206 treatment on growth and AKTSer473 phosphorylation in the MCF7AC1 as well as long-term estrogen deprived T47D (T47D-LTED) cell lines were analyzed by cell proliferation and IB assays. Results: In MCF7AC1 cells unstimulated with estrogen, ENDX at 5 μM but not at 0.01 and 0.1 μM concentrations inhibited growth, and induced apoptosis, suggesting an ER α -independent effect. Further, ENDX at 5 μM displayed three-fold greater effects in downregulating the phosphoproteome compared to the other concentrations, with minimal impact on the total proteome. Protein kinase C beta (PKC β) and AKT1 were identified as the prevalent upstream kinases for ENDX downregulated protein phosphorylations. Notably, in estrogen unstimulated MCF7AC1 and T47D cells, ENDX at 5 μM attenuated phosphorylation of AKTSer473 and AKT substrates in vitro in the presence of insulin and in vivo. In MCF7AC1 cells, PMA-induced phosphorylation of PKC β 1 as well as

AKTSer473 and AKT substrate phosphorylations were blocked by ENDX at 5 μ M, with ENDX inducing PKC β 1 protein degradation both in the presence of insulin and PMA. Further, ENDX effects on growth and AKTSer473 phosphorylation were phenocopied by siRNA-mediated PKC β 1 knockdown as well as treatment with the pan-AKT inhibitor, MK-2206. Notably, the potent PKC β 1 kinase inhibitor, enzastaurin, had no effects either on PKC β 1 protein degradation nor on downstream AKT signaling. Conclusion: Taken together, these findings suggest that ENDX may exert anticancer activity via dual effects on blocking ER α as well as by targeting PKC β 1 for degradation, thus suppressing AKT signaling and induction of apoptosis. These preclinical findings will be studied in a planned neoadjuvant trial comparing ENDX with exemestane and ovarian function suppression (EVANGELINE) that will activate in the Fall of 2022.

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5:00 PM - 6:15 PM

P3-11-05

Efficacy of Gonadal steroids on aromatase inhibitor-resistant ER+ breast cancer: Insights from single-cell trajectory analysis of a patient-derived xenograft model

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Background: While estrogen typically promotes the progression of hormone-dependent breast cancer via the activation of estrogen receptor (ER)- α , estrogen-induced suppression of ER+ breast cancer has been clinically observed. Our previous study demonstrated that estrogen increased the percentage of cells expressing IL24, linking to the estrogen-dependent growth inhibition of an ER+ aromatase inhibitor (AI)-resistant tumor (Mori et al. *Cancers*, 2021). To continue our evaluation, we investigated whether progesterone (P4) and dihydrotestosterone (DHT) would affect the growth of this estrogen-suppressive tumor. Methods: An estrogen-suppressive patient-derived xenograft (PDX) model (named GS3) was established from an AI resistant ER+/HER2- brain metastatic breast cancer. E2 (1mg), P4 (10mg), DHT (12.5mg), or placebo pellets were implanted in mice carrying GS3 for in vivo drug efficacy examination. Beside tumor growth response, immunohistochemistry (IHC) and RNA sequencing of PDX specimens were conducted to decipher molecular changes after each treatment. The single-cell RNAseq analysis was further performed to examine gene expression profiles in individual cells. Results: ER α , ER β , Progesterone receptor (PR), and androgen receptor (AR) genes in GS3 are wild-type and are not amplified. Measurements of tumor volume showed that E2, E2+P4, and DHT suppressed the growth of GS3. The Tumor growth was not modulated by P4 treatment. IHC indicated that the number of Ki-67+ cells were decreased after E2, E2+P4, and DHT treatments, but were not changed after P4 treatment. PR+ cells appeared after E2 and E2+P4 treatments, and the AR+ cells increased after DHT treatment. Bulk-RNA sequencing indicated that E2 and E2+P4 treatments resulted in comparable gene expression patterns, while those of placebo and P4-treated tumors were similar. GSEA analysis showed that in E2 treatment, the hallmark estrogen response gene sets were upregulated, and the hallmark G2M checkpoint

gene set was downregulated. However, in DHT treatment, the hallmark interferon alpha/gamma response gene sets and androgen response gene set were upregulated, and the hallmark TNFA signaling via NFkB gene set was downregulated. Single-cell RNA sequencing analysis of Placebo/E2/DHT samples revealed 9 clusters; cells from E2-treated and DHT-treated tumors were placed in different clusters based on principle component analysis of Highly Variable Genes, although both E2 and DHT treatments resulted in tumor regression. DHT promoted cell cycle arrest, but it did not increase IL24 expression. The hallmark oxidative phosphorylation and androgen response gene sets were upregulated in all clusters from DHT-treated tumors. Trajectory analysis of single cells revealed that three major branches associated with clusters selective to the treatments of placebo, E2, and DHT were separated from a common branch which are consist of G2M phase cells. Conclusions: E2 and DHT were effective suppressor of GS3, but not P4. Based on the results from IHC, bulk-RNAseq, and Single-cell RNAseq, the mechanism of DHT-induced tumor regression is different from that by E2. Our results suggest that DHT/E2 could be treatment options for patients with relapsed ER+ AI-resistance breast cancer.

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Chromatin landscape analysis based on ATAC-seq and RNA-seq reveals that GRHL2 is a novel key transcription factor for endocrine therapy resistance

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Current data using gene expression and DNA modification profiles yield limited information for evaluating the potential resistance to therapies. Recent studies show that the chromatin landscape is dynamic and defines cell identity and disease status. Thus, changes in open chromatin sites could provide important information on disease progression and identify potential therapeutic targets. The majority of breast cancers express estrogen receptor (ER) and initially respond to endocrine therapies blocking ER activity. However, endocrine therapy resistance (ETR) occurs de novo or follows an initial response. Recent studies have identified new drivers of ETR, such as mTOR and CDK4/6. Therapy with these inhibitors in combination with endocrine therapy have improved patient survival, but the molecular mechanism of ETR is not fully understood and additional therapeutic options for ETR are needed. To investigate the molecular mechanisms of ETR, we established in vitro Long-Term Estrogen Deprivation (LTED) model using multiple human ER-positive breast cancer cell lines. These cells showed differential time-dependent patterns of ESR1 expression upon LTED with ESR1 upregulation in some cell lines and downregulation in others. LTEDs with ESR1 upregulation were sensitive to fulvestrant, while the others were resistant. We analyzed time-course of chromatin landscape transitions during acquisition of ETR in ESR1 up- and downregulated LTEDs cells by Assay for Transposase Accessible Chromatin (ATAC-seq) combined with RNA-seq. Because transcription factors play a primary key role in gene expression and in cell-fate changes including response to therapies, we performed bioinformatic analysis to uncover differential open chromatin sites, select enhancer signatures and identify digital footprints of transcription factors. Unlike ChIP-seq, which identifies binding sites for a known transcription factor, ATAC-seq permits analysis of all sites potentially accessible to the transcriptional machinery and predict occupancy by ~700 different transcription factors at once. With these algorithms, we found that Grainyhead-like 2 (GRHL2) is associated with development of both ESR1 overexpressed and downregulated types of LTEDs. Furthermore, RNA-seq analysis showed that GRHL2 target genes are upregulated in LTEDs. Furthermore, in the METABRIC database, high GRHL2 expression is significantly associated with poor outcome in ER+ breast cancer patients treated with endocrine therapy. Taken together, these data suggest that GRHL2 may

be a novel important transcription factor in endocrine therapy resistant breast cancer regardless of fulvestrant sensitivity. Our studies provide evidence that chromatin landscape analysis, coupled with the transcription factor network algorithm, is capable of identifying novel biomarkers or therapeutic targets, This approach will expand the range of translational research as it is applicable to many cancers and diseases.

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P3-11-07

Inhibition of FASN as a potential treatment of advanced endocrine therapy-resistant breast cancer

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INTRODUCTION: The past decade has seen significant advancement in increasing survival in estrogen receptor alpha (ER α) positive breast cancer. The use of selective estrogen receptor down-regulators and modulators (SERMs) (e.g. fulvestrant and tamoxifen), mTOR inhibitors (e.g. everolimus), aromatase inhibitors (AIs), and cyclin-dependent kinase inhibitors (e.g. palbociclib, ribociclib, and abemaciclib) have helped to extend overall survival of breast cancer patients. Unfortunately, resistance to endocrine therapy is a common occurrence and all patients will eventually succumb to their disease. Fatty acid synthase (FASN) is a key enzyme in lipid biosynthesis and is overexpressed in more aggressive and therapy-resistant tumors, including breast cancers. FASN inhibitor, TVB-2640, has been evaluated in multiple tumor cell lines and in a phase 1 clinical study, and showed partial responses in 5 patients and multiple patients with prolonged stable disease (≥ 16 weeks). **METHODS:** We generated tamoxifen- and fulvestrant-resistant MCF7 cells by long term exposure to tamoxifen (MCF7/TamR cells) and fulvestrant (MCF7/FR cells), and palbociclib-resistant (MCF7/RB1Crispr and ZR75/RB1Crispr) cells were generated through CRISPR/Cas9 knockout of the retinoblastoma (RB) gene. We assessed the impact of TVB-3166 inhibitor (and analog of TVB-2640 with slightly lower molecular weight for in vitro use) on proliferation, viability, cell cycle, and apoptosis in these cells. We evaluated the impact of TVB on proliferation and ER α expression in patient derived explants, and tumor growth in xenografts. RNA sequencing of tamoxifen- and fulvestrant-resistant cells was performed to investigate alterations in gene expression. Subcellular localization of ER α was assessed using subcellular fractionations. Palmitoylation and ubiquitination of ER α were assessed by immunoprecipitation. ER α and p-eIF2 α protein levels were analyzed by western blotting after treatment with TVB with or without the addition of palmitate or BAPTA. **RESULTS:** TVB treatment leads to a marked inhibition of proliferation in tamoxifen-, fulvestrant- and palbociclib-resistant cells compared to the parental cells. RNA sequencing of explants of patients with ER α positive disease showed down regulation of ESR1 related genes and genes involved in invasiveness. RNA sequencing of fulvestrant-resistant cells showed that treatment with TVB results in down regulation of EMT and E2F target genes, cholesterol homeostasis genes and mTORC1 signaling. Additionally, TVB significantly inhibited tumor growth in mice and decreased proliferation of primary tumor explants compared to untreated controls. FASN inhibition significantly reduced ER α levels most prominently in endocrine resistant cells and altered its subcellular localization. Furthermore, we showed that the reduction of ER α expression upon TVB treatment is mediated through the induction of endoplasmic reticulum stress in tamoxifen-resistant cells. **CONCLUSION:** Our preclinical data provide evidence that FASN inhibition by TVB-3166 presents a promising therapeutic strategy for treatment of endocrine-resistant breast cancer. Further clinical development of FASN inhibitors for endocrine resistant breast cancer should be considered.

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Inhibition of Sirtuin 3 Sensitizes Breast Cancer Cells to Fulvestrant

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Endocrine therapy can lead to nutrient deprivation by reducing glucose and glutamine uptake and total cellular ATP production. The ability of cells to bypass this metabolic stress is fundamental to how they regulate BC growth and acquire endocrine resistance. Sirtuins (SIRT3) are NAD⁺-dependent deacetylases and regulate a widerange of intracellular processes including metabolism. SIRT3, activated by calorie restriction, modulates mitochondrial adaptation to low energy input. It has a key role in mitochondrial integrity and function, regulating cell survival, death and metabolic pathways, regulating the shift to amino-acid and fatty-acid catabolism. SIRT3 can maintain ROS levels at the appropriate levels for sustaining a proliferative phenotype, preventing apoptosis and promoting carcinogenesis. A role of SIRT3 in epigenetic regulation has also been reported. We used Differential Dependency Network analysis to compare the wiring of the SIRT3 and key metabolism-related genes in matched antiestrogen- sensitive vs. resistant breast cancer (BC) cells, which identified several novel signaling hubs including CDKN2A (p16), linking SIRT3 to cell proliferation. The ability of SIRT3 to sense and respond to changes in energy, coupled with their deacetylase/deacetylase functions, could provide a mechanism for the cell to rewire signaling and maintain a newly acquired drug-resistant phenotype. Using endocrine sensitive (LCC1) and resistant (LCC9) BC cells, we confirmed the higher expression of SIRT3 in LCC9, compared to LCC1 cells. Upregulation of SIRT3 expression within 24 hrs of Fulvestrant (ICI 1 μ M) treatment ($p=0.0176$) in LCC1 was shown, but no effect was observed in LCC9 cells. Conversely, treatment with 17 β -estradiol (E2- 10 nM) did not significantly affect SIRT3 expression in either LCC1 or LCC9 cells. Inhibition of SIRT3 activity, using the LC0296 inhibitor (15 μ M), reduced growth rate in LCC1 and SIRT3-silenced LCC9 cells under treatment with ICI (1 nM and 1 μ M, respectively) ($p < 0.0001$, $p < 0.001$ respectively). Treatment with SIRTUIN 3 inhibitor and ICI induced apoptosis in LCC1 and SIRT3-silenced LCC9 cells compared to the untreated control and ICI only treated

cells ($p < 0.001$). The combination SIRT3 inhibitor ($15 \mu\text{M}$) plus ICI ($0.5 \mu\text{M}$) increased ROS production in LCC9-SIRT3 silenced cells in 24 hours of treatment compared to the untreated control and ICI only treated cells ($p < 0.001$). SIRT3 inhibitor ($15 \mu\text{M}$) decreased LCC1 cell spheroid formation ($p < 0.05$), however it didn't show additive effect to the effect of ICI ($0.5 \mu\text{M}$) in the same conditions. The combination of SIRT3 inhibitor ($15 \mu\text{M}$) and ICI ($1 \mu\text{M}$) reduced the growth of LCC9 SIRT3-silenced cells in detached condition compared to untreated control and ICI only treated cells ($p < 0.001$). The results show that SIRT3 may have a role in Fulvestrant response in BC cells; the mechanism is under investigation in our laboratory.

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Extracellular vesicle-based biomarker assay for the monitoring of the efficacy of frontline endocrine therapy + CDK4-6 inhibitors in metastatic breast cancer.

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CONTEXT: Endocrine therapy combined with CDK4/6 inhibitor is the standard frontline treatment for the vast majority of HR+/HER2- metastatic breast cancer (MBC) patients. Despite an overall survival benefit, patients eventually progress and mechanisms of resistance to this combination are not well identified. Non-invasive monitoring of the efficacy of treatment could help into tailoring therapeutic regimen. Extracellular vesicles (EVs) are a group of heterogeneous nanosized bioparticles (30-1000nm), released by almost all cell types - including tumor, platelets, and immune cells - carrying informative biological material emanating from the mother cell and circulating in the blood stream. In this project, we ambition to assess whether the vesiclemia, i.e. plasmatic extracellular vesicle concentration can be used as a clinic-biological parameter to assist in the monitoring of patients. **METHODS:** EPICURE is an ongoing pilot prospective cohort study of heterogeneous and massive data integration, i.e. multi-omics approaches in MBC patients. The present study focused on patients with HR+/HER2- MBC receiving frontline endocrine therapy+CDK4/6. Plasma samples were drawn every 3 months during the treatment until progression. The workflow for the enrichment of circulating EVs was developed from frozen plasma. A semi-automatized isolation procedure using size exclusion chromatography combined with the newly developed interference light microscopy apparatus Videodrop allowed to routinely separate plasmatic EVs and quantify vesiclemia in a fast and reliable manner for a large number of samples (longitudinal follow-up of MBC patients). **RESULTS:** 26 patients were included and monitored for vesiclemia. Median age was 58.5y (± 13.7). Metastatic disease sites were distributed as follows: bone metastases (21; 84%), liver (21; 84%), thoracic (10; 40%), node (2; 8%), brain (1; 4%), others (2; 8%). Endocrine therapy included aromatase inhibitors (20; 77%), fulvestrant (6; 29%), GnRH agonists (5; 19%) and CDK4/6 inhibitors palbociclib (15; 57%), abemaciclib (8; 31%) and ribociclib (3; 11%). With a median follow-up time of 22.1 months (95%CI 21.2 - not reached), median progression free survival was 21.8 months (95%CI 18.1 - not reached). Median time on treatment was 19.4 months (IQR 11.6 - 22.1). Objective response rate was confirmed in 12 patients (6 with complete response). Out of the 26 patients, 12 stopped the frontline treatment due to disease progression. 135 longitudinal follow-up samples were analyzed for EVs. All patients who progressed rapidly after treatment initiation (i.e median PFS < 6 months) had an increased vesiclemia at the months 2 and 6 after inclusion. Conversely, patients who had a median PFS >18m had a stable vesiclemia during this period. **CONCLUSION** This study aims to use circulating EVs as a therapeutic companion to anticipate treatment resistance and tumor progression in MBC patients. Our preliminary data suggest that the vesiclemia could be used as a predictive tool to anticipate treatment failure, and thus might be used to tailor treatments in time.

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Estrogen receptor reprogramming by HOXB13 and GATA3 in ER-positive breast cancer cells

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Background: The Breast Cancer Index (BCI) is a gene expression-based signature comprising two functional biomarker panels. The Molecular Grade Index (MGI) is composed of five genes that measure tumor proliferation. BCI (H/I) is a ratio of the HOXB13 and IL17BR genes and measures estrogen signaling. Integration of MGI and BCI (H/I) provides a single prognostic score that quantifies the risk of both late (5-10 years) and overall (0-10 years) distant recurrence. BCI (H/I) has been validated to predict benefit from extended endocrine therapy across multiple adjuvant endocrine treatment backgrounds in several prospective-retrospective studies. Hormone receptor responses are dependent on genome-wide hormone receptor binding patterns. In hormone-dependent cancers, nuclear receptor binding patterns are frequently reprogrammed by other transcription factors. The homeobox transcription factor HOXB13 has previously been shown to reprogram genome-wide binding of the androgen receptor (AR) during prostate cancer tumorigenesis, where it colocalizes with FOXA1 at reprogrammed AR binding sites. Similarly, the transcription factor GATA3 was found to mediate enhancer accessibility at regulatory regions involved in estrogen receptor (ER)-mediated transcription. We have shown previously that HOXB13 overexpression reprograms and expands the ER binding pattern in breast cancer cells. In this study, we have further characterized the role of HOXB13 in reprogramming the ER cistrome and evaluated potential interactions with GATA3. Methods: HOXB13 was expressed in MCF-7 and T47D cells by electroporating HOXB13 mRNA or eGFP mRNA as control. Cells were harvested after 18 hours and analyzed by western blot and chromatin immunoprecipitation followed by high-throughput sequencing (ChIP-seq) using antibodies against ER, HOXB13, FOXA1, GATA3 and histone H3K27ac. Chromatin accessibility was assessed by ATAC-seq. After aligning reads with Bowtie2, peak calling, data integration and motif enrichment analysis was performed using HOMER v4.10. Results: ChIP-seq analysis of T47D cells expressing HOXB13 confirmed previous results in MCF-7 cells, where binding of HOXB13 to a significant number of genomic binding sites induced changes in binding of ER, FOXA1 and GATA3 compared to control cells. Integrative analysis of ATAC-seq and ChIP-seq data revealed that HOXB13-induced reprogramming results in open chromatin that frequently exhibits increased acetylation of histone H3K27, a hallmark of transcriptional activation. While both increased chromatin accessibility and H3K27 acetylation were associated with HOX and AP-1 motif enrichment of the underlying DNA sequences, newly open chromatin was specifically co-enriched for motifs for pioneering factors such as FOXA1 and GRHL1. Conclusion: This study lends further support to a model of HOXB13-mediated reprogramming of the ER cistrome in breast cancer. Motif analysis of HOXB13-induced chromatin opening suggests interactions with other pioneer transcription factors including FOXA1 and GRHL1, while HOXB13-induced transcriptional

activation is associated with motifs for activating factors such as AP-1. These results will be expanded to inducible cell lines to further characterize the effects of HOXB13 expression on ER binding and function.

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5:00 PM - 6:15 PM

Discussion 1 + Q&A: PD7-01, PD7-02, PD7-03 & PD7-04

Presenting Author(s) and Co-Author(s):

Barbara O'Brien

Laura Crandon

12/7/2022

5:00 PM - 6:15 PM

Discussion 2 + Q&A: PD7-05, PD7-06, PD7-07 & PD7-08

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12/7/2022

5:00 PM - 6:15 PM

Poster Spotlight Discussion 7: Brain Metastases

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12/7/2022

5:00 PM - 6:15 PM

PD7-01

PD7-01 Trastuzumab deruxtecan for the treatment of patients with HER2-positive breast cancer with brain and/or leptomeningeal metastases: A multicenter retrospective study (ROSET-BM study)

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Background: Brain metastases (BM) occur in 20%-50% of patients (pts) with HER2-positive (HER2+) metastatic breast cancer (MBC), and their presence is a poor prognostic factor. Leptomeningeal carcinomatosis (LMC) occurs in 12%–43% of pts with MBC. Therapeutic options for BC pts with BM and/or LMC are limited. Results of the DESTINY-Breast01 and DESTINY-Breast03 studies have shown the clinical benefit of trastuzumab deruxtecan (T-DXd) in HER2+ MBC pts with stable BM; however, the study populations were small and did not include pts with active BM (untreated or progressive) and/or LMC. This data gap is addressed in the present study. Methods: ROSET-BM (UMIN000044995) is a multicenter, retrospective chart review study of pts who received T-DXd for HER2+ MBC with BM and LMC between May 25, 2020, and April 30, 2021, in a standard-of-care setting. Overall response rate (ORR), progression-free survival (PFS), and overall survival (OS) were evaluated. Additionally, in the pts with brain imaging data, intracranial (IC)-ORR and IC-PFS were evaluated by independent radiologists to provide central review according to RECIST v1.1. Active BM were determined by independent central review (ICR). Pts whose baseline and pre-baseline brain imaging data were compared and confirmed increased tumor size, or pts with new lesions were classified as active BM. LMC was determined by ICR using brain imaging. Results: In the study period, 62 sites participated, enrolling 113 pts with HER2+ MBC and BM were treated with T-DXd. After exclusion of data from 9 who did not meet the criteria for inclusion, 104 pts were included in the analysis. In the 104 pts, 70.2% (n=73) were active BM, 16.3% (n=17) were active BM with LMC, 5.8% (n=6) were stable BM, 1.9% (n=2) were only LMC, and 5.8% (n=6) were not classified. Symptomatic BM were observed in 30.8% (n=32). Median number of prior lines of therapy was 4 (range, 1–15). Median duration of follow up from first T-DXd treatment was 11.2 months. ORR assessed by investigator was 55.7% (complete response [CR], 5.2%) in all pts, 51.7% (CR, 6.9%) in symptomatic BM pts (n=29), and 57.4% (CR, 4.4%) in asymptomatic BM pts (n=68). Among all pts, median PFS was 16.1 months (95%CI, 12.0–n/a), and median OS was not reached (OS at 1 year was 74.9%). In the 19 pts with LMC, 1-year PFS and OS were 60.7% (95%CI, 34.5–79.1) and 87.1% (95%CI, 57.3–96.6), respectively (neither reached the median). Of the 89 pts with brain lesion imaging data (at both baseline and follow-up), IC-ORR

was 62.7% (CR, 0.0%). IC-PD was observed in 5.9% (n=3) of pts. Median IC-PFS was 16.1 months (95%CI, 12.2–n/a). In all pts, the most common event and adverse event leading to discontinuation of T-DXd were PD (27 pts, 26.0%) and interstitial lung disease (19 pts, 18.3%), respectively. Conclusion: The results of this retrospective chart review show that T-DXd has promising efficacy in HER2+ MBC pts with active BM and LMC. This study was funded by Daiichi Sankyo Co., Ltd.

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12/7/2022

5:00 PM - 6:15 PM

PD7-02

PD7-02 Trastuzumab Deruxtecan in patients with Unstable Central Nervous System Involvement from HER2-Low Advanced Breast Cancer: The DEBBRAH Trial

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Background: The antibody-drug conjugate trastuzumab deruxtecan (T-DXd) significantly improved survival outcomes of HER2-low advanced breast cancer (ABC) patients (pts) compared to standard chemotherapy in the DESTINY-Breast04 trial. DEBBRAH is assessing the efficacy and safety of T-DXd in HER2[+] and HER2-low ABC pts with a history of brain metastases (BM) and/or leptomeningeal carcinomatosis (LMC); here, we report results of HER2-low ABC pts. Methods: DEBBRAH (NCT04420598) is a multicenter, open-label, five-cohort, non-comparative, phase 2 study across 18 hospitals in 2 countries. A total of 39 pts aged ≥ 18 years with pretreated HER2[+] or HER2-low ABC with stable, progressing, or untreated BM and/or LMC, were enrolled in 5 cohorts: (1) HER2[+] ABC with non-progressing BM after radiotherapy and/or surgery; (2) HER2[+] or HER2-low ABC with asymptomatic untreated BM; (3) HER2[+] ABC with progressing BM after local treatment; (4) HER2-low ABC with progressing BM after local treatment; (5) HER2[+] or HER2-low ABC with LMC. Pts received 5.4 mg/kg T-DXd intravenously once every 21 days until disease progression, unacceptable toxicity, or consent withdrawal. Primary endpoint for cohorts 2 and 4 was intracranial overall response rate (ORR-IC) according to RANO-BM. Secondary endpoints included overall response (ORR) according to RECIST v1.1, progression-free survival (PFS), duration of response (DoR), clinical benefit rate (CBR); and safety and tolerability as per NCI-CTCAE v.5.0. Primary analysis is the estimation of ORR-IC (H_0 : ORR-IC $\leq 5\%$; H_1 : ORR-IC $\geq 40\%$) based on the one-sided binomial exact test. Sample size was planned to attain an 80% power at a nominal α level of 0.05 in each cohort. Results from cohort 2 should be considered descriptive since formal testing has to be performed in the whole cohort of pts with HER2[+] or HER2-low ABC and asymptomatic untreated BM. Results: From Oct 23, 2020, through Feb 15, 2022, 6 pts and 7 pts were allocated into cohorts 2 and 4, respectively. One patient with LMC included in cohort 4 was excluded from analysis. Median age was 54 (range 40–73) years. Median number of previous lines of therapy for advanced disease was 7 (range, 4-8) and 3 (range, 2-4) for cohorts 2 and 4, respectively. Median follow-up was 9.5 months (range, 1.6-

15.7). At data cutoff (Apr 29, 2022), no patient of cohort 2 and 3 (50.0%) pts of cohort 4 remained on therapy. In cohort 2, ORR-IC was 66.7% (4 of 6 pts had intracranial partial response [PR]; 95% CI, 22.3–95.7). In cohort 4, ORR-IC was 33.3% meeting the primary endpoint (2 of 6 pts had intracranial PR; 95% CI, 4.3–77.7; P = .033). Overall, ORR-IC in all pts was 50% (6 of 12 pts; 95% CI, 21.1–78.9) and CBR was 66.7% (8 of 12 pts; 95% CI, 34.9–90.1). Combining pts with measurable intracranial or extracranial disease from cohorts 2 and 4, ORR, CBR and median DoR were 41.7% (5 of 12 pts; 95% CI, 15.2–72.3), 50.0% (6 of 12 pts; 95% CI, 21.1–78.9), and 7.2 months (95% CI, 2.5–16.4), respectively. Median PFS was 5.7 months (95% CI, 4.7-NA) among these pts. The most common treatment emergent adverse events (TEAEs) of any grade (G) were fatigue (58.3%; 8.3% G≥3) and nausea (50.0%; 0% G≥3). Two (16.7%; 0% G≥3) cases of interstitial lung disease/pneumonitis were reported. Serious unrelated TEAEs occurred in 2 (16.7%) of 12 pts; 1 case of general pain (G3) and 1 case of venous embolism (G5) that led to death. There were no drug-related deaths due to TEAEs. Conclusions: T-DXd showed a preliminary antitumor activity in pretreated HER2-low ABC pts with asymptomatic untreated or progressing BM after local treatment. The substantial response of BM to T-DXd in this setting is promising and warrants further investigation.

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PD7-03

PD7-03 Translational Breast Cancer Research Consortium Trial 022: Neratinib and Trastuzumab-Emtansine for HER2+ Breast Cancer Brain Metastases (BCBM)

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PURPOSE: Treatment options for patients (pts) with HER2+ BCBM remain limited. We previously reported that neratinib monotherapy is associated with a volumetric central nervous system objective response rate (CNS ORR) of 8%, whereas the combination of neratinib and

capecitabine resulted in a volumetric CNS ORR of 49% (in lapatinib-naïve pts). Preclinical data suggest that neratinib may overcome resistance to trastuzumab-emtansine (T-DM1) and that the combination has potential CNS efficacy. Here, we report results of neratinib plus T-DM1 in pts with HER2+ BCBM. PATIENTS AND METHODS: In this prospective, multicenter, phase II study, pts with measurable HER2+ BCBM received neratinib 160 mg orally once daily plus T-DM1 3.6 mg/kg IV every 21 days in three parallel-enrolling cohorts. Cohort 4A enrolled pts with previously untreated brain metastases. Cohort 4B enrolled pts with BCBM progressing after prior local CNS-directed therapy without prior exposure to T-DM1. Cohort 4C enrolled pts with BCBM progressing after prior local CNS-directed therapy who had previous exposure to T-DM1. Diarrhea prophylaxis with colestipol and loperamide was required during cycle 1. Cohorts 4A and 4B were single-stage with a planned enrollment of 20 patients; cohort 4C had a two-stage design, with a requirement for at least 1 of the first 9 pts to achieve a response in order to enroll a total of 24 patients. The primary endpoint was Response Assessment in Neuro-Oncology-Brain Metastases (RANO BM) in each cohort separately. Correlative studies included patient-reported outcomes (PROs) for gastrointestinal toxicity. RESULTS: We enrolled 6, 17, and 21 patients to cohorts 4A, 4B, and 4C, during 11/07/2018 – 11/01/2021. Enrollment was stopped prematurely due to slow accrual. Across Cohorts 4A-4C, the median number of prior lines of chemotherapy prior to enrollment was 2 (range 1-10); 25% received prior lapatinib and no patients received prior tucatinib. In cohorts 4B and 4C (prior CNS-treated cohorts), 33% had prior CNS surgery and >94% had prior CNS radiation. Among evaluable patients, CNS ORR in cohorts 4A (n=6), 4B (n=16), and 4C (n=21) was 50.0% (95% CI 18.8- 81.2%), 25.0% (95% CI 8.3-52.6%), and 38.1% (95% CI 19.0-61.3%), respectively. Median (range) number of cycles completed for 4A, 4B, and 4C was 4.5 (1-15), 4 (range 0-49+), and 6 (0-23); three patients on Cohort 4B remain on protocol therapy (cycles 14, 45, and 49). The overall survival at 12-months for cohorts 4A, 4B, and 4C was 83.3% (95% CI, 58.3-100%), 86.2% (95% CI 70-100%), and 83.3% (95% CI 67.6-100%). Diarrhea was the most common grade 3 toxicity (19.0–33.3% across cohorts); one grade 4 liver function event occurred in cohort 4B. Updated efficacy results will be reported at the meeting; PRO analyses are ongoing. CONCLUSION: Intracranial activity was observed for the combination of neratinib plus T-DM1 across all three enrolled cohorts, including those with prior T-DM1 exposure, suggesting synergistic effects of this treatment combination. Our data provide additional evidence for consideration of neratinib-based combinations in pts with HER2+ BCBM.

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5:00 PM - 6:15 PM

PD7-04

PD7-04 Capecitabine treatment for patients with central nervous system metastases from breast cancer

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BACKGROUND: Central nervous system (CNS) is a common site of metastases from breast cancer (BC). The efficacy of systemic therapy for CNS metastases from HER2-negative BC is limited. Although new anti-HER2 therapies seem to be more effective in this scenario, these drugs are not widely available yet. Chemotherapy with capecitabine is often used in patients (pts) with CNS metastases, but data supporting its activity is scarce. We aimed to evaluate the effectiveness of capecitabine for CNS metastases from BC.

METHODS: This retrospective study included pts with BC and confirmed CNS metastases treated with capecitabine at a tertiary cancer center from 2010-2021. Study endpoints included intracranial objective response rate (CNS-ORR) and intracranial disease control rate (CNS-DCR), intracranial progression-free survival (CNS-PFS), and overall survival (OS). Survival analysis were estimated by Kaplan-Meier method and compared using log-rank test.

RESULTS

Among 209 pts included, 41.6% were hormone receptor-positive (HR+) HER2-negative 33.9% HER2-positive, and 26.4% triple-negative (TNBC). Most pts had ECOG 0-1 (56.9%) and had received < 2 chemotherapy lines (77.9%) before capecitabine. Brain parenchymal metastases were present in 85.5%; 43.1% had ≥ 5 brain lesions. Radiotherapy was performed in 90.4% of the cases and CNS surgery in 27.5%. Among 124 pts accessible for intracranial response, CNS-ORR and CNS-DCR were 31.4% and 79% in 3-months. In 6 months, 76 pts were accessible, and CNS-ORR and CNS-DCR were 23.6% and 73.6%. The median CNS-PFS was 5.6 months and median OS was 7.9 months. Table 1 shows CNS-ORR and CNS-DCR at 3 months according to immunohistochemical subtype. Although TNBC had higher 3-month IORR (48%), this subgroup had a worse prognosis compared to HR+ (OS: HR = 1.87, CI 95% = 1.28 – 2.73, p = 0.001). mOS was 8.7 months and 9.1 months for HR+ and HER2+ subtypes respectively, and 4.5 months for TNBC. OS was worse in patients with ECOG-PS ≥ 2 (p = 0.017) and was not influenced by the number or size of brain metastases, number of previous chemotherapy lines and previous surgery or radiotherapy to CNS.

CONCLUSION

Our results showed that pts with CNS metastases from BC still have a poor prognosis. TNBC subtype and ECOG-PS ≥ 2 were detrimental prognostic factors. Nevertheless, among pts accessible for intracranial response, satisfactory CNS-DCR was observed with capecitabine, suggesting activity of this drug for selected pts.

Intracranial response rate (CNS-ORR) and disease control rate (CNS-DCR) of central nervous system metastases from breast cancer treated with capecitabine.

	HR+HER2- BC (n=50)	HER2+ BC (n=49)	TNBC (n=25)	P-value*
CNS-ORR, n (%)	12 (24)	15 (31)	12 (48)	0.113
CNS-DCR, n (%)	47 (94)	36 (73)	15 (60)	0.001

*Fisher's exact test.

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5:00 PM - 6:15 PM

PD7-05

PD7-05 Survival of patients with brain metastases at initial breast cancer diagnosis over the last decade

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Background

Brain metastases (BM) is a challenging presentation of breast cancer (BC) and has historically been associated with poor prognosis. The risk of BM is higher in patients (pts) with hormone receptor (HR) negative, human epidermal growth factor receptor 2 (HER2)-positive, or triple negative (TN) tumors.

There have been significant advances in the treatment of metastatic BC over the past several years, and long-term outcomes after a diagnosis of breast cancer brain metastases (BCBM) are lacking; therefore, this study aimed to identify clinical predictors of BM at initial BC diagnosis, to describe trends in overall survival (OS) over the past decade, and to identify factors associated with OS after BM diagnosis.

Methods

We evaluated pts with de novo stage IV BC using the Surveillance, Epidemiology and End Results (SEER) database from 2010-2019. A multivariate logistic regression model was conducted among all pts with stage IV BC to assess predictors of BM at initial BC diagnosis. OS probabilities were estimated using the Kaplan-Meier method and log rank test was used to compare differences between groups. Among pts with BM at initial BC diagnosis, univariate analyses were performed to determine the effects of each variable on OS. A Cox proportional hazards regression was used to assess the independent association of several variables with OS.

Results

A total of 425,110 pts with BC were identified from 2010-2019; 25,113 had stage IV BC at diagnosis and among these, 1,939 pts had BM at initial BC diagnosis. For this last group

median age was 60 years and median follow up was 54 months .

We performed a logistic regression model to evaluate the factors correlated with BM at initial BC diagnosis among all stage IV BC pts and found that lobular vs ductal histology (OR 0.68; 95% CI 0.55-0.85), HR-/HER2+ vs HR+/HER2- tumors (OR 1.93; 95% CI 1.64-2.29), and the presence of bone (OR 1.19; 95% CI 1.07-1.32), liver (OR 1.25; 95% CI 1.12-1.39), lung (OR 1.72; 95% CI 1.55-1.89), or lymph node (OR 1.21; 95% CI 1.03-1.42) metastases, were significantly associated with this presentation.

The table shows OS by tumor subtype among all pts with BM at initial BC diagnosis, as well as the survival rate at 2, 5 and 8 years. We observed significant differences in survival by tumor subtype, where pts with HR+/HER2+ disease had the longest OS (median 18 months; 95% CI: 13-22 months; p = < 0.0001) and the highest rate of OS at 8 years (12.2%; 95% CI 7.61%-17.95%). In contrast, TN BC had a median OS of 6 months (95% CI 5-8 months) and a rate of OS at 8 years of 2.57% (95% CI 0.1%-5.48%).

Multivariate analysis among pts with BM at initial BC diagnosis revealed differences in OS in those who were >64 years vs < 50 years (Hazard Ratio [HzR] 1.51; 95% CI 1.29-1.77), married vs single (HzR 0.79; 95% CI 0.70-0.91), lower vs higher income (HzR 1.45; 95% CI 1.19-1.76), tumor grade III/IV vs grade I (HzR 1.68; 95% CI 1.24-2.28), TN subtype vs HR+/HER2- (HzR 2.13; 95% CI 1.81-2.49), as well as pts with additional liver (HzR 1.34; 95% CI 1.20-1.51) or lung metastases (HzR 1.34; 95% CI 1.20-1.49).

We did not observe significant changes in OS over time (adjusted HzR 0.996 per year; 95% CI: 0.96-1.02, p = 0.837).

Conclusions:

Over the last decade, the median OS of pts with BM at initial BC diagnosis has remained poor. However, a substantial minority of pts survive 5 or more years, with long-term survival rates higher in pts with HER2+ tumors. In addition to tumor subtype, OS varied according to age, the presence of metastases to other organs, and sociodemographic factors.

		N	Median OS in months (95% CI)	% OS at 2 years (95% CI)	% OS at 5 years (95% CI)	% OS at 8 years (95% CI)
Tumor subtype	HR+/HER2-	725	14 (12-16)	34.43 (30.72-38.17)	10.56 (7.86-13.72)	5.53 (3.28-8.61)
	HR+/HER2+	310	18 (13-22)	42.24 (36.36-47.99)	20.31 (15.09-26.07)	12.2 (7.61-17.95)
	HR-/HER2+	238	14 (11-17)	34.19 (27.87-40.60)	14.29 (9.53-19.97)	11.2 (6.18-17.89)
	Triple negative	334	6 (5-8)	10.27 (7.09-14.11)	3.21 (1.43-6.19)	2.57 (0.1-5.48)
	Unknown	332	4 (3-4)	15.68 (11.74-20.14)	5.35 (2.82-9.06)	0.89 (0.09-4.21)
All pts		1939	10 (9-11)	28.3 (26.17-30.46)	10.51 (8.87-12.31)	5.94 (4.44-7.73)

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Carlos T. Vallejo, MD: No financial relationships to disclose

Nancy U. Lin, MD: Affinia Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Aleta Biopharma: Consulting Fees (e.g., advisory boards) (Ongoing); Artera: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Daichii-Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Denali Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Genentech: Contracted Research (Ongoing); Janssen: Consulting Fees (e.g., advisory boards) (Ongoing); Merck: Contracted Research (Ongoing); Olema Pharmaceuticals: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Pfizer: Contracted Research (Ongoing); Prelude Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted

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12/7/2022

5:00 PM - 6:15 PM

PD7-06

PD7-06 Characteristics of Long-Term Survival in Breast Cancer Brain Metastasis after Stereotactic Radiation

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Background: Advances in imaging and systemic therapy have improved the survival for patients with breast cancer brain metastases (BCBM). However, an improved understanding of patients

with long-term survival after stereotactic radiation (SRT) for BCBM is warranted and could allow for better prognostication and personalized treatment. Methods: This is a single institution retrospective review of 188 patients who underwent SRT sessions to 685 BCBM from August 2004 to June 2020. Patients who were lost to follow up within 2 years after SRT were excluded. Patients were stratified into 2 groups: those with overall survival (OS) from SRT less than 2 years (short-term survival, STS) and those with OS from SRT of at least 2 years (long-term survival, LTS). Patient, tumor, and treatment characteristics were compared between the 2 groups via the student t-test and Chi-square testing as appropriate. The Kaplan-Meier (KM) method was used to calculate OS, local control (LC), and distant intracranial control (DIC) from the date of SRT. The reverse KM method was used to estimate follow-up from SRT. Results: The median follow up from BCBM diagnosis was 52.8 months (95% CI: 40.5-75.2 months). Of the 685 treated BCBMs, 552 (81%) received stereotactic radiosurgery (SRS) to a median dose of 21 Gy (12-24 Gy) and 133 received fractionated stereotactic radiation therapy (FSRT) to a median dose of 25 Gy (20-35 Gy) in 3-5 fractions. The 2-year LC, DIC, and OS was 78.4%, 26.5%, and 38.3%, respectively. The 5-year OS was 19%. There were 72 patients (38%) in the LTS group and 116 patients (62%) in the STS group. The LTS group had lower rates of invasive lobular carcinoma (0% vs 6%, $p=0.001$) and higher rate of HER2+ disease (61% vs 30%, $p<0.001$). The LTS group had lower rates of concurrent extracranial metastasis (74% vs 89%, $p=0.008$) and lung metastasis (33% vs 53%, $p=0.009$), though there were no differences in the rates of bone or liver metastasis. The LTS group had less BCBM at the time of SRT (mean 1.9 vs 2.5, $p=0.013$) and more often received SRT to a single BCBM (65% vs 42%, $p=0.002$). There were no significant differences in age or performance status between the groups. Conclusion: Prognosis for patients with BCBM is heterogeneous, as a minority of patients have prolonged OS after SRT. These patients more often have limited BCBM, HER2+ disease, and a lower extracranial disease burden.

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5:00 PM - 6:15 PM

PD7-07

PD7-07 Somatic alterations in primary tumors of patients (pts) with metastatic breast cancer (MBC) may predict likelihood of brain metastasis

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Background: Despite advances in treatment options, outcomes remain poor for many pts with breast cancer brain metastases (BCBMs). Identifying genomic predictors of brain metastasis from primary tumors could lead to better stratification of pts at risk and drive the development of preventative strategies. The objective of this study was to describe the landscape of genomic alterations in primary tumors from pts with MBC who subsequently did or did not develop BCBMs.

Methods: We performed a case control study to identify somatic alterations in primary tumors associated with a higher incidence of brain metastases. We reviewed outcomes for 2562 unique MBC patients from a single institution who underwent targeted next-generation DNA sequencing of > 280 cancer-related genes (OncoPanel) from their tumor between July 1, 2013 and December 31, 2020. Pts were included in this analysis if they had at least 2 years of follow-up from date of metastatic diagnosis and OncoPanel testing on a primary breast tumor. We compared single nucleotide variants (oncogenic or likely oncogenic), copy number variation (amplification and deep deletions) and tumor mutation burden in the primary tumors of pts in this cohort. Copy number variation was corrected for Panel version and tumor purity. Wilcoxon rank sum test and Fisher exact test was used to compare genomic differences between groups. False discovery rate was used to correct for multiple hypothesis testing and $q < 0.1$ was considered significant

Results: A total of 369 pts were included in the final analytic cohort. Of these, 115 were diagnosed with brain mets (cases, BM group) and 224 were not (controls, nBM group). The BM group was enriched for patients with HER2-positive breast cancer (33 vs 12.5%), consistent with previous work. In the whole cohort, the most common and clinically significant somatic alterations (oncogenic single nucleotide variants or copy number high amplification or two copy deletion) are shown in Table 1. When adjusting for subtype there were no significantly enriched SNVs in BM vs nBM group. When adjusting for subtype, FGFR1 amplification was significantly enriched in hormone receptor positive HER2 negative (HR+ HER2-) patients with BM (log2 odds ratio 1.22, $q < 0.1$). Tumor mutation burden was not significantly different in primary tumors between the BM and nBM groups (median TMB 7.3 vs 6.1, Wilcoxon $p = 0.08$).

Pathway analysis combining all subtypes revealed that RTK_RAS pathway (log2 odds ratio 1.64, q value < 0.1) and TP53 pathway (log2 odds ratio 1.15, q value < 0.1) gene sets were significantly enriched in the BM group. When controlling for subtype, pathway analysis revealed that RTK_RAS pathway gene set was significantly enriched in HR+ HER2- BM group (log2 odds ratio 1.36 $q < 0.1$).

Conclusions: In this case control series of patients with metastatic breast cancer with or without brain metastases, we found that primary tumors that are enriched for somatic alterations in the RTK_RAS and TP53 pathway may be associated with higher risk of developing brain metastases. Further validation in larger cohorts is warranted.

Table 1

Table 1: Frequency of somatic alterations in primary tumor by brain metastasis outcome			
GENE	No brain metastasis (nBM, n = 224)	Brain metastasis (BM, n = 115)	Cohort (n = 339)
PIK3CA	36%	35%	36%
TP53	25%	48%	32%
CCND1	16%	11%	14%
GATA3	12%	11%	12%
CDH1	10%	14%	12%
ERBB2	10%	33%	18%
FGFR1	8%	10%	8%
BRCA2	6%	7%	6%
ARID1A	4%	6%	5%
PTEN	5%	8%	6%

Disclosure(s):

Sheheryar Kabraji, BMBCh: No financial relationships to disclose

Yvonne Y. Li, PhD: No financial relationships to disclose

Melissa E. Hughes, MSc: No financial relationships to disclose

Hersh V. Gupta, BSc: No financial relationships to disclose

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5:00 PM - 6:15 PM

PD7-08

PD7-08 Gene Expression Profiling of Breast Cancer Brain Metastasis shows enrichment for non-luminal subtypes with potential prognostic implications

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Background: The incidence of breast cancer (BC) brain metastases (BM) is increasing as a result of both improved diagnostic techniques and longer survival due to better treatment approaches. However, the biological complexity of BCBMs is still poorly understood. We here evaluate the genomic profile of BCBMs and assess its prognostic implications.

Methods: Clinical data and BM samples (FFPE) from BC patients undergoing neurosurgery (2003-2019) at three institutions were collected. Hormone receptor (HR) and HER2 status were evaluated on the BCBM. RNA extracted from BM samples was used to measure the expression of 758 BC-related genes and 18 housekeeping genes using the Breast Cancer 360 Panel on an nCounter platform (NanoString Technologies). Intrinsic molecular subtyping was determined using the previously reported PAM50 subtype predictor (Parker et al. JCO 2009). Median overall survival from neurosurgery (OS) was calculated using the Kaplan-Meier method. The correlations between expression of each gene/PAM50 signature, BC subtype and OS were studied using univariate and multivariate Cox-models.

Results: Sixty-five BCBM samples were analyzed: 32% (N=21) were HR+/HER2-, 38% (N=25) HER2+ and 29% (N=19) HR-/HER2-. With a median follow-up of 33 months, no clinical variable was significantly associated with OS, despite a trend towards a shorter survival for patients with HR-/HER2- BMs, as compared to patients with HR+/HER2- and HER2+ subtypes (median OS 9.4 versus 22.1 and 20.0 months, respectively, log-rank p=NS).

The intrinsic subtype distribution, as assessed by gene-expression profiling, was 37% Basal-like, 46% HER2-enriched (HER2-E), 15% Luminal B and 2% Normal-like. Non-luminal subtypes (basal-like and HER2-E) were extensively represented, both overall and in each BC subtype (52% in HR+/HER2- subgroup, 96% in HER2+ subgroup, see Table).

The PAM50 basal-like signature was significantly associated with a worse OS (HR 2.7, 95% CI 1.0-7.2, p=0.045), even after correcting for BC subtype (HR 5.2, 95% CI 1.1-23.4, p=0.032). In fact, even within the subgroup of HR+/HER2- BCBMs, the PAM50 basal-like signature was strongly associated with a worse OS (HR 92.6, 95% CI 5.0-1860.1, p=0.003) and patients with basal-like HR+/HER2- BCBMs presented a median OS similar to patients with HR-/HER2- BCBMs (mOS 9.0 vs 9.4 months).

We identified 36 genes whose high expression was significantly associated with a worse OS (p< 0.05) and one gene (LINC02381) whose high expression was significantly associated with better OS (p< 0.05); for 33 of these genes (BCL11A, BMP2, BNIP3, CAV1, CDH3, CDK6, CKB, CRYAB, CXCL12, EGFR, EYA4, FOXC1, FZD8, FZD9, GABRP, GAS1, GDF5, GPC4, IL6, KRT17, KRT5, KRT6B, KRT7, LAMB3, LINC02381, MYC, NOTCH1, PRKX, PSAT1, RUNX3, SNAI1, SPRY2, TTYH1), the association was confirmed even after correcting for BC subtype (p< 0.05).

Conclusions: Non-luminal intrinsic subtypes are extensively represented in resected BCBMs, even if clinically classified as HR+/HER2-. Our data suggest that basal-like genomic features might be enriched in BCBMs and might be associated with worse survival.

Distribution of PAM50 intrinsic subtyping on the 65 brain metastases evaluated according to hormone receptor (HR) and HER2 status

PAM50 Intrinsic subtype	HR+/HER2- BCBM N (%)	HER2+ BCBM N (%)	HR-/HER2- BCBM N (%)
HER2-enriched	6 (29%)	21 (84%)	3 (16%)
Basal-like	5 (24%)	3 (12%)	16 (84%)
Luminal B	9 (43%)	1 (4%)	-
Normal-like	1 (5%)	-	-
Luminal A	0	0	0

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5:00 PM - 6:15 PM

Discussion 1 + Q&A: PD8-01, PD8-02, PD8-03, PD8-04, PD8-05 & PD8-06

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5:00 PM - 6:15 PM

Discussion 2 + Q&A: PD8-07, PD8-08, PD8-09 & PD8-10

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5:00 PM - 6:15 PM

Poster Spotlight Discussion 8: Symptom Management and Associated Toxicities

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5:00 PM - 6:15 PM

PD8-01

PD8-01 PantoCIN: Pantoprazole's effectiveness as prophylaxis against delayed Chemotherapy-Induced Nausea and Vomiting (CINV) in patients receiving adjuvant or neoadjuvant breast cancer chemotherapy

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Background: Rates of delayed CINV remain high at over 50% following adjuvant chemotherapy for breast cancer, despite the use of multiple antiemetics. Delayed CINV is complex, distressing to patients and its incidence is underestimated by physicians. Anti-emetics used with early breast cancer chemotherapy are often directed against acute rather than delayed CINV. Chemotherapy is virtually eliminated from the circulation prior to the delayed phase (24-120 hours post-chemotherapy), suggesting the etiologies for acute and delayed CINV may differ. Chemotherapy and steroids can alter the gastric environment and acid secretion, while chemotherapy can cause gastroesophageal mucositis. We hypothesized that the altered gastric environment, combined with disrupted gastroesophageal mucosa, could contribute to delayed nausea in a proportion of patients. Anecdotal experience suggested proton pump inhibitors, such as Pantoprazole, reduced symptoms in this setting. Methods: This study incorporated a double-blinded crossover design to determine whether Pantoprazole would reduce the incidence of delayed CINV in patients receiving adjuvant, or neoadjuvant breast cancer chemotherapy. Patients were randomized to either pantoprazole or placebo from Day 1-5 after cycle 1, changing to the other intervention for cycle 2. CINV symptoms during the delayed phase were assessed using the Multinational Association of Supportive Care in Cancer (MASCC) Antiemesis Tool and recorded in real time by patients using the PantoCIN ePRO application. With 160 patients, this approach had an 80% power to detect a statistically significant effect (one-sided α (type 1) error of 0.025) of Pantoprazole, if the true effect of Pantoprazole is a 10% reduction in the rates of any delayed CINV compared to placebo. The primary endpoint was the proportion of patients with complete absence of both nausea and vomiting during days 2-5, with severity of CINV and patient preference for intervention described as secondary endpoints. Results: 160 patients were recruited between June 2019 and October 2021, from 10 different cancer centers in New Zealand. Primary statistical analysis has shown a significant reduction in absolute CINV with pantoprazole as the primary end point, with incidence of any CINV symptoms reducing from 61.0% to 49.6% (OR=1.8, 95% confidence interval (1.0 to 3.3); p-value=0.04), in patients with full data. There was also a clear preference for patients to prefer the blinded pantoprazole arm of the 2 cycles of treatment under study, with the proportion of participants who preferred pantoprazole to placebo being 49% and the proportion who preferred placebo to pantoprazole was 25.2%, (difference in proportions 23.8% and 95% confidence interval 12.4 to 35.2; p=0.0017). Conclusion: CINV is a common and distressing complication of early breast cancer chemotherapy, which persists despite the use of a range of current antiemetics. Pantoprazole is a cheap, well-tolerated agent without significant drug interactions, which clearly ameliorates this symptom in a significant proportion of patients and should be considered as a standard prophylactic intervention.

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PD8-02

PD8-02 Metformin (MET) for the prevention of Alpelisib (ALP)-related Hyperglycemia (HG) in PIK3CA-mutated, Hormone Receptor-Positive (HR[+]) HER2-Negative (HER2[-]) Advanced Breast Cancer (ABC): The METALLICA study.

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Background: HG is an on-target AE of PI3K inhibition, reported in 63.7% (36.6% G \geq 3) of HR[+]/HER2[-] ABC patients (pts) treated with ALP plus fulvestrant in SOLAR-1. HG was the most frequent adverse event (AE) leading to ALP discontinuation (6.3%). MET reduces systemic insulin resistance and suppress PI3K and Ras signaling. METALLICA is assessing the prophylactic use of MET for prevention of ALP-induced G3-4 HG in PIK3CA-mutated, HR[+]/HER2[-] ABC pts with normal fasting glycemia or prediabetic criteria. Methods: This is an open-label, single-arm, two-cohort, phase 2 trial. Pts aged \geq 18 years, ECOG PS of 0–1, and PIK3CA-mutated, HR[+]/HER2[-] ABC, progressing to an aromatase inhibitor (AI)-containing regimen, \leq 2 previous endocrine therapy (ET) and \leq 1 prior chemotherapy regimens for ABC

were eligible. Pts were enrolled into cohorts according to glycemia at baseline: (A) pts with normal fasting glycemia < 100 mg/dL and glycosylated hemoglobin (HbA1c) < 5.7%; (B) pts with prediabetic fasting glycaemia 100–140 mg/dL and/or HbA1c 5.7–6.4%. Pts received oral ALP 300 mg/day, starting from C1D8, in combination with ET; fulvestrant, letrozole, or exemestane as per standard of care; and oral MET 1000 mg/day on days 1-3 and 2000 mg/day thereafter. The primary endpoint was G3-4 HG incidence as per NCI-CTCAE v.4.03 at 2 first cycles of treatment. Assessment of glycemia was performed by rigorous self-monitoring blood glucose and local laboratory confirmation in fasting conditions. Secondary endpoints included objective response (ORR), clinical benefit rate (CBR), duration of response (DoR), progression-free survival (PFS), and safety. Sample size was based on a Simon's two-stage design in cohorts A (H0: G3-4 HG \geq 25%; H1: G3-4 HG \leq 10%) and B (H0: G3-4 HG \geq 40%; H1: G3-4 HG \leq 15%). We planned to attain 80% power at the nominal one-sided α level of 0.05 for each cohort. Results: Between Aug 30, 2020, and Mar 10, 2022, 68 pts were enrolled at 18 sites (48 cohort A, 20 cohort B). Median age was 55 (range, 29–79) years and 58.8% pts had visceral disease and an ECOG PS 0. A total of 66 (97.1%) pts had been previously treated with a CDK4/6i and 13 (19.2%) pts had received chemotherapy for advanced disease. Sixty-three (92.6%) pts received fulvestrant as ET (45 cohort A, 18 cohort B). With a median follow-up of 8 (range, 1.6–14.9) months, 28 (41.2%) pts remain on study treatment. Disease progression was the main reason for discontinuation, reported in 32 (47.1%) pts. The primary endpoint of the study was reached, with 1 (2.1%) pts (95%CI, 0.8–9.5; $p < 0.001$) in cohort A and 3 (15%) pts (95%CI, 4.5–33; $p = 0.012$) in cohort B experiencing a G3-4 HG episode over the 2 first cycles of treatment. For patients on fulvestrant, G3-4 HG rates were 1 pts (2.2%) and 3 (16.7%) pts for cohorts A and B, respectively. No ALP discontinuation related to HG was reported during the first 2 treatment cycles. Median PFS in all patients was 7.4 months (95%CI, 6–NA). Among pts with measurable disease, ORR was 14 (36.8%) pts (95%CI, 21.8–54). At the time of this analysis, DoR and CBR were still immature. The most common AEs were diarrhea (67.6%; 13.2% $G \geq 3$), nausea (67.6%; 0% $G \geq 3$), and fatigue (45.6%; 2.9% $G \geq 3$). Serious AEs occurred in 15 (22.1%) pts. The main serious AEs were rash (2.9% $G \geq 3$) and vomiting (1.5% $G \geq 3$). No additional pts reported $G \geq 3$ HG after the first 2 cycles. The dose of ALP was reduced according to the protocol in 19 (27.9%) pts. Eight (11.8%) pts permanently discontinued ALP due to AEs, none of whom related to HG. No treatment-related deaths were reported. Conclusions: Prophylactic use of MET substantially reduced the incidence and severity of ALP-related HG with no additional toxicities and could be a new standard for PIK3CA-mutated, HR[+]/HER2[-] ABC pts receiving ALP plus fulvestrant or other ET.

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12/7/2022

5:00 PM - 6:15 PM

PD8-03

PD8-03 Beta blockers and/or ACE inhibitors as cardioprotective strategy for patients affected by nonmetastatic breast cancer who are receiving an anthracycline-based chemotherapy (SAFE - NCT02236806): final results of a randomized trial

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Introduction. Several studies have evaluated cardioprotective strategies to prevent myocardial dysfunction in patients who are receiving cardiotoxic therapies. Angiotensin-converting enzyme inhibitors and β -blockers are recommended first-line agents for heart failure. However, the optimal approach still represents a controversial issue. We hypothesized whether pharmacological cardioprotection could reduce subclinical heart damage in patients with breast cancer who are being treated with an anthracycline-based chemotherapy. **Patients and methods.** The SAFE trial was a 4-arm, randomized, phase 3, double-blind, placebo-controlled, national multicentric study conducted at eight oncology departments in Italy. The study recruitment was conducted between July 2015 and June 2020. A prespecified interim analysis on 174 women at 12 months was reported in 2020. Patients were eligible for trial inclusion if they had indication to receive primary or postoperative systemic therapy using an anthracycline-based regimen. Patients with a prior diagnosis of cardiovascular disease were excluded. Cardioprotective therapy (bisoprolol, ramipril, or both drugs compared with placebo) was administered for one year from the initiation of chemotherapy or until the end of trastuzumab therapy in case of ERBB2-positive patients. Doses for all groups were systematically up-titrated up to the daily target dose of bisoprolol (5mg, once daily), ramipril (5mg, once daily), and placebo, if tolerated. The primary end point was defined as detection of any subclinical impairment (worsening 10%) in myocardial function and deformation measured at 24 months using 3-dimensional (3D) echocardiography, left ventricular ejection fraction (LVEF), and global longitudinal strain (GLS). ClinicalTrials.gov identifier: NCT2236806. **Results.** 262 women (median age, 48 years; range, 24-75 years) were enrolled and treated in the study. We analyzed patients who had completed the pre-planned cardiological assessment at 24 months. Baseline demographic, tumor, and cardiovascular profiles were similar between groups. All patients received an anthracycline-based chemotherapy, 215 patients received at least three cycles of anthracyclines (range 1-6), 223 patients received also a taxanes-based chemotherapy, and 84 cases were treated with adjuvant trastuzumab. Sixty patients were treated with neoadjuvant chemotherapy, 157 cases received adjuvant endocrine therapy, and 128 patients had postoperative radiation therapy. GLS worsened 10% or greater in 68% of patients enrolled in the placebo arm, 15%, 13%, and 13% in the ramipril, bisoprolol, and ramipril plus bisoprolol arms, respectively ($P < 0.05$). A reduction of 10% or greater in 3D-LVEF was observed in 19% in the placebo arm, 11% in the ramipril arm, 11% in the bisoprolol arm, and 7% in the ramipril plus bisoprolol arm ($P < 0.05$). Study drugs were well tolerated with no serious adverse events, the ramipril plus bisoprolol arm showed significantly more toxic effects and had a significantly higher rate of allocated treatment discontinuation as compared to the other arms. **Conclusions.** Cardioprotective pharmacological strategies in patients who were affected by breast cancer and were receiving an anthracycline-based chemotherapy are well tolerated and protect against cancer therapy-related LVEF decline and heart remodeling.

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PD8-04

PD8-04 The role of Yoga as a complementary therapy in women undergoing treatment for breast cancer: A randomized controlled trial

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Background: Yoga has been tested in multiple small-randomized studies for its impact on quality of life (QOL) on breast cancer (BC). We conducted a randomized controlled trial, to study the effect of yoga on disease free survival as the primary endpoint in women with operable breast cancer. (NCT02161900). Methods: Women with non-metastatic BC during and after standard treatment, were randomized to yoga and conventional exercise(YCE) versus conventional exercise only(CE). The primary endpoint was disease free survival (DFS) with secondary endpoints of overall survival (OS) and QOL, which was assessed using the EORTC QLQC30, BR23, Brief fatigue inventory (BFI), Visual pain scores (VPS) and a spirituality questionnaire (SQ). EORTC QLQ was assessed at baseline (BL), 6-9 months (mo), 18-21 mo. BFI and VPS at BL, 6-8 mo and 12-15 mo and SQ at BL and 12-15 mo. We report the final analysis of DFS, OS and QOL in 850 women randomized to the study. The groups were balanced for clinic-pathologic factors in both arms. Results: Of the 850 women randomized on the study, 426 were on YCE arm and 424 on CE arm. The median age was 47 versus (vs) 48 years, median pT size was 3 vs 2.85cm, grade 3 tumors were 82.7 vs 82.1%, hormone receptor positive was in 69% vs 69.4% and HER2neu positive was in 14.4 vs13.7% in YCE and CE arms respectively. At a median follow-up of 80 months the disease free survival was 80% vs 76.7% (HR= 0.85, 95% CI= 0.64 – 1.14, p=0.28), and overall survival was 85.4% vs 83.1% (HR= 0.86, 95%CI = 0.61 – 1.21, p=0.38) in YCE and CE respectively. Physical(p=0.043) and emotional function (0.017), fatigue (p=0.002), pain (p=0.031), appetite loss (< 0.001) arm symptoms (0.035) and systemic therapy side effects (0.036) reduced at 6-9mo in YCE, with sustained improvements in physical (p=0.036) and emotional function (p=0.008) at 54mo. The median score of fatigue after adjuvant therapy measured by QLQ C30 was lower in YCE compared to CE (11.11vs 22.22, p = 0.002). Similarly, in BFI the baseline median scores of

severity of fatigue were 5 in YCE and 6 in CE which reduced to 3 at one year in both groups. A further reduction to 0 was observed in the YCE arm at 2 years and then sustained till 4 years compared to the median score of fatigue in CE which stayed at 3. ($p=0.04$, 0.03 2 and 4 years respectively). In VPS the number of patients experiencing severe pain in YCE group were less than CE group with specific reduction noted in pain over the breast/ chest wall ($p=0.018$ at 24mo). Lastly SQ assessed spirituality and showed no difference, but less deterioration compared to baseline scores were noted in YCE. Fifty-three percent women on YCE showed an improvement in QOL from baseline compared to 47% in CE, however the global score of QOL did not differ significantly between the two arms. This cohort had overall compliance of 61% to yoga and physiotherapy in YCE with 91.75% compliance among those who did yoga for 6-9mo and 85% to physiotherapy alone in CE. Conclusions: Yoga resulted in a 15% relative improvement in DFS and 14% in OS, that did not reach statistical significance in this trial. Yoga is a low-risk, low-cost therapy that improves day-to-day activity, including pain, fatigue and quality of life in women with breast cancer. This is the first study where the long term benefits in quality of life have been noted with the addition of yoga for women undergoing treatment for breast cancer.

Disclosure(s):

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5:00 PM - 6:15 PM

PD8-05

PD8-05 Effectiveness of Electroacupuncture Versus Auricular Acupuncture in Reducing Pain and Improving Quality of Life in Breast Cancer Survivors with Chronic Musculoskeletal Pain

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Introduction: Chronic musculoskeletal pain is common and debilitating among breast cancer survivors. Recently, the Personalized Electroacupuncture (EA) versus Auricular Acupuncture (AA) Comparative Effectiveness (PEACE) trial demonstrated that both acupuncture methods reduced pain more than usual care (UC) in cancer survivors. However, the comparative effectiveness between EA and AA among breast cancer survivors is unknown. Here, we report the results of subgroup analysis of breast cancer survivors enrolled in the PEACE trial.

Methods: PEACE is a three-arm, parallel, single center randomized trial investigating the effectiveness of EA and AA versus UC for chronic musculoskeletal pain in 360 cancer survivors. Patients in both EA and AA received ten weekly treatments. Patients in UC could receive ten EA treatments after week 12. The primary endpoint was the change in mean Brief Pain Inventory (BPI) pain intensity from baseline to week 12; change from baseline to week 24 and change in quality of life were secondary endpoints. We analyzed the subset of 46% of trial participants with a primary diagnosis of breast cancer. We conducted constrained linear mixed model analyses, which constrained all arms to have a common pre-randomization baseline mean. Model-based mean estimates at weeks 12 and 24 were compared between arms using model contrasts. Results: Among 165 breast cancer survivors, the baseline mean pain severity was 5.35 (95% Confidence Interval [CI]: 5.04, 5.66). At week 12, the BPI pain severity score was 2.69 (2.26, 3.13) in EA, 3.60 (3.17, 4.02) in AA, and 5.06 (4.47, 5.65) in UC. At week 24, the mean BPI pain severity was 2.84 (95% CI: 2.40, 3.28) in EA and 3.67 (95% CI: 3.23, 4.10) in AA. EA reduced pain severity significantly more than AA at both week 12, (-0.90 [-1.45, -0.36], p=0.001) and week 24 (-0.82, [-1.38, -0.27], p=0.004). There were no differences between EA and AA in improvements in PROMIS physical health or mental health component scores, but both EA and AA significantly improved both PROMIS scores at week 12 compared to UC. Mild toxicities were reported, more patients dropped out of the AA arm due to ear pain. Conclusions: EA was more effective than AA at reducing pain severity, but both similarly improved physical and mental health scores. Breast cancer survivors with chronic musculoskeletal pain may consider EA before AA.

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PD8-06

PD8-06 Incidence of Acute and Persistent Clinically Meaningful Chemotherapy Induced Peripheral Neuropathy in Patients with Early-Stage Breast Cancer Receiving Taxane Therapy: SWOG S1714 (NCT# 03939481)

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Background: Taxanes play an important role in the treatment of early-stage breast cancer. Chemotherapy induced peripheral neuropathy (CIPN) is a complication of taxane therapy and can lead to treatment dose reduction or discontinuation, which may ultimately affect overall survival, and can substantially impact quality of life and functional status in survivors. The trajectory of CIPN symptoms is not well described. Methods: SWOG S1714 enrolled participants 18 years or older with Stage I-III primary non-small cell lung, primary breast, or primary ovarian/fallopian tube/peritoneal cancer starting treatment with a taxane-based regimen. Participants with baseline neuropathy were eligible to enroll. Neuropathy was assessed with the patient-reported European Organization for Research and Treatment of Cancer QLQ-CIPN20 (CIPN-20). The occurrence of clinically meaningful sensory neuropathy was defined as an increase of 8 or more points (on a 0-100 scale, with a higher score indicating more severe symptoms) between baseline and follow-up in the sensory neuropathy subscale of the CIPN-20. Assessments occurred at baseline and at 4, 8, and 12 weeks +/- 14 days and 24, 52, 104, and 156 weeks +/- 28 days after registration. Results: Among N=1336 enrolled participants, 1321 were eligible (99%). Of the eligible participants, we will report on the 1198 (90.7%) with breast cancer. The median age was 55 years (range 23-84) and 99.3% were female. The breast cancer cohort included 72.2% White, 11.7% Black, 4.9% Asian, and 11.0% Hispanic/Latino participants. Paclitaxel (every week for 12 weeks or every 2 weeks for 8 weeks) was administered to 56.2% and docetaxel (every 3 weeks for 12-18 weeks) to 43.8%. The mean baseline patient-reported CIPN-20 sensory neuropathy subscale score was 6.2 (standard deviation 12.0). Through one full year of follow up, 1084 participants (90.5%) were evaluable for sensory neuropathy at any time point. At individual assessment times, clinically meaningful sensory neuropathy was reported by 18.7% of participants at week 4, 33.0% at week 8, 46.3% at week 12, 44.8% at week 24, and 47.4% at week 52. Clinically meaningful sensory neuropathy at one or more assessments was reported by 67.8% of participants. Conclusions: In this large prospective cohort of racially/ethnically diverse participants with breast cancer receiving taxane-based therapy, 2 out of every 3 experienced clinically meaningful sensory neuropathy symptoms during the first year of treatment and nearly 50% continue to experience clinically meaningful sensory neuropathy symptoms at the end of the first year. Given the high incidence of symptoms during taxane treatment and persistence of symptoms after treatment completion, it is critical to develop effective methods to predict, prevent, and treat this toxicity. Follow up of data at 104 and 156 weeks will further characterize the trajectory of long term CIPN symptoms. Funding: NIH/NCI/NCORP grant UG1CA189974

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5:00 PM - 6:15 PM

PD8-07

PD8-07 The Changing Informational Needs of Young Women Affected by Breast Cancer: A National Needs Assessment

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Background: Nearly 9% of new breast cancer diagnoses in the United States are in women under the age of 45. In 2012, Living Beyond Breast Cancer (LBBC) conducted a four-phase needs assessment of young women diagnosed with breast cancer at or before age 45, which identified needs and service gaps in resources addressing the unique needs of this age group and explored how these women prefer to receive emotional support and breast cancer information. In 2020, LBBC conducted another assessment to better understand young women's service preferences and information needs. The 2020 assessment focused specifically on demographic differences and targeted content areas, including sexual health and long-term impacts on physical and emotional health. Methods: An 88-item online questionnaire was administered via REDCap between August and September 2020. Inclusion criteria were women diagnosed with breast cancer at or before age of 45 who were living in the United States. The survey included questions about respondents' experiences with treatment side effects, communication with their healthcare providers, and how they sought emotional support services, and breast cancer information. Questions centered on sexual, physical, and emotional health needs of respondents throughout their treatment journey. Special focus was placed on participants' demographic information, including race/ethnicity, cancer stage, and time elapsed since diagnosis. Results: Overall, breast cancer diagnosis and treatment caused significant physical and emotional impacts on women diagnosed before age 45 (N=717), and a woman's race/ethnicity, cancer stage, and time elapsed since diagnosis resulted in differences in their experiences. In addition, how a woman preferred to receive emotional support services and breast cancer information differed based on her race/ethnicity, and cancer stage. Many participants (64%) also reported significant impacts to their sexual health, yet their healthcare providers were unable to address those needs. Compared to women diagnosed at other stages, those diagnosed with stage III and stage IV breast cancer reported significantly higher

percentages of problems with little or no interest in sex. How a woman preferred to receive emotional support services and breast cancer information differed based on her race/ethnicity, and cancer stage. The 2020 survey also showed that although eight years have passed since the original LBBC needs assessment, the percentage of young women reporting discussions about fertility with healthcare providers (48%) remain largely unchanged. Additionally, more respondents in the 2020 survey reported accessing genetic counseling (72%) and testing services (90%) than the 2012 survey participants, but in 2020, the data indicated significant disparities in both counseling and testing based on race/ethnicity. Conclusion: Young women diagnosed with breast cancer before age 45 reported several significant differences in service preferences and information needs based on race/ethnicity and cancer stage. While some aspects of the breast cancer experience have improved, there remain several gaps in care and survivorship needs, including sexual health. Informational materials and supportive programming may address these gaps by accounting for differences among the diversity of people diagnosed in this age group.

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PD8-08

PD8-08 Employment status change in a cohort of young women with breast cancer in Mexico

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Background: Breast cancer diagnosis and treatment generates disruption in multiple aspects in the life of patients, including work-related outcomes. The disruption in employment may exacerbate the economic burden on patients and their families, contributing to financial toxicity and ultimately impacting quality of life, especially in young women. However, the evidence of employment status at diagnosis for this group and its trajectory thereafter is limited. This study

aims to document the first change in employment experienced by Mexican young women with a recent diagnosis of breast cancer and determine which factors are associated with a decrease in work activities. Methods: Mexican women from the Joven & Fuerte prospective multicenter cohort, aged ≤ 40 , diagnosed with stage I-III breast cancer between 2015-2021 with at least 6 months of follow-up were included. Participants with a documented disease recurrence, missing employment status information, diagnosis of a new primary breast cancer or a second type of cancer were excluded from the analysis. Patients completed surveys at baseline, 6 months, and yearly for up to 5 years to assess sociodemographic characteristics, employment status, medical and treatment data. Employment status was categorized on a scale as follows: full-time > part-time > student > medical leave > unemployed. Only the first employment status change was included in this analysis. The Kaplan-Meier failure estimate was employed to calculate the increase or decrease in employment status at 1 year and 2 years post-diagnosis. Competing risk regression models were undertaken to explore variables associated with a decrease in employment status. Results: A total of 142 women with a median age at diagnosis of 36.5 years (IQR 33-39) and median follow-up of 17 months were included in the analysis. Baseline employment status for these patients was: employed - full time (27%), employed - part time (14%), student (1%), medical leave (4%) and unemployed (54%). At 12 months, 18.5% of participants had a reduction in their work activity (95% CI 12.8 - 26.4%) and this proportion further increased to 25.8% at 24 months (95% CI 18.7 - 34.8%). In contrast, 11.8% (95% CI 7.3 - 19.0%) and 23.2% (95% CI 15.9 - 33.2%) of participants exhibited an increase in their work activity at 12 and 24 months, respectively. The most common patterns in first employment status change were from unemployed to employed - full time (19%), employed - full time to employed - part time (13%) and employed - full time to unemployed (13%). In univariable analysis, having a partner at diagnosis demonstrated a lower hazard for experiencing a decrease in work activities; in contrast, postmenopausal status at 1 year was associated with a higher hazard of experiencing a decrease in employment status. However, in a competing-risks model including both partner and menopausal status, only the latter was associated with a higher hazard for experiencing a reduction in work activity (SHR=3.05, 95% CI 1.38 - 6.72, $p=0.006$). Age, education, monthly income, number of people who contribute to the household, having a partner at diagnosis, number of children, being financially responsible for another person, mastectomy, chemotherapy, radiotherapy and endocrine treatment were not associated with a higher probability of reduction in work activity. Conclusion: This cohort is one of the few initiatives assessing the impact of diagnosis and treatment of BC in young patients, specifically Latin American women. Our results show that there are relevant employment status changes after BC, possibly as a consequence of their treatment. Physical and psychological elements of menopause might influence the decrease in work status. Further studies are needed to deepen our understanding of employment changes in Latin American young women and guide interventions that address unintended limitations of work activities.

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PD8-09

PD8-09 Impact of Neighborhood Disadvantage on Biological and Clinical Indicators of Anxiety and Breast Cancer Survival

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Introduction: Women living in disadvantaged neighborhoods consistently having worse breast cancer survival. Recent studies have identified that disparities by neighborhood disadvantage persist after controlling for patient, tumor, and National Comprehensive Cancer Network-guideline concordant treatment. This suggests unaccounted mechanisms by which neighborhood disadvantage “gets under the skin” to impact to shorter breast cancer survival.

Methods: Women with stage 0-3 breast cancer between 1998-2005 were enrolled in a clinical trial for stress management 2-10 weeks post-surgery and before initiating adjuvant treatment. At baseline, women provided an evening-time serum cortisol sample and were administered a structured clinical interview of anxiety symptoms (Hamilton Anxiety Rating Scale; HAM-A). Of the 240 women who enrolled in the study and completed baseline procedures, home addresses were provided by 225 women (93.8%). The addresses were used to determine the Area Deprivation Index (ADI), a validated measure of neighborhood disadvantage. Women were categorized as low (1-3) versus high (4-10) ADI. Linear regression analysis was used to assess the relationship between ADI and serum cortisol and logistic regression to assess whether ADI group predicted the presence of clinically significant anxiety per the HAM-A. Cox regression analysis was used to determine predictors of breast cancer-specific survival.

Results: The average age of our population was 50.4 years old (range 23-70 years) and the majority were non-Hispanic White (63.6%). Most patients had stage 1 (37.8%) or 2 (38.2%) disease. The majority lived in advantaged neighborhoods (low ADI, 77.8%). On the HAM-A, 46.8% of women reported clinically significant anxiety symptoms. When controlling for age, stage, and type of surgery, women with a high ADI had higher cortisol levels than women in with a low ADI (Beta=.19, $t(117)=2.18$, $p=.031$). Moreover, accounting for age, stage, and type of surgery, women with a high ADI were nearly two times as likely to have clinically significant anxiety symptoms in the HAM-A clinical interview (OR 1.99, 95%CI 1.01, 3.90, $p=.046$).

Moreover, after controlling for study condition (stress intervention vs. control), age, stage, Black race, and treatment, women with living in neighborhoods with an increasing ADI (disadvantaged neighborhoods) had shorter 5-year breast cancer-specific survival (HR=.096 95%CI 0.02, 0.64) compared to women living in neighborhoods with a lower ADI (advantaged neighborhoods).

Conclusion: This study identified that neighborhood disadvantage is significantly associated with higher levels of cortisol, clinical anxiety, and shorter 5-year breast cancer-specific survival. Future studies need to evaluate stress pathways as a potential mechanism by which neighborhood disadvantage impacts breast cancer-specific survival.

Table 1. Multiple Regression Illustrating Relationship between ADI and Serum Cortisol

Variable	Unstandardized		Standardized		
	B	SE	B [95% CI]	β	p
ADI (REF = Low ADI 1-3 (v. high ADI 4-10))	2.62	1.20	[0.24, 5.00]	0.19	.031*
Age	-0.14	0.06	[-0.26, -0.02]	-0.21	.022*
Surgery Type (REF= lumpectomy (v. mastectomy))	0.54	1.12	[-1.67, 2.74]	0.05	.632
Stage (0-3)	0.07	0.69	[-1.29, 1.44]	0.01	.916
Total Model	<i>Adjusted R</i> ² = .07, <i>F</i> [4,117] = 3.13, <i>p</i> = .017				

Note: SE = Standard Error; CI = Confidence Interval; ADI = Area Deprivation Index; *p<.05

Table 2. Logistic Regression Illustrating Relationship between ADI and Anxiety on HAM-A Clinical Interview

Table 2. Logistic Regression Illustrating Relationship between ADI and Anxiety on HAM-A Clinical Interview

Variable	HAM-A Clinically Significant Anxiety				
	Unstandardized		Standardized		
	<i>B</i>	SE	OR	OR [95% CI]	<i>p</i>
ADI (REF = Low ADI 1-3 (v. high ADI 4-10))	0.69	0.35	1.99	[1.01, 3.90]	.046*
Age	-0.03	0.02	0.97	[0.94, 1.00]	.064
Surgery Type (REF= lumpectomy (v. mastectomy))	0.13	0.17	1.13	[0.81, 1.59]	.472
Stage (0-3)	0.03	0.30	1.03	[0.58, 1.85]	.917
Total Model	<i>Cox and Snell R</i> ² = .04, $\chi^2(4) = 9.34$, <i>p</i> = .053,				

Note: HAM-A = Hamilton Anxiety Rating Scale; SE = Standard Error; CI = Confidence Interval; OR=Odd's Ratio; ADI = Area Deprivation Index; **p*<.05

Disclosure(s):

Neha Goel, MD: No financial relationships to disclose

Molly Ream, PhD: No financial relationships to disclose

Alexandra Hernandez, MD, MPH: No financial relationships to disclose

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Daniel S. O'Neil, MD, MPH: No financial relationships to disclose

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5:00 PM - 6:15 PM

PD8-10

PD8-10 Identifying racial and ethnic disparities in psychosocial care among adults with metastatic breast cancer (mBC): A retrospective analysis across six New York health systems

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Background: More than 150,000 men and women are currently living with mBC in the United States. A diagnosis of mBC and its associated treatment can have pronounced consequences on patients' psychosocial well-being. However, to date, few studies have described patterns of psychosocial care among this population. Identifying disparities in psychosocial care utilization at the systems level may uncover gaps in mBC supportive care more broadly. Using a large retrospective cohort inclusive of patients treated at six health systems across New York City (NYC), we sought to determine if there were racial or ethnic differences in receipt of outpatient psychosocial care and psychosocial medications.

Methods: Adults diagnosed with mBC between 2010-2020 were identified using ICD-9 and ICD-10 diagnosis codes from the INSIGHT-Clinical Research Network database, which includes electronic health record, administrative, and clinical data from 12 million patients who received care across six NYC health systems. Receipt of outpatient psychosocial care was operationalized using Common Procedure Terminology codes for receipt of any outpatient psychotherapy or counseling visit with a licensed provider. Receipt of psychosocial medications (e.g., antidepressants, anxiolytics, sleep aids, benzodiazepines) were identified using RxCUI codes. Associations between race/ethnicity and outpatient psychosocial care and medications use was evaluated using logistic regression. Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated for all estimates.

Results: We included 6,934 adults with mBC. Mean age was 61 (SD: 14) years and < 1% were male. Overall, 42% were non-Hispanic white, 17% non-Hispanic Black, 12%, Hispanic/Latinx, 4.8% Asian/Native Hawaiian/Pacific Islander, and 24.4% "other or unknown." Only 159 patients (2.3%) had ≥ 1 outpatient psychosocial care visits with a mean of 17 (SD: 42) visits per patient.

Of the overall cohort, 4,308 patients (62%) were prescribed at least one psychosocial medication during the study period. Both psychosocial outpatient care and psychosocial medication use differed by race/ethnicity (see Table). Compared to Non-Hispanic Whites, Black (OR 1.81; 95% CI 1.12-2.90) and Hispanic/Latinx (OR 4.46; 95% CI 2.96-6.77) mBC patients were more likely to have a documented outpatient psychosocial visit. Black (OR 0.63; 95% CI 0.54-0.72) and Asian (OR 0.40; 95% CI 0.32-0.50) mBC patients were less likely to be prescribed psychosocial medications compared to Non-Hispanic White patients.

Conclusion: Among a large, diverse cohort of mBC patients treated across NYC, we observed low utilization of outpatient psychosocial care. This finding may be attributable in part to patterns of referral/use of psychosocial support in the private practice setting that cannot be captured in administrative data. Sub-optimal health insurance coverage for psychosocial support may also be responsible for low utilization of outpatient psychosocial care. In contrast, psychosocial medication use was far more prevalent than outpatient care among our mBC cohort with significant differences observed by race/ethnicity. Identified differences suggest that unmet needs may exist and warrant further investigation.

Table. Psychosocial Outpatient Care & Medication Use by Race/Ethnicity

	Non-Hispanic White N=2910 (%)	Non-Hispanic Black N=1161 (%)	Hispanic/Latinx N=864 (%)	Asian/Native Hawaiian/ Pacific Islander N=330 (%)	Other/Unknown N=1669 (%)
Outpatient care	42 (1.4)	30 (2.6)	53 (6.1)	0 (0)	34 (2)
Medication use	1969 (67.7)	658 (56.7)	578 (66.9)	150 (45.5)	953 (57)

Disclosure(s):

Laura Pinheiro, PhD, MPH: Pfizer: Contracted Research (Ongoing)

Anjile An, MPH: Pfizer: Contracted Research (Ongoing)

Desiree Walker, n/a: No financial relationships to disclose

Anne Marie Mercurio, n/a: Blue Note Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Medidata Solutions: Consulting Fees (e.g., advisory boards) (Ongoing), Travel, Accommodations, Expenses (Ongoing)

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Discussion 1 + Q&A: PD9-01, PD9-03, PD9-04 & PD9-05

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Discussion 2 + Q&A: PD9-06, PD9-07, PD9-08 & PD9-09

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5:00 PM - 6:15 PM

Poster Spotlight Discussion 9: Immune Landscape and Microenvironments

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Disclosure(s):

W. Fraser Symmans, MB.ChB.: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Delphi Diagnostics: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing); Eiger Biopharmaceuticals: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); IONIS Pharmaceuticals: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Pfizer: Contracted Research (Ongoing); transcriptional measure of endocrine activity: unrelated patent (Ongoing)

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5:00 PM - 6:15 PM

PD9-01

PD9-01 Stromal mediators of lymphocyte exclusion and dysfunction in triple negative breast cancer

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Triple negative breast cancer (TNBC) is the most aggressive breast cancer subtype with poor prognosis and limited treatment options. One of the mechanisms contributing to this is the ability of TNBC tumors to evade anti-tumour response, limiting the success of immune-checkpoint therapy. In recent studies of the tumor microenvironment, stromal cells have emerged as potential important mediators of lymphocyte function in TNBC. Multi-omics studies from our group and others have elucidated the heterogeneity of stromal cells and their interactions with immune cells in TNBC. However, the clinical relevance and functional characteristics of these relationships remain poorly explored. Our previous work revealed functionally distinct subpopulations of stromal cells in breast cancer: endothelial cells, myofibroblast-like cancer-associated fibroblasts (myCAFs), inflammatory-CAFs (iCAFs), and perivascular-like cells which resemble pericyte and smooth muscle cells in immature and differentiated states (impVLS; dPVLs), respectively. Here we directly explored the clinical relevance of these stromal subpopulations and their association with immune evasion in a large independent TNBC cohort with long-term survival data. Using markers derived from our single-cell multi-omics studies, we performed multiplex immunofluorescence using the OPAL9 platform on tumor microarrays from 222 TNBC patients to mark myCAFs, iCAFs, dPVLs, endothelial cells, CD8 and/or PD1 positive T-cells. Digital imaging analysis (QuPath) revealed a significant negative correlation between the abundance of stromal cells and CD8 T cells. This

cytotoxic T-cell exclusion is primarily driven by smooth muscle dPVLs. Parallel to this T-cell exclusion, our functional studies demonstrate that stromal cells suppress T-cell proliferation. Using multiple ex vivo co-culture models of primary TNBC CAFs and peripheral blood mononuclear cells (PBMCs) from healthy and matched donors, we show that CAFs suppress the proliferative capability of CD4 and CD8 T-cells. ScRNA-seq of these co-culture models demonstrate that CAF educated T cells are driven into a LAG3+ exhausted state enriched for canonical pathways of immunosuppressive cytokine signaling. Our findings suggest that manipulation of these stromal subpopulations could elicit a more effective immune response in a subset of patients through inhibiting T-cell dysfunction and exclusion.

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Julia Chen, MBBS Bsc(Med)Hon MMED FRACP: No financial relationships to disclose

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Alex Swarbrick, PhD: No financial relationships to disclose

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5:00 PM - 6:15 PM

PD9-02

PD9-02 MHC class I and PD-L1 expression in triple-negative breast cancer subtypes: impact on T-cell infiltration and clinical outcome

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Background: Triple-negative breast cancer (TNBC) is a heterogeneous group of cancer with dismal prognosis. In an effort to discover therapeutic targets, TNBC has been further stratified into molecular subtypes. Immune checkpoint inhibitors targeting programmed cell death protein 1 (PD-1) and its ligand (PD-L1) have been increasingly utilized for the treatment of TNBC. Difficulty remains, however, in appropriate patient selection for treatment, as many PD-L1-positive cancers fail to show durable responses to PD-1/PD-L1 inhibition. Major histocompatibility complex (MHC) class I molecules play a crucial role in the presentation of tumor antigenic peptides to cytotoxic T cells. Loss of MHC class I expression in tumor cells represents a possible mechanism of immunotherapeutic resistance in PD-L1-positive cancers. However, little is known about the clinical impact and value of MHC class I expression in TNBC subtypes. Thus, this study examined MHC class I expression in TNBC subtypes with attention to PD-L1 expression and T cell infiltration. Materials and methods: MHC class I and PD-L1 expression were assessed by immunohistochemistry in 256 TNBC samples using tissue microarray. Immunohistochemistry for the TNBC molecular subtype-surrogate markers [cytokeratin 5/6 (CK5/6), CK14, epidermal growth factor receptor (EGFR), and androgen receptor (AR)], CD3, and CD8 was also performed. TNBC subtypes were classified into three subtypes: basal-like (BL), luminal AR (LAR), and unclassifiable type (UN). Results: All immunohistochemical markers were interpretable in 240 cases. TNBCs were classified into BL (65.8%), LAR (11.3%), and UN (22.9%) subtypes. Loss of MHC class I expression was found in 62 of 240 (25.8%) cases and was observed in 23.4% of BL, 40.7% of LAR, and 25.9% of UN subtype. PD-L1 expression in tumor-associated immune cells ($\geq 1\%$) was seen in 69.2% (166/240). Among 166 PD-L1-positive TNBC cases, loss of MHC class I expression was seen in 16.4% of BL, 31.3% of LAR, and 20.0% of UN subtype. Loss of MHC class I expression was associated with low stromal TILs density and low CD3+ and CD8+ T-cell infiltration in BL subtype. CD3+ and CD8+ T-cell infiltration in TNBC subtype had a positive correlation with PD-L1 expression. In PD-L1 positive BL subtype, MHC class I lost expression showed a lower infiltration with CD3+ and CD8+ T-cells than MHC class I intact expression. In BL subtype, PD-L1 expression was associated with better disease-free survival and loss of MHC class I expression was associated with poor overall survival. However, MHC class I and PD-L1 expressions were not independent prognostic factors for disease-free or overall survival. Conclusions: Loss of MHC class I expression was found in TNBC, including PD-L1 positive cases. In PD-L1 positive BL subtype, loss of MHC class I expression was associated with low CD3 and CD8+ T-cell infiltration. Our results suggest that the evaluation of PD-L1 and MHC class I expression together is very important for the selection of potential responders to anti-PD-1/PD-L1 therapy for the TNBCs, especially the BL subtype.

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ji shin lee, n/a: No financial relationships to disclose

nah ihm kim, n/a: No financial relationships to disclose

min ho park, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

PD9-03

PD9-03 Breast Cancer Microenvironment Change After Neoadjuvant Endocrine Treatment

Breast Cancer Microenvironment Change After Neoadjuvant Endocrine Treatment

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Background: Estrogen receptor positive (ER+) / HER-2 negative breast cancer (BC) is considered to be an immunologically cold tumor compared to triple negative breast cancer. Therefore, the tumor microenvironment (TME) of ER+ / HER-2 negative BC is understudied.

The receptor activator of nuclear factor- κ B ligand (RANKL)-RANK pathway was first identified, as mediator of T and dendritic cells interaction, but it is mostly known for its role as key regulator of bone remodeling and pathophysiology of bone metastases. RANK is a member of the tumor necrosis factor receptor (TNFR) superfamily that is activated upon RANKL binding, promoting cell proliferation, survival and differentiation. The RANKL-RANK pathway also emerged as a major mediator of hormone-driven breast carcinogenesis. The aim of this study is to investigate the TME and the immune response during neoadjuvant endocrine therapy (NET) and to correlate this with the treatment response in a real life setting.

Methods: Expressions of immune checkpoint receptors and immune cells were examined immunohistochemically in pre- and post- NET on a cohort of 44 ER+ / HER-2 negative BC patients. They were treated with tamoxifen (N=8), an aromatase inhibitor (N=36) or a combination of an aromatase inhibitor with a PI3K inhibitor (N= 7) for a median duration of 6 months (range 1-32) months. Monoclonal antibodies for PD-L1, PD-1, TIM-3, LAG-3, CTLA-4, CD4, CD68, FOXP3, RANK and RANKL were used. All staining were done according to validated protocols and scoring was done by a pathologist specialized in breast cancer. Positivity was defined as staining > 1% on TILs. Response to NET was evaluated according to tumor size change on imaging and Ki-67 change.

Results: The median age was 62.5 (44–90.3) years. Diameter of tumor size decreased with a mean of 7.818 mm ($p < 0.0001$) during NET and the value of Ki-67 value decreased significantly after NET (value, $p < 0.0004$). An increase in PD-L1 expression after NET showed a trend towards significant ($p = 0.088$) and RANK expression on TILs significantly decreased with a median of 30% (range= -70 to 85) ($p = 0.0007$) after NET. A good response to NET defined as a decrease in tumor size and/or decrease of Ki-67 was found to be associated with a longer duration of NET, a change of CD4+ T-cells, a change of RANK expression on TILs and a higher number of CD68+ tumor-associated macrophages before the start of NET and also RANK expression on TILs before the start of NET.

Conclusion: The immune micro-environment plays an important role in ER+ / HER-2 negative BC. NET influences the composition and/or functional state of the infiltrating immune cells. Furthermore, changes in the immune micro-environment are also associated with treatment response.

Breast Cancer Microenvironment Change After Neoadjuvant Endocrine Treatment

	Continuous parameters		
	(median (min-max))		
	Before NET	After NET	p value
Tumour Size	23.5 (6-65)	13 (0-70)	<0.001
Ki-67	15 (1-45)	3 (1-45)	<0.001
sTIL	5 (1-85)	5 (1-80)	0.08
CD-68	15 (5-40)	10 (5-50)	0.11
CD-4	5 (1-13)	10 (1-70)	0.03
FOXP3	22.5 (0-60)	15 (1-60)	0.14
FOXP3/CD-4	2.307(0-15)	1 (0.03-12)	0.04
	Categorical parameters n (%)		
	Before NET	After NET	p value
PD-L1	4 (9)	11 (25)	0.088
PD-1	8 (18)	15 (34)	0.16
CTLA-4	10 (23)	12 (27)	0.69
TIM-3	28 (64)	23 (52)	0.53
LAG-3	19 (43)	29 (66)	0.22

Comparison of continuous and categorical parameters before and after NET. Comparison of the continuous parameters was done using Wilcoxon signed rank test. Comparison of the categorical parameters was done using a Chi-square test. sTIL: stromal tumour infiltrating lymphocytes and NET: neoadjuvant endocrine therapy. Bold values denote statistical significance at the $p < 0.05$ level.

Disclosure(s):

Gizem Oner, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

PD9-04

PD9-04 Immunological and clinical consequences of durvalumab treatment in combination to neoadjuvant chemotherapy in triple-negative breast cancer patients

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Background: The implementation of immune checkpoint inhibitors in the therapy of different cancer types has provided promising results, but only a limited number of patients respond. Therefore, biomarkers to identify these responding patients are urgently needed. Methods: The GeparNuevo was a randomized, double-blind phase II trial in which triple-negative breast cancer (TNBC) patients were treated with neoadjuvant chemotherapy (NACT) consisting of nanoparticle albumin-bound paclitaxel in an initial phase followed by treatment with epirubicin and cyclophosphamide. Placebo or durvalumab were given throughout the neo-adjuvant treatment and in the “window” sub-cohort also prior to chemotherapy. Primary objective of this report was to evaluate changes in the blood immune cell repertoires of TNBC patients receiving durvalumab (anti-PD-L1) versus placebo in combination with NACT. At up to 4 different time points during therapy, blood samples were taken and underwent immunomonitoring using multicolor flow cytometry. The absolute counts of the major immune cell subtypes in the blood as well as the frequencies of different immune cell subpopulations and their functional phenotypes along treatment were determined and correlated to clinico-pathologic characteristics of the patients and to treatment response. Results: 120 out of 174 patients included in the GeparNuevo trial underwent blood immunomonitoring; 63 patients belonged to the “window” sub-cohort. Durvalumab administration almost completely blocked the detection of the inhibitory ligand PD-L1 and induced changes in the composition of the immune cell subpopulations. Evaluation of the “window” sub-cohort, in which an enhanced, but not significant pathological clinical response was observed within the immunomonitoring patients, identified different markers correlating with clinical response to durvalumab. Higher frequencies

of CD4+ T cells at recruitment as well as increased frequencies of T cells bearing the gamma delta TCR along treatment were some of the characteristics of patients responding to durvalumab treatment. Conclusions: The flow cytometry-based immunomonitoring of the clinical trial identified different immune-relevant biomarkers at recruitment as well as during treatment that predict clinical response to durvalumab. After validation of this data in an independent patient cohort, these markers could be implemented for an improved patient stratification to immunotherapy.

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PD9-05

PD9-05 Stromal tumor-infiltrating lymphocytes identify early-stage triple-negative breast cancer patients with favorable outcomes at 10-year follow-up in the absence of systemic therapy: a pooled analysis of 1835 patients

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Background: The prognostic value of stromal tumor-infiltrating lymphocytes (TILs) as a biomarker for triple-negative breast cancer (TNBC) has been extensively demonstrated in patients (pts) receiving (neo)adjuvant systemic therapy. In addition, several small studies suggest that a subset of pts with early-stage TNBC and high TILs have excellent long-term outcomes, even in the absence of systemic therapy [1-3]. However, data on the absolute risk of TNBC recurrence according to TIL levels in the absence of systemic therapy are limited and critical to inform the design of future systemic therapy de-escalation clinical trials.

Methods: We conducted an individual patient data pooled analysis of 12 international cohorts of pts with TNBC treated with locoregional therapy but no systemic therapy. TNBC was defined as tumors with estrogen and progesterone receptor of < 1% and HER2 negative (IHC 0, 1+ or IHC 2+ and FISH negative) per local evaluation. TILs were locally assessed in hematoxylin & eosin-stained slides according to the International Immuno-Oncology Biomarker Working Group guidelines (www.tilsinbreastcancer.org). We used the Kaplan-Meier method to assess survival outcomes according to prespecified TIL thresholds: 30% and 50%. Confidence intervals (CI) for survival probabilities were calculated using a percentile bootstrap method. The primary endpoint was invasive disease-free survival (iDFS, STEEP 2.0 definition). Key secondary outcomes included recurrence-free survival (RFS), distant disease-free survival (DDFS) and overall survival (OS).

Results: 1,835 pts diagnosed with TNBC between 1982 and 2017 who did not receive systemic therapy were included. The median age at diagnosis was 56 (IQR 38-71). Menopausal status was known in 1,184 women, of whom 78% were post-menopausal. The median tumor size was 2.0 cm (IQR 1.2-2.6). Most pts (87%) had no axillary lymph node involvement (N0). Most tumors were invasive ductal carcinoma (74%) and grade 3 (70%). The median level of TILs was 15% (IQR 5-40). The median duration of follow-up was 30.4 years (95% CI 29.9, 31.1). A total of 950 (52%) iDFS, 828 (45%) RFS, 767 (42%) DDFS events, and 604 (33%) deaths were observed. In multivariable analyses, higher TILs were independently associated with improved iDFS, RFS, DDFS, and OS beyond clinicopathological factors (likelihood ratio $p < 10e-6$). Each 10% increment in stromal TILs was associated with an 8% (95% CI: 6-11), 10% (95% CI: 7-13), and 13% (95% CI: 10-15) reduction in the risk of experiencing an iDFS, RFS or DDFS event, and with a 12% (95% CI: 9-15) reduction in the risk of death. iDFS, RFS, DDFS and OS rates according to different TIL thresholds and nodal status are shown in the Table. Of note, the RFS estimates (which exclude second non-breast primaries and contralateral breast cancers) were consistently higher than the iDFS counterparts (which include both), consistent with a high rate of contralateral breast cancers and second primary tumors in this cohort. Notably, patients with node-negative—and especially stage I—TNBC with high TILs had excellent survival rates at 10-

year follow-up.

Conclusion: TILs are highly prognostic in pts with systemically untreated early-stage TNBC. Pts with pN0 (and especially stage I) TNBC with high TILs exhibited very favorable long-term outcomes even in the absence of systemic therapy. These data define the natural history of TIL-rich TNBC pts and are crucial to identifying the optimal patient population for future chemotherapy and immunotherapy de-escalation clinical trials.

References:

- [1] Leon-Ferre et al, 2017, PMID: 28913760
- [2] Park et al, 2019, PMID: 31566659
- [3] de Jong et al, 2022, PMID: 35353548

Table

Outcome	Year	All pts		NO		Stage I	
		sTILs ≥30% (n=620)	sTILs ≥50% (n=388)	sTILs ≥30% (n=539)	sTILs ≥50% (n=348)	sTILs ≥30% (n=244)	sTILs ≥50% (n=150)
IDFS [95% CI]	5	75% [73-78]	79% [75-82]	78% [75-81]	81% [78-85]	83% [78-87]	89% [84-93]
	10	64% [61-67]	67% [63-71]	68% [64-71]	70% [66-75]	71% [66-77]	75% [69-81]
RFS [95% CI]	5	80% [77-83]	84% [81-87]	83% [80-86]	87% [84-90]	88% [85-92]	94% [91-97]
	10	72% [69-76]	75% [72-79]	76% [73-80]	79% [75-83]	79% [75-84]	82% [76-87]
DDFS [95% CI]	5	83% [80-85]	88% [85-90]	86% [83-89]	90% [88-93]	90% [86-93]	95% [92-98]
	10	76% [73-79]	82% [78-85]	80% [77-83]	85% [82-88]	83% [78-87]	90% [85-94]
OS [95% CI]	5	89% [86-91]	91% [89-94]	91% [89-93]	94% [92-96]	95% [93-97]	99% [97-100]
	10	82% [79-85]	85% [82-88]	86% [83-88]	89% [86-92]	88% [85-92]	94% [90-97]

5 and 10-year survival endpoints according TIL level, nodal status, and stage

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12/7/2022

5:00 PM - 6:15 PM

PD9-06

PD9-06 Histopathological and molecular immune landscape and DNA damage response signatures to predict response to carboplatin and docetaxel in TNT trial TNBC cohort

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Background The TNT trial (NCT00532727) showed no evidence of carboplatin (C) superiority over docetaxel (D) overall in metastatic triple negative breast cancers (TNBC), but a C benefit was observed in the pre-specified sub-group analysis in patients with a gBRCA1/2 mutation (Tutt et al, Nat Med 2018). Given only ~30% of patients have a gBRCA1/2 mutation, broader predictive biomarkers of response are needed. In this cohort we previously found that DNA Damage Response (DDR) signatures were associated with improved C response in chemotherapy (CT) naïve patients only (Tovey et al, ASCO 2020). Since DDR activities influence tumour immune-microenvironment, we explored the predictive ability of immune cell markers and performed integrative analyses on multi-omics features to identify novel TNBC subgroups. Patients and Methods Tumour infiltrating lymphocytes (TILs) were evaluated on haematoxylin and eosin stained primary tumour (PT) slides for 222/376 TNT patients. Formalin-fixed paraffin-embedded PT tissues from 186/376 TNT patients were successfully profiled using total RNA-sequencing. Matched recurrence (REC) was also sequenced for 13 patients. Twenty-five immune signatures were assessed. Logistic regression and restricted mean progression free survival (PFS) were applied to delineate the relationship of these features with treatment outcomes. Random forest clustering of multi-omics DDR and immune biology markers, including gene expression signatures and mutation/methylation status, was applied to identify subgroups. We further molecularly characterised these clusters through supervised clustering of 693 gene expression "modules" (sets of co-expressed genes), immune cell deconvolution and genomic scars. Results Immune gene expression signatures and TILs were highly correlated. Average immune infiltration based on ConsensusTME was lower in mutated/methylated tumours compared with BRCA1 wildtype tumours (p=0.04). Immune signature score markers decreased from PT to REC, demonstrating a dynamic immune microenvironment. In the overall population and when restricting to prior CT treated patients,

high immune infiltration (gene expression based & TILs) was associated with response to D while C response rates were not associated with immune scores (interaction p-values < 0.05). This did not translate to a PFS benefit. Multi-omics clustering identified 6 biological subgroups including immune enriched, immune depleted, DDR deficient and proficient clusters as well as 2 small clusters with no obvious distinguishing features. Immune enriched TNBC were predominantly basal-like immune activated with high B-cell/T-cell diversity. Immune depleted TNBC showed higher activity of proliferation and DDR pathway modules. DDR proficient tumours had low expression of immune markers and enrichment for ESR1/PGR expression, markers of extra cellular formation, cell structure, lipid metabolism and proliferation. The DDR deficient cluster was enriched for proliferation and demonstrated high number of TILs despite no apparent enrichment for gene expression-based immune modules. In the prior CT treated cohort, the immune enriched cluster had preferential response to D (62.5% (D) vs. 29.4% (C) ; $p=0.02$). The immune depleted cluster had preferential response to C (8.0% (D) vs. 40.0% (C); $p=0.01$). Numbers were too small to assess differential response within the other clusters or in the CT naïve cohort. Conclusions Tumours with high immune features have high response to D while those with low immune features have preferential response to C in advanced TNBC. Combining multi-omics markers of DDR deficiency and immune biology can identify clusters of patients with distinct biological profiles and differential treatment specific response rates.

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5:00 PM - 6:15 PM

PD9-07

PD9-07 Role of immunosuppressive JNK pathway in the tumor microenvironment among Triple Negative Breast Cancer subtypes in IBCSG Trial 22-00

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BACKGROUND: Although the triple-negative breast cancer (TNBC) tumor microenvironment (TME) has been deeply characterized, much remains unknown about pathways attributing to an immunosuppressive TME in this disease. The phosphorylation of JNK (c-Jun N-terminal kinase) pathway has been associated with promoting an immunosuppressive phenotype, enhancing TNBC aggressiveness. Here, we aimed to explore the role of the JNK pathway in TNBC using a gene signature inferring the level of JNK phosphorylation. For this purpose, we used the TNBC cohort from the phase III adjuvant IBCSG 22-00 trial, which evaluated low-dose cyclophosphamide and methotrexate (CM) chemotherapy showing no clinical benefit in the overall population. **METHODS:** JNK gene signature was developed in TNBC samples by integrating RNA-seq gene expression data and phospho-JNK-targeted proteomic data in The Cancer Genome Atlas. Stochastic subsampling was performed to select the candidate markers. LASSO regression was performed to determine the final transcriptional signature to reflect JNK phosphorylation. The signature was then applied in a cohort composed of 498 TNBCs selected using stratified 1:3 relapse cases and non-relapse subcohort ratio from the IBCSG 22-00 trial. RNA-seq data from FFPE tumor samples were available for 347 patients. The JNK signature was calculated as the mean of the products between gene expression and signature coefficients, defining high and low levels using the median cut-off. Immune hot tumors were defined according to TNBC molecular subtypes or tumor-infiltrating lymphocytes (TILs) levels higher than 30%. Multivariable Cox models were used for disease-free survival (DFS) analysis. Wilcoxon test was used to evaluate the association between gene signatures and the levels of JNK. **RESULTS:** Tumors with either immunomodulatory (IM) phenotype or high TILs showed better DFS when presenting low levels of JNK compared to high levels (HR = 0.75, 95% CI, 0.57 to 0.99; P-value = 0.024 and HR = 0.62, 95% CI, 0.43 to 0.89, P-value = 0.0013). No significant differences in DFS were observed in other TNBC subtypes or tumors with low TILs, further highlighting the relevance of JNK signaling pathway in tumors presenting immune infiltration. Moreover, immune hot tumors with high levels of JNK were enriched for angiogenesis and eosinophils signatures and linked to immunosuppression. The immune targets B7-H3, CSF1R, GITR, and GARP were significantly associated with high levels of JNK.

Of note, these genes are involved in the immune escape, activation of macrophages, and regulation of Tregs population. On the other hand, low levels of JNK were associated with higher levels of activated CD8+ T cells, pointing to an anti-tumor immune response, as well as with higher levels of the immune targets PDL-1, CTLA4, CD47, DCIR, and TIGIT. Of interest, a significant DFS benefit was found in IM tumors with high levels of JNK when treated with low-dose CM, compared to those who were not (HR = 0.52, 95% CI, 0.28 to 0.99; P interaction = 0.045). CONCLUSIONS: We developed a JNK gene signature to estimate the phosphorylation level of JNK from gene expression data in TNBC, and validated the associated biological and prognostic value in the IBCSG 22-00 trial. Our results are in line with the immunosuppressive effect described by the JNK gene signature and highlight the heterogeneity of immune response in immune hot TNBCs. Of note, high levels of JNK were associated with worse DFS, as well as with a benefit from low-dose CM potentially related to the immunomodulatory effect described for metronomic regimens. Overall, our findings suggest a potential role of the JNK signature in identifying TNBCs with an immunosuppressive TME and provide the rationale to explore its role as a biomarker for immunotherapy. Further validation of these findings is required.

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PD9-08

PD9-08 ImPrint immune signature in 10,000 early-stage breast cancer patients from the real-world FLEX database

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BACKGROUND: Immune checkpoint inhibitors in combination with chemotherapy have demonstrated an improvement of pathologic complete response (pCR) in patients with HR-HER2- and MammaPrint (MP) High Risk, HR+HER2- tumors in the I-SPY2 TRIAL. However, not all patients benefit from immune checkpoint blockade and these new agents come with additional financial burden and significant long-lasting side effects such as adrenal insufficiency. Thus, it is imperative to better understand who benefits. Response Predictive Subtypes (RPS) were developed in the I-SPY2 TRIAL using pre-treatment expression data

from 987 MP High Risk patients; 39% of HR+HER2- tumors and 63% of HR-HER2- tumors were identified as immune sensitive. In I-SPY2.2, RPS tumor classification uses ImPrint, a 53-gene signature that has been independently validated to predict the likelihood of a pCR with PD1-PDL1 immune checkpoint inhibitors with high sensitivity and specificity. Using a real-world dataset of 10,000 patients enrolled in the FLEX trial, we identified immune sensitive (ImPrint+) patients within immunohistochemistry (IHC) subtypes and within MP and BluePrint (BP) subgroups.

METHODS: FLEX (NCT03053193) is an ongoing registry trial with 97 sites open in the United States and 2 international sites. Patients enrolled in FLEX have early-stage breast cancer and receive standard of care MP testing with or without BP molecular subtyping and consent to clinically annotated full genome data collection. MP is a 70-gene risk of distant recurrence signature that classifies patients as Low Risk or High Risk. MP High Risk can be further stratified into High 1 and High 2, which have demonstrated differences in chemosensitivity and pCR rates in the I-SPY2 TRIAL (NCT01042379). BP, an 80-gene molecular subtyping signature, categorizes patients' tumors as Luminal-, HER2- or Basal-Type.

RESULTS: Of the 10,021 patients, 9.1% of the FLEX patient population are ImPrint+ and are predicted to have a meaningful pCR rate with immune checkpoint inhibitors. Younger (≤ 50 years) or pre/peri-menopausal patients, patients with larger or node-positive tumors, and patients of Black or Latin race/ethnicity independently had a higher likelihood of having ImPrint+ tumors (Table 1). ImPrint+ tumors were identified in all clinical subtypes by IHC. There is a higher likelihood of ImPrint+ tumors being MP High 2 or BP Basal-Type tumors. Within BP Basal tumors, 74.7% of HR+ and 66.0% of HR- tumors were ImPrint+.

CONCLUSIONS: The focus of immune therapy trials has been on patients with HR-HER2-, MP High Risk patients. Indeed, most patients who are predicted to benefit have MP High 2 or BP Basal-Type tumors, including some HR+ patients, which is consistent with I-SPY2 results. Importantly, this large real-world dataset enables the identification of populations who may benefit from immune therapy outside of traditional clinical trial populations and supports the testing of checkpoint inhibitors in the immune-positive subtype. Younger women and patients of Black or Latin race/ethnicity who typically have more aggressive tumors also have higher proportions of ImPrint+ tumors. Thus, it is critical that these populations be included in clinical trials. This first look at immune sensitivity in over 10,000 FLEX patients with ImPrint generates preliminary data and hypotheses that will be explored in future FLEX substudies, including an analysis of lobular cancers and long-term outcomes in ImPrint+ patients across all races and ages.

Clinical characteristics of ImPrint+ and ImPrint- tumors

[Table 1.tif](#)

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12/7/2022

5:00 PM - 6:15 PM

PD9-09

PD9-09 Molecular differences between younger versus older estrogen receptor positive / human epidermal growth factor receptor-2 negative breast cancers

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Background: The RxPONDER and TAILORx trials demonstrated benefit from adjuvant chemotherapy in patients < 50 years with node-positive breast cancer and Recurrence Score (RS) 0-25, and with node-negative disease and RS 16-25, respectively. Neither trial showed benefit in older women with RS < 26. It is unclear what explains the interaction between age and adjuvant chemotherapy benefit. Methods: We analyzed transcriptomic and genomic data from n=4,507 ER+/HER2- breast cancers to compare differences in estrogen receptor (ER), proliferation, and immune-related gene expressions, and somatic mutation patterns and mutation burden between younger (< 50 years of age) and older (>55 years) patients. We restricted our analysis to patients in the lower 80% range of in silico RS distribution to mimic the RxPONDER and TAILORx populations. Results: Five data sets were analyzed independently to assess consistency of results (TCGA n=530; microarray cohort A n=865; Cohort B n=609, METABRIC n=867, SCAN-B n=1636). Older patients had significantly higher somatic mutation

burden and more frequent copy number gain in ESR1, LATS1, ARID1B, SGK1, and MYB genes (odds ratio [OR] > 8.5, FDR < 0.05), but lower frequency of GATA3 mutations (12% versus 26%, P < 0.0001). Younger patients had higher rate of ESR1 copy number loss (OR: 0.45, FDR: 0.03). There was no difference in proliferation-related gene expression. ESR1 mRNA expression was significantly lower in younger women in all cohorts (P < 0.001). A regression model of ESR1 mRNA expression using age and ER IHC positivity indicated that lower ER expression in younger patients is primarily driven by lower ESR1 mRNA per cancer cell and not by fewer ER positive cells. We also assessed four gene signatures associated with endocrine therapy sensitivity including a 4-gene ERS, a 7-gene ERS-Lum, a 106-gene ERS-Pos signature, and a 59-gene ERS-Neg signature associated with endocrine resistance. In the TCGA and METABRIC cohorts, the ERS, ERS-Lum, and ERS-Pos signatures were all lower (FDR < 0.03) while the ERS-Neg signature was higher (FDR < 0.001) in younger patients. Similarly, in both microarray cohorts, and in the SCAN-B-cohort, the ERS-Pos signature was lower and the ERS-Neg signature was higher in younger patients (FDR < 0.002). Next, we assessed 4 different immune cell signatures that have been associated with response to chemotherapy. In the TCGA, B-cell, T-cell, Mast-cell, and TIS signatures were significantly higher (FDR < 0.05). In the microarray Cohort-A, B cells and mast cells were significantly higher, and the T cell and TIS signatures showed a trend for higher expression. In Cohort-B, T cells, B cells, TIS, and dendritic cells signatures were significantly higher in younger patients. Significantly higher expression of immune gene signatures in younger patients were also seen in the METABRIC and SCAN-B data sets. The ER-related and immune-related gene signatures showed negative correlation and joint analysis defined three subpopulations in younger women: (i) immune-high/ER-low, (ii) immune-intermediate/ER-intermediate and (iii) immune-low/ER-intermediate, whereas in older women the dominant pattern was immune-low/ER-high. Conclusion: ESR1 mRNA and ER-associated gene expression is lower in ER positive cancers of younger compared to older patients, while immune infiltration is higher. The cytotoxic and endocrine effects of adjuvant chemotherapy could both contribute to the survival benefit seen in younger patients, but the relative contributions of these effects may vary by ER and immune phenotype. We hypothesize that in immune-high/ER-low cancers, the cytotoxic effect of chemotherapy may drive the benefit, whereas in immune-low/ER-intermediate cancers chemotherapy induced ovarian suppression may play a more important role.

Disclosure(s):

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5:00 PM - 6:15 PM

PD9-10

PD9-10 Independent validation of the HER2DX genomic test in HER2-positive breast cancer treated with neoadjuvant docetaxel, carboplatin, trastuzumab +/- pertuzumab (TCH/TCHP): a correlative analysis from a multicenter academic study.

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Background: HER2DX (Prat et al. EBiomedicine 2022) is a 27-gene prognostic (risk-score) and predictive (pathological complete response [pCR]-score) assay in early-stage HER2+ breast cancer based on clinical data and the expression of 4 gene signatures (immune, proliferation, luminal differentiation and HER2 amplicon). Here, we aim to evaluate, for the first time, the ability of HER2DX to predict pCR following neoadjuvant TCH or TCHP in HER2+ disease. Methods: Standardized HER2DX was performed in a central lab on baseline pre-treatment FFPE tumor biopsies from the GOM-HGUGM-2018-05 study in Spain, a consecutive retrospective series of patients (pts) with newly diagnosed stage I-III HER2+ breast cancer eligible for neoadjuvant therapy. Pts received standard 6 cycles of docetaxel, carboplatin and trastuzumab (TCH) or TCH with pertuzumab (TCHP) regimens. Primary aim was to test the ability of HER2DX pCR score to predict pCR (ypT0/is ypN0). Secondary objectives were to test the ability of HER2DX pCR score to predict pCR independently of clinical-pathological variables and the PAM50 subtype (HER2-enriched versus not), and to evaluate the association of HER2DX pCR score with the HER2DX risk-score. Logistic regression and receiver-operator curve (ROC) analysis were assessed. Statistical analyses were performed in R code 4.0.5. Results: HER2DX was evaluated in 155 pts (97%) enrolled in the study with available RNA (as of June 2022). Mean age of pts was 50 (range 22-74) and 55.2% of pts (n=85) were pre-menopausal. Clinical T2-4 disease represented 77.4% of cases (n=120), clinical node-positive disease (cN1-3) represented 63.9% of cases (n=99), and 68.0% of tumors (n=105) were hormone receptor-positive. The overall pCR rate was 57.4% (95% confidence interval [CI] 50-65): 52.2% (95% CI 40-64) with TCH (n=67) and 61.4% (95% CI 50-72) with TCHP (n=88). The proportion of HER2DX low-, medium- and high-pCR groups was 34.2%, 34.8% and 31.0%, respectively. HER2DX pCR score (as a continuous variable from 0 to 100) was significantly associated with pCR (odd ratio [OR]=1.03, p=5.91e-07). The pCR rates in HER2DX pCR-high and pCR-low groups were 75.0% and 28.0% (OR=7.6, 95% CI 3.2-19.1, p=7.14e-06), respectively. In pts treated with TCHP, the pCR rates in HER2DX pCR-high and pCR-low groups were 85.7% and 27.3% (OR=16.0, 95% CI 4.3-59.01, p=3.2e-05), respectively. The AUC ROC of HER2DX pCR score (as a continuous variable) and pCR status was 0.746 (in all pts) and 0.812 (in pts treated with TCHP). HER2DX pCR score was significantly associated with pCR independently of hormone receptor status, Ki67, age, menopausal status, pertuzumab use, clinical stage and PAM50 HER2-enriched subtype. The proportion of HER2DX low- and high-risk of relapse disease was 32.0% and 68.0%, respectively. The

correlation of HER2DX pCR score and HER2DX risk-score was weak (coefficient=-0.17), as previously described. Proportion of cases according to both HER2DX scores and absolute difference of pCR rates between TCHP and TCH in each combined group is shown in Table. Conclusion: The HER2DX genomic test predicts pCR following neoadjuvant TCH or TCHP regimens independently of clinical-pathological variables and intrinsic subtype. The combination of both HER2DX scores might help better tailor systemic therapy in patients with newly diagnosed stage I-III HER2+ breast cancer.

Disclosure(s):

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12/7/2022

7:00 PM - 10:00 PM

Open Satellite Events

12/8/2022

7:00 AM - 8:15 AM

P4-01-01

RIBANNA 5th interim analysis: Matched-pair analysis of progression-free survival (PFS) across treatment cohorts and comparison of frontline ribociclib + endocrine therapy PFS data from RIBANNA vs MONALEESA trials, in HR+, HER2- ABC

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Background: Ribociclib (RIB) plus endocrine therapy (ET) has demonstrated a statistically significant survival benefit across the three phase 3 MONALEESA (ML) trials, irrespective of menopausal status, line of therapy, or combination partner. RIBANNA (CLEE011ADE03), a prospective, noninterventional study assessing the efficacy and safety of RIB + ET, or ET monotherapy or chemotherapy (CT) in first-line (1L) setting in pre-, peri- and postmenopausal patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor-2-negative (HER2-) advanced breast cancer (ABC) is ongoing in Germany since October 2017 to gain insights into real-world scenario. In the 5th interim analysis (IA) from RIBANNA, a matched-pair analysis of 1L PFS data from the three treatment cohorts and comparison of 1L PFS data on RIB + ET from RIBANNA versus (vs) ML trials will be performed.

Methods: Pre-, peri- and postmenopausal women receiving RIB + ET, ET monotherapy, or CT as 1L treatments for HR+, HER2- ABC, in accordance with German treatment guidelines, were included. Propensity score matched (PSM) analysis of PFS data from the 3 treatment cohorts will be conducted to reduce the bias due to confounding variables. In addition to safety analyses, comparison of 1L PFS data on RIB + ET from RIBANNA vs ML trials will be performed.

Results: By the cutoff date of the 4th IA (October 11, 2021), data were available for 2187 pts, including 1849 (83.0%), 193 (78.1%), and 145 (73.6%) pts from the RIB + ET, ET monotherapy, and CT cohorts in 1L setting, respectively (Table 1). Of these 2187 pts, 1111 postmenopausal pts received 1L RIB + letrozole; 357 postmenopausal pts received 1L RIB + fulvestrant, and 158 pre- and perimenopausal pts received 1L RIB + anastrozole/letrozole. The unadjusted Kaplan-Meier estimate for median PFS was 31.7 months (95% confidence interval [CI], 28.5–36.2) in the RIB + ET cohort, 25.7 months (95% CI, 18.0–not reached) in the ET monotherapy cohort, and 15.3 months (95% CI, 9.5–17.5) in the CT cohort. The most frequent treatment-emergent adverse events (grade 3 or 4) in the RIB + ET and ET monotherapy cohorts were neutropenia (14.8% and 6.6%, respectively) while that in CT cohort was general physical health deterioration (9.1%).

Conclusions: In RIBANNA, a diverse pt population is being analyzed in a real-world setting; treatment with RIB + ET has been observed to be well adopted. The 5th IA is planned in October 2022 and data will be presented in SABCS 2022, which will include PSM analysis to compare 1L PFS data across treatment cohorts as well as comparison of 1L PFS data on RIB + ET from RIBANNA vs ML trials. The safety profile of RIB was found to be similar to those observed in ML trials.

Table 1. Patient demographics and baseline clinical characteristics from the 4th IA

Table 1. Patient demographics and baseline clinical characteristics from the 4th IA

Demographic variable	1L RIB + ET (n=1849)	1L ET monotherapy (n=193)	1L CT (n=145)
Mean age, years (SD)	65.5 (11.6)	70.7 (11.5)	61.6 (11.6)
Menopausal status*, n (%)			
Postmenopausal	1640 (88.7)	178 (92.2)	123 (84.8)
Premenopausal/ perimenopausal	192 (10.4)	13 (6.7)	20 (13.8)
ECOG performance status*, n (%)			
0	818 (44.2)	67 (34.7)	61 (42.1)
>1	1031 (55.8)	125 (64.8)	84 (57.9)
Mean time since initial diagnosis, years (SD)	5.9 (7.3)	6.8 (8.3)	4.7 (6.1)
Grading at initial diagnosis*, n (%)			
G1	113 (6.1)	5 (2.6)	2 (1.4)
G2	1095 (59.2)	117 (60.6)	73 (50.3)
G3	466 (25.2)	39 (20.2)	55 (37.9)
Metastatic sites*, n (%)			
CNS, liver, and lung	761 (42.6)	51 (26.8)	94 (67.1)
Bone only	551 (30.8)	91 (47.9)	21 (15.0)
Skin, lymph nodes, and others	434 (24.3)	45 (23.7)	20 (14.3)

*Remaining cases are missing
CNS, central nervous system; CT, chemotherapy; ECOG, Eastern Cooperative Oncology Group; ET, endocrine therapy; IA, interim analysis; RIB, ribociclib; SD, standard deviation

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12/8/2022

7:00 AM - 8:15 AM

P4-01-02

Results from a dose escalation phase 1b study of palbociclib and avelumab in advanced breast cancer in the PAveMenT Trial

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Background CDK4/6 inhibitors may trigger anti-tumour immunity, both through tumour cell intrinsic and extrinsic mechanisms, which can be enhanced by immune checkpoint blockade in pre-clinical studies. Although most triple negative breast cancers (TNBC) are resistant to CDK4/6 inhibition, palbociclib (palbo) has activity in pre-clinical models of the luminal androgen receptor (LAR) subtype. Here we report the dose finding phase 1b cohort A of the PAVeMenT trial combining avelumab and palbociclib. Methods The PAVeMenT phase 1b trial consists of a dose finding phase (cohort A), to be followed by an expansion in androgen receptor positive (AR+) TNBC (Cohort B). The phase 1B phase investigated palbo dosing schedules (75mg intermittent dosing (ID), 100mg continuous dosing (CD) and 125mg ID) in combination with the anti-PD-L1 antibody, avelumab 10mg/kg 2-weekly (cohort A) to determine the optimal schedule for cohort B. The CD dose-level was pre-specified as the preferred schedule if tolerated, due to the proliferative nature of TNBC and potential for tumour re-growth with ID. Patients with previously treated advanced breast cancer (ABC) of any histology with measurable disease and adequate organ function, who had not received prior immunotherapy or CDK4/6 inhibitors or more than 2 lines of chemotherapy for ABC, were eligible for cohort A. Dose-limiting toxicities (DLTs) were defined as Grade(G) 4 neutropenia, complicated G3 neutropenia or G4 thrombocytopenia, or \geq G3 immune toxicity during cycle 1. AR staining of \geq 10% using the SP107 antibody (Ventana) was considered AR+. PD-L1 was evaluated using CC23 Pharma Dx antibody (DAKO) and PD-L1 positive defined as CPS score of \geq 10%. Results Fourteen patients were recruited to Part A, all female, 12 with TNBC, two with ER positive/HER2 negative ABC, median age 53.5 years. Three evaluable patients received palbo 75mg/day ID without DLTs, therefore two further dose levels were opened in parallel. Three evaluable patients received palbo 125mg/day ID without DLTs. Due to a DLT of fever with G3 neutropenia in one of 3 patients receiving palbo 100mg CD, 3 further evaluable patients received 100mg CD without DLTs. Two patients were not evaluable for DLTs having not received a full cycle of treatment so were replaced. One case of grade 3 colitis and one case of grade 2 hypothyroidism (both 100mg CD) occurred outside the DLT period. Amongst 12 patients with TNBC, metastatic tissue was available for 11, archival breast tissue for one. Four of 12 patients were AR+. Five of 10 TNBC patients with sufficient tissue were PD-L1 positive, all of whom had previously tested negative with the SP142 antibody (Ventana). One of the 5 PD-L1+ and 2/5 PD-L1 negative TNBC cases were also AR+. TNBC patients received a median of 2 cycles of treatment (range 1-17). Both ER+ patients were AR+ and PD-L1 negative; one progressed after 4 cycles, the other remains on treatment at 12 cycles. The 100mg CD schedule was selected for cohort B. Conclusions All schedules were tolerable, with activity observed in patients with both ER positive and TNBC cancers. Cohort B of the study is open to recruitment for patients with AR+ TNBC. NCT04360941.

Disclosure(s):

Alicia F. Okines, MBChB, MD(Res), FRCP: Astra Zeneca/DS: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Gilead: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Lilly: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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7:00 AM - 8:15 AM

P4-01-03

Progression-free survival and patient-reported outcomes in HR+, HER2- ABC patients treated with first-line ribociclib + endocrine therapy (ET) or ET monotherapy or chemotherapy in real world setting: 5th interim analysis of RIBANNA

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Background: Ribociclib in combination with endocrine therapy (ET) has demonstrated survival benefits in a broad patient population with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (ABC). RIBANNA (CLEE011ADE03) is an ongoing, prospective, noninterventional study assessing the efficacy and safety of first-line (1L) ribociclib in combination with ET in routine clinical practice in women with HR+, HER2- ABC. This study will provide insights into the use of ribociclib in combination with ET with regard to effectiveness and patient-reported outcomes (PRO) in the real-world setting in a large patient population.

Methods: Patients with HR+, HER2- ABC starting their 1L treatment with ribociclib + ET, or ET monotherapy, or chemotherapy (CT) were included. Data after disease progression to second-line (2L) and further lines of therapy are being collected too. The progression-free survival (PFS) in 1L, 2L and PFS2 (time from inclusion into the trial in the 1L setting until progression from 2L to third-line therapy) for individual treatment sequences will be analyzed using the Kaplan-Meier method. PRO for all the patients in the 1L and 2L treatment cohorts are being evaluated using the Morisky Medication Adherence Scale (MMAS-8), questionnaires related to quality-of-life (EORTC QLQ-C30) and its breast cancer-specific module (EORTC QLQ-BR23) as well as the Hospital Anxiety and Depression Scale (HADS). Data were collected at baseline and at every 3 months until the end of treatment.

Results: By the cutoff date (October 11, 2021) of the fourth interim analysis, data were available for 2187 patients (Table 1). Overall, 633 patients progressed after 1L therapy, including 27.6%, 30.6%, and 43.4% of patients from the 1L ribociclib + ET, ET monotherapy, and CT cohorts, respectively. A total of 286 patients received CDK4/6 inhibitors in 2L, which represents 48.3%, 37.3%, and 27.0% of patients from the 1L ribociclib + ET, ET monotherapy, and CT cohorts, respectively. The PFS in 1L, 2L and PFS2 results for individual treatment sequences will be presented at SABCs 2022. PRO compliance rates at baseline were 88.2%, 89.8%, and 89.4% for EORTC QLQ-C30 global health status, QLQ-BR23, and HADS-D/A, respectively, in the overall population, and 84.5% for MMAS-8 in the 1L ribociclib + ET cohort. Data for patient-reported adherence to 1L ribociclib + ET and for questionnaires related to global health-related

quality of life, functioning, and symptoms from patients receiving treatment in 1L and 2L settings will be analyzed and presented at SABCS 2022.

Conclusion: The RIBANNA study has shown diverse population characteristics among patients who received ribociclib treatment in a real-world setting. The 5th interim analysis is planned in October 2022. Data on PFS, PFS2, specific therapy sequences and PRO from 1L and 2L that will provide insights on therapy sequencing strategy will be presented at SABCS 2022.

Table 1. Patient disposition at the data cutoff date (October 11, 2021)

Table 1. Patient disposition at the data cutoff date (October 11, 2021)

Patients	Total (N = 2187)	Ribociclib + endocrine therapy (n = 1849)	Endocrine monotherapy (n = 193)	Chemotherapy (n = 145)
First-line treatment, n (%)	2187 (100.0)	1849 (100.0)	193 (100.0)	145 (100.0)
Second-line treatment, n (%)	633 (28.9)	511 (27.6)	59 (30.6)	63 (43.4)
Third-line treatment, n (%)	239 (10.9)	183 (9.9)	25 (13.0)	31 (21.4)

Disclosure(s):

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7:00 AM - 8:15 AM

P4-01-04

Phase IV multicenter study evaluating RWE and the safety of talazoparib in patients with locally advanced or metastatic negative HER2 breast cancer and a BRCA1/2 mutation (ViTAL) - Cohort 2: patients treated according to the EMA

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Background: Talazoparib (TALA) is a highly potent, dual-mechanism PARP inhibitor that has demonstrated clinical benefit in EMBRACA Phase III trial for patients with germline BRCA1/2 (BRCA1/2)-mutated locally advanced or metastatic HER2- breast cancer. Objective: The aim of the study is to ensure the effectiveness and safety of TALA in the real-world setting among patients with locally advanced or metastatic HER2- breast cancer, with somatic or germline BRCA1/2 mutation. Methods: VITAL is an ambispective, multicentric, longitudinal, phase IV study. It includes two ambispective cohorts: - Cohort 1: patients treated through the French Early Access Program and inclusion of patients with somatic BRCA1/2 mutation was allowed. - Cohort 2: patients treated according to the European Marketing Approval granted in 09/21/2021. The primary endpoint of the study is the Time to Treatment Discontinuation (TTD) which is defined as time between the date of first dose of TALA and the date of last dose or death. Results: From November 2018 to May 2021, 85 patients were included in Cohort 2, Patients' characteristics are: - a median age of 49.0 years; - 65.8% ER+ BC / 34.2% TNBC; - 42.1% mBRCA1 / 55.3 % mBRCA2 / 2,6% mBRCA1 and mBRCA2. - 85.7% ECOG PS 0 or 1; - 23.4% de novo mBC. - Visceral, bones and CNS metastases were found in 59.0%, 61.5% and 10.3% of patients respectively. - No breast or ovarian cancer family history at 1st degree was found in 39 patients (50.0%). - 38.5% were chemo-naïve; - 21.8% received prior platinum in (neo)adjuvant or metastatic setting, with a median of prior cytotoxic regimen of 1 - For patients with ER+/HER2- ABC the median number of prior endocrine therapy was 1 and 62.0% of these patients received a CDK4/6 inhibitor prior to TALA. - 8 patients (10.3%) had CNS metastases. Out of the 78 treated patients, 57 patients (73.0%) experienced a TALA permanent discontinuation for Progressive disease (80.7%), toxicity (12.3%), cancer-related death (1.8%), or other reasons (1.8%). The median TTD for TALA is 9.6 months [6.7;10.8] with 34.5% of patients still on treatment at 12 months. After discontinuation of TALA, 59.0% of patients received a subsequent treatment with a TTD of 3.9 months [2.1 ; 45]. The most common subsequent treatments were non-platinum chemotherapy (67.4%), platinum therapy (6.5%) and other (26.1%). The Clinical Benefit Rate assessed by the investigators is 87.6% (Complete Response for 14.1%, Partial Response for 56.3% and Stable Disease for 17.2%). The median

duration of CNS metastases control was 10.2 months, and 25.0% of patients had a control of CNS metastases. At least one adverse events (AEs) was recorded in 67.9% of patients. Hematologic adverse events (AEs) (any grade) occurred in 55.1% (anemia 37.2%, thrombocytopenia 16.7%, neutropenia 15.4%). Most common non-hematologic AEs were Nausea (15.4%) and asthenia (15.4%). Related Serious Hematologic AEs occurred in 6 patients (7.7%) including 3 (3.8%) thrombocytopenia and 3 (3.8%) anemia. Related Serious Non-hematologic AEs (metrorrhagia) were seen in 1 patient (1.3%). AEs associated with temporary drug interruption, dose modification and permanent drug discontinuation occurred in 26 (33.3%), 22 (28.2%), and 7 (12.3%) patients respectively. The mOS is not mature for this analysis. Conclusions: ViTAL is the largest study that reports real-world data with TALA. Outcomes and safety in Cohort 2 (patients treated with TALA according to the European Marketing Approval), are consistent with the results of EMBRACA study and with the Cohort 1. (Litton et al. NEJM 2018)

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-01-05

Machine learning to predict treatment response and tolerability in HR+, HER2– advanced breast cancer: German study AI4ANNA

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Background: Predicting the probability of tumor progression and tolerability with sufficient accuracy remains a significant challenge in advanced breast cancer. The objective of AI4ANNA study was to assess the predictive potential of machine learning (ML) methods with respect to tumor control and safety outcomes using German study data (RIBECCA, RIBANNA) and to identify the most relevant baseline factors for prediction. Methods: Anonymized study data from two studies of ribociclib and endocrine therapy in patients with advanced HR+, HER2– breast cancer were used for predictive analysis. RIBECCA (N=487) was a multicenter, open-label, single-arm, phase 3b trial, and RIBANNA (N=1904) is an ongoing non-interventional study evaluating the real-world efficacy and safety of first-line ribociclib in combination with aromatase inhibitor/fulvestrant, endocrine monotherapy or chemotherapy. Study baseline features were used to develop prediction models for a variety of tumor control (including progression-free survival (PFS), overall response rate (ORR) at week 24, death) and safety outcomes (including general number of adverse events (AEs) as well as selected AEs belonging to blood system, cardiac, hepatobiliary, and gastrointestinal disorders). LASSO (Least Absolute Shrinkage and Selection Operator) and XGBoost (eXtreme Gradient Boosting) ML algorithms were employed

to train prediction models. LASSO was selected as a representative of fully interpretable, linear models and XGBoost as a representative of highly flexible, nonlinear models. Predictive performance of these two algorithms was compared and predictive value of single baseline features was assessed using feature permutation importance method. Results were validated internally within the training study (10 times repeated 5-fold stratified cross-validation) as well as externally, ie, implementation and training of the prediction models on one study and validation on the other and vice versa. Results: Moderate predictive signal (at baseline) could be identified for the following two outcomes: ORR (area under the curve [AUC] mean 0.628 [RIBANNA] and 0.626 [RIBECCA]) and PFS (AUC mean 0.626 [RIBANNA], 0.604 [RIBECCA]). Model performance could be validated with very similar AUCs by cross-study evaluation. Patients could be assigned to one of three risk groups. The most important features for ORR prediction included the presence of locally advanced cancer and metastases presenting as bone only disease and for PFS the presence of liver metastases, histological grade and prior (neo)adjuvant treatment. For three safety endpoints, a predictive signal (AUC >0.6) was identified only in one study but not in the other (AEs "QT prolongation", "leukopenia grade 3/4" and serious AE "vomiting"). However, insufficient predictive signals were found for all other outcomes. Conclusion: Prediction models for tumor control and safety outcomes were trained on a broad number of clinical baseline features. Moderate predictive signals could be identified for ORR and PFS. Even though the predictive performance (AUC) seems to be limited, patients could be assigned to one of three differently behaving risk groups at the baseline. The key predictive features for PFS included clinically known prognostic factors like liver metastasis, histological grade and prior (neo)adjuvant treatment.

Disclosure(s):

Peter A. Fasching, MD: Agendia: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Biontech: Contracted Research (Ongoing); Cepheid: Contracted Research (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Ongoing); Genentech: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Merck Sharp & Dohme: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Pierre Fabre: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing); Sanofi Aventis: Consulting Fees (e.g., advisory boards) (Ongoing); SeaGen: Consulting Fees (e.g., advisory boards) (Ongoing)

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12/8/2022

7:00 AM - 8:15 AM

P4-01-06

LP-184, an acylfulvene class small molecule therapeutic, is synthetically lethal in HR deficient and PARP inhibitor resistant triple negative breast cancer

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Triple-negative breast cancer (TNBC) is the most aggressive subtype of breast cancer accounting for approximately 15% to 20% of all newly diagnosed breast cancer cases. TNBCs are defined by lack of expression of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER-2). Due to its special molecular phenotype, it is not sensitive to endocrine therapy or targeted therapy. Therefore, chemotherapy such as anthracyclines or taxanes is the main systemic treatment, but the efficacy of conventional postoperative adjuvant chemoradiotherapy is poor. ~35% of TNBC tumors show abnormalities in the HR pathway, making them sensitive to poly (ADP-ribose) polymerase (PARP) inhibitors (PARPi) and DNA-damaging agents. Although more than 40% BRCA1/2-deficient patients fail to respond to PARPi and a substantial proportion of patients acquire PARPi resistance over time. TNBCs heterogeneous nature, poor prognosis and limited treatment options presents the urgent need of development of novel agents targeting tumor specific alterations. Lantern Pharma is advancing LP-184, an acylfulvene-derived prodrug that is specifically activated in tumors that overexpress the oxidoreductase enzyme Prostaglandin Reductase 1 (PTGR1), for the treatment of solid tumor indications including TNBC. LP-184 has multiple mechanisms of action (MOA). While It is synthetically lethal in tumors harboring DNA damage repair defects including Homologous Recombination (HR) deficiencies, it can also interrupt transcription. LP-184 efficacy was tested in a panel of breast cancer cell lines and patient derived TNBC xenografts models, both sensitive as well as resistant to PARP inhibitors and anthracyclines. LP-184 demonstrated nanomolar potency in six NCI-60 breast cancer cell lines (median IC50 = 327 nM). Subcutaneous patient-derived TNBC xenograft mouse models were used to determine tumor volume responses to LP-184 treatment in vivo. Xenograft tumors were derived from 10 treatment-naive HR deficient (HRD score > 50) primary TNBC patients with known BRCA1/2 loss of heterozygosity (LOH), 7 of which subsequently progressed on PARP inhibitor Olaparib. LP-184 (4mg/kg i.v., (q2d x 5 then 7 days off)x2) led to complete and durable regression in all 10 TNBC HRD-PDX models tested as compared to control (p < 0.0001). A tumor growth inhibition range of 107-141% was achieved across all the 10 models. For LP-184, T/C at the control group end day was 0% in 10/10 models, whereas across the same models for Olaparib, T/C was 0% in 2/10 models and ranged from 15 - 90% in 8/10 models. Terminal

body weight change was only a transient weight loss < 4% with LP-184 treatment across all models. LP-184 exhibited superior potency than olaparib in TNBC PDX models that carry HRD mutations including PARP resistant models and was well tolerated in mice. As acylfulvene-induced damage is primarily repaired by transcription-coupled nucleotide-excision repair (TC-NER) and HR pathways, response to LP-184 is influenced by tumor DNA damage repair pathway status. Recent data highlight an important role of super enhancer driven core transcription regulatory circuits in the pathogenesis of TNBCs. Our results support the superior efficacy of LP-184 in TNBCs, likely linked to the multiple MOAs, and establish LP-184 as a promising new agent for future clinical testing in TNBC patients. We finally propose that LP-184 may be broadly efficacious in solid tumors with HR and/or TC-NER pathway defects, such as pancreatic, prostate, ovarian and bladder cancers.

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-01-07

FS-1502, an anti-HER2 ADC, in Patients with HER2-Expressing Advanced Solid Tumors: A Phase 1a Dose-Escalation Study

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Background: FS-1502 is a HER2-targeting antibody drug-conjugate with a cleavable β -glucuronide linker and an antimitotic agent (monomethyl auristatin F) which showed promising antitumor activity in preclinical studies. We are evaluating the safety and tolerability of FS-1502 in patients with HER2-expressing advanced solid tumors (NCT03944499). Methods: Patients with HER2-expressing advanced solid tumors who had failed prior standard of care therapies were enrolled in a single-arm, open-label, dose-escalation phase Ia study in China. FS-1502 was given IV once in 21-day or 28-day cycles. The primary endpoint was incidence of dose-limiting toxicity (DLT). Adverse events (AEs), objective response rate (ORR) and duration of response (DoR) were also assessed. Data cutoff was December 30, 2021. Results: A total of 67 patients, 64 with breast cancer and 3 with other solid tumors, with median 3 prior therapies (range 1-10), were enrolled in 5 sites and treated with FS-1502 at doses of 0.1-3.5 mg/kg. Two DLTs, as defined by the protocol, were observed, with one G2 decrease in creatinine clearance at 3.0 mg/kg and one G3 thrombocytopenia with hemorrhage at 3.5 mg/kg. No Grade 4/5 events were observed. Grade 3 TRAEs were observed in 24 (35.8%) patients with the most common AEs of hypokalemia (14.9%) and decreased platelet count (9.0%). ORRs were observed at doses at or above 1.0 mg/kg with an ORR of 66.7% (4/6) at the recommended phase 2 dose (RP2D) of 2.3 mg/kg. Median duration of response (DoR) across all dose levels was 9.2 months (95%CI 5.6-NR). ORR for HER2-low patients was 42.9% (3/7). Plasma concentration and exposure (AUC) based on total ADC and total antibody increased dose proportionally at ≥ 1.0 mg/kg, with a T1/2 of 2.4-4.9 days. The incidence and magnitude of immunogenicity were low. While no MTD was determined, the 2.3mg/kg dose once in a 21-day cycle was selected as the RP2D based on safety, antitumor activity and PK data. Conclusions: FS-1502 was well-tolerated and demonstrated encouraging antitumor activity in both HER2-high and -low patients. Phase Ib and phase II clinical trials with FS-1502 are currently ongoing in various solid tumor indications including breast, gastric, and colorectal cancer.

Disclosure(s):

Qiao Li, MD: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

P4-01-08

Efficacy of PARP Inhibitors in Patients With BRCA1/2-related Breast Cancer with Prior Platinum Exposure: A Systematic Review and Meta-Analysis

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Background: Approximately 5% of breast cancer patients carry a deleterious germline BRCA1/2 mutation, which leads malignant cells to be deficient in the repair of DNA double-strand breaks via homologous recombination. The poly(adenosine diphosphate–ribose) polymerase (PARP) enzymes are important on DNA single-strand break repair and PARP inhibitors (PARPi) cause an accumulation of unresolved DNA damage in tumors with BRCA1/2 mutations, resulting in cell death. However, because platinum salts also ultimately cause double-strand DNA breaks and may have overlapping mechanisms of resistance with PARPi, the efficacy of PARPi in patients with prior platinum therapy is unknown. We sought to evaluate the efficacy of PARPi in patients with BRCA1/2-related breast cancer and previous platinum exposure. Methods: We performed a systematic review and meta-analysis of studies that evaluated the efficacy of PARPi in patients with advanced or metastatic breast cancer and germline BRCA1/2 mutations.

Two independent investigators identified double-blind, randomized controlled trials (RCTs) that included the subgroup of previous exposure to platinum. PubMed, Embase, and Cochrane databases were searched for papers up to June 26, 2022. Data extraction from published reports and quality assessment were performed under Cochrane recommendations. Hazard ratios (HRs) with a 95% confidence interval (CI) were pooled, and a p-value of < 0.05 was considered statistically significant. The software Review Manager 5.3 was selected for conducting the statistical analysis. The primary endpoint of interest was progression-free survival (PFS). Results: Out of 2069 database results (487 on PubMed; 1376 on Embase; and 206 on Cochrane), 42 studies were selected for full review, and 4 RCTs, with a total of 249 patients, were included in the final investigation. The PARPi included were Olaparib, Talazoparib, Niraparib, and Veliparib. Pooled analysis showed that PARPi improved PFS in breast cancer patients with prior treatment with platinum-based therapy compared to the control group [HR = 0.72; 95% CI, 0.53-0.97; p = 0.03]. In comparison, the population without previous platinum exposure had a similar but slightly greater benefit from PARPi [HR = 0.68; 95% CI, 0.52-0.89; p = 0.005]. A subgroup analysis containing only the three randomized trials with PARPi monotherapy confirmed the central tendency favoring PARPi over physicians' choice of single-agent chemotherapy in patients with prior platinum-therapy; however, because of small numbers and wide confidence interval it was not statistically significant [HR = 0.72; 95% CI, 0.51-1.01; p = 0.06]. Conclusions: Our findings suggest that PARPi are associated with longer PFS in patients with advanced breast cancer and previous exposure to platinum therapy, decreasing the concerns about cross-resistance between the drug classes. Nonetheless, more extensive studies are still necessary to investigate the efficacy of PARPi in patients with prior platinum exposure and truly platinum-resistant disease.

Progression-free survival of included studies

Study	Intervention	Hazard Ratio (95% CI)		Events/patients	
		PARPi	Control	PARPi	Control
BRAVO, 2021	Niraparib	0.78 (0.39-1.58)		18/23	14/21
BROCADE3, 2020	Veliparib*	0.70 (0.34-1.44)		19/27	14/16
EMBRACA, 2018	Talazoparib	0.76 (0.40-1.45)		38/46	25/30
OlympiAD, 2017	Olaparib	0.67 (0.41-1.14)		50/60	21/26

* Veliparib plus carboplatin-paclitaxel

Disclosure(s):

Alice D. Marinho, n/a: No financial relationships to disclose
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12/8/2022

7:00 AM - 8:15 AM

P4-01-09

Characterization of breast cancer brain metastases overall and progression-free survival and timing of cyclin-dependent kinase 4/6 inhibitor use: Retrospective single institution experience

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Background Approximately 15% of patients (pts) with hormone receptor (HR)+ human epidermal growth factor receptor 2 (HER2)- breast cancer will develop brain metastases (BM) (Kuksis et al, *NeuroOnc* 2021). Cyclin dependent kinase 4/6 inhibitors (CDK4/6i) with an endocrine therapy partner are recommended 1st line treatments in HR+HER2- metastatic breast cancer (MBC). Preclinical models show that CDK4/6i can cross the blood brain barrier (BBB). In vitro assays have shown that abemaciclib crosses the BBB more effectively than palbociclib or ribociclib (George et al, *Front Oncol* 2021). The efficacy of CDK4/6i in patients with breast cancer BM is not well described. **Methods** We examined prior treatment data for 368 pts with HR+HER2- BM who received a CDK4/6i between 2015 to 2021. The primary endpoint was overall survival (OS) from the time of starting CDK4/6i after BM development. CNS progression free survival (PFS) was assessed in pts who received CDK4/6i after BM development. We examined the relationship between OS, type and timing of CDK4/6i in multivariate analyses. Statistical analyses were conducted using R 4.1.2 software. **Results** Of the total cohort of 368 pts, 23% (n=86) had de novo MBC and 77% (n=282) had relapsed MBC. At initial presentation of MBC 79% (n=290) of pts had no BM, 19% (n=71) had BM and extracranial disease and 2% (n=7) had BM only. 56% (n=205) received a CDK4/6i before BM development, 37% (n=136) received a CDK4/6i after BM development and 7% (n=27) received a CDK 4/6i both before and after BM development. The most common CDK4/6i used first was palbociclib (85%, n=312) followed by abemaciclib (13%, n=47) and ribociclib (2%, n=9). At the time of data cutoff 277 pts were dead, 55 were alive and 36 were lost to follow up. The median follow-up of surviving pts from BM development was 32 months. 163 pts received a CDK4/6i post BM: palbociclib (66%, n=108), abemaciclib (31%, n=51) and ribociclib (3%, n=4). Of these 163 pts 83% (n=136) received a CDK4/6i as their 1st or 2nd systemic treatment post BM. In the cohort of 163 pts who received a CDK4/6i post BM, 9% did not receive local BM therapy, 40% had whole brain radiotherapy (WBRT), 34% had stereotactic surgery (SRS) alone and 17% had surgery +/- SRS. The median CNS PFS for pts who received a CDK4/6i after BM was 21

months with palbociclib and 14 months with abemaciclib (p value 0.11). Too few pts received ribociclib for analysis. CNS PFS was 21 months for pts receiving a CDK4/6i only after BM development and 10 months for those who received CDK4/6i both before and after BM diagnosis (p = 0.01). Pts who died prior to CNS progression were censored. Median OS from the time of starting CDK4/6i after BM development for pts receiving a CDK4/6i only after BM development was 25 months versus 12 months for those who received it both before and after BM development (p = 0.03). There was no statistically significant difference in OS when adjusting for the type of local BM treatment received, time from initial MBC diagnosis to BM, or the Breast Graded Prognostic Assessment (GPA) score (Sperduto et al, IJROBP 2020). Conclusions This observation suggests that there is a greater OS benefit from the time of starting CDK4/6i after BM development in pts who receive CDK4/6i solely after BM development compared to pts who received a CDK4/6i both before and after BM development. This is not unexpected given the known OS benefit associated with early use of these agents. Our unique observation of longer CNS PFS for patients who did not receive CDK4/6i prior to BM but who received it afterward suggests that CDK4/6i exposure prior to BM development may lead to development of resistance mechanisms that reduces CNS efficacy upon rechallenging with CDK4/6i after BM development. There was no statistically significant difference in post-BM CNS PFS by type of CDK4/6i received. This motivates investigation of biomarkers for patient selection and our ongoing work in collecting a matched comparison cohort of HR+HER2- pts with BM who never received CDK4/6i.

Disclosure(s):

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Yuan Chen, PhD: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

P4-01-10

Evaluating the safety of tucatinib in combination with trastuzumab and capecitabine for human epidermal growth factor 2 (HER2)-positive metastatic breast cancer in a real-world setting

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Background: Tucatinib, a highly selective tyrosine kinase inhibitor (TKI) for human epidermal growth factor 2 (HER2) receptor, received FDA approval in combination with trastuzumab and capecitabine for metastatic HER2-positive breast cancer based on the HER2CLIMB trial. While the efficacy data is promising, the tucatinib-containing triplet regimen is associated with significant toxicity and many drug-drug interactions (DDIs). The toxicity profile of tucatinib in regards to adverse events (AEs) and DDIs has not been reported outside of the HER2CLIMB trial. Additionally, with the development of many new HER2 targeted therapies including antibody-drug conjugates (ADCs) such as trastuzumab deruxtecan, efficacy in regards to therapy sequence is still unknown. Here, we describe the safety and efficacy of tucatinib in a real-world setting. Methods: This single-center, retrospective, cohort study included patients (pts) with a diagnosis of HER2- positive locally advanced or metastatic breast cancer pts that were newly initiated on tucatinib therapy at the Duke Breast Oncology Clinic following FDA approval from April 17, 2020 to June 9, 2021. Pts were evaluated for the pre-specified outcomes for the duration of tucatinib therapy, until progression of disease, or for at least 6 months follow-up. AEs reviewed included palmar-plantar erythrodysesthesia syndrome (PPE), diarrhea, fatigue, rash, anemia, thrombocytopenia, neutropenia, nausea, vomiting, mucositis, hepatotoxicity, and nephrotoxicity, defined according to the Common Terminology Criteria for Adverse Events (CTCAE) grading criteria. Overall response was categorized as complete response, partial response, stable disease, or progressive disease, defined according to the Response Evaluation Criteria in Solid Tumors (RECIST) criteria, at first staging after therapy

initiation. The overall response rate was stratified by prior standard therapies, pts who did not receive capecitabine therapy with tucatinib, and the presence or absence of brain metastases. Results: A total of 23 pts (N=23) were included in the cohort, 52% of which had brain metastases and 9% with leptomeningeal disease. Pts had a median of 3 prior lines of therapy in the metastatic setting including: lapatinib (9%), neratinib (30%), trastuzumab deruxtecan (13%), trastuzumab emtansine (74%). All pts experienced AEs, most of which were mild or moderate severity. The most common AEs reported were fatigue (70%), PPE (61%), nausea (61%), and anemia (61%). Severe AEs occurred in 6 pts (26%) with grade 3 or 4 hepatotoxicity in 13%. Only 2 pts discontinued therapy due to AEs (grade 4 hepatotoxicity, grade 2 fatigue). Due to capecitabine intolerance, 13% received tucatinib and trastuzumab doublet therapy. There were 9 pts (39%) that experienced a DDI with tucatinib requiring therapy modification or close monitoring. At first staging, partial response was seen in 26% while 35% demonstrated stable disease and 30% progressive disease. Pts with previous neratinib therapy demonstrated a partial response of 14% and a stable disease response of 29%. No pts with previous trastuzumab deruxtecan or omission of capecitabine therapy experienced a partial or stable disease response. Conclusions: The rate of AEs were similar in a real-world setting compared to the HER2CLIMB trial with a lower rate of severe adverse events, however, a higher rate of hepatotoxicity. Given the high rate of drug interactions identified with tucatinib, concurrent medications should be reviewed for appropriate therapy adjustments and monitoring. Additional data is needed in regards to sequencing and impact on therapy efficacy.

Disclosure(s):

Heather Moore, PharmD, BCOP, CPP: Daiichi Sankyo/AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing)

Carey Anders, MD: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Athenex: Consulting Fees (e.g., advisory boards) (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Terminated, December 1, 2020); Elucida: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); G1-Therapeutics: Contracted Research (Ongoing); Genentech: Consulting Fees (e.g., advisory boards) (Ongoing); Immunomedics: Consulting Fees (e.g., advisory boards) (Ongoing); IPSEN: Consulting Fees (e.g., advisory boards) (Ongoing); Jones and Bartlett: Royalty (Ongoing); Lilly: Contracted Research (Ongoing); Merck: Contracted Research (Ongoing); Nektar: Contracted Research (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Pfizer: Contracted Research (Ongoing); Puma: Contracted Research (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Tesaro: Contracted Research (Ongoing); UpToDate: Royalty (Ongoing); ZION: Contracted Research (Ongoing)

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7:00 AM - 8:15 AM

P4-01-12

BAT8006, a novel FR α ADC with strong bystander effect, for the treatment of advanced solid tumor

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FR α is overexpressed in a number of cancers, including ovarian , breast, lung cancer, and endometrial carcinoma, yet limited expression in normal tissue. Efficacy of anti-FR α ADC have been demonstrated in clinical trials for high FR α expression ovarian cancer. These results validate FR α as a viable target for cancer treatment. We have developed a novel FR α ADC with strong bystander killing effect, BAT8006, which consists of a high-affinity antibody, an enzymatically cleavable linker and a topoisomerase I inhibitor as the payload, with DAR of 8. BAT8006 shows high affinity for the FR α antigen (KD < 0.5 nM) and FR α -expressing tumor cells. Upon binding to FR α on cell surface, BAT8006 internalizes effectively and traffics to the lysosome where payload is proteolytically released. BAT8006 demonstrated potent in vitro cell

growth inhibitory activity to FR α -positive cells with IC50 values of ~ 1 nM. In an in vitro bystander killing assay, proliferation of FR α -negative cells was potently inhibited by addition of culture medium of BAT8006-treated FR α -positive cells, but not that of BAT8006-treated FR α -negative cells, indicating the bystander killing effect of the released payload in the culture medium. Less than 0.03% of the payload was released from BAT8006 when incubated with human or monkey plasma for 4 days in 37°C, suggesting the stability of BAT8006 in blood circulation. BAT8006 led to potent and dose-dependent tumor regression in patient-derived xenograft (PDX) model of SCLC. Furthermore, single dose of 2.5 mg/kg of BAT8006 showed complete eradication of tumor in choriocarcinoma JeG-3 xenograft mice model. In PDX of ovarian cancer, 2.5 mg/kg of BAT8006 (DAR8) demonstrated superior tumor inhibition activity than 5 mg/kg of BAT8006 with DAR4, suggesting the high DAR approach of BAT8006 would be more effective. In addition, BAT8006 showed favorable pharmacokinetic and safety profiles in cynomolgus monkeys with the highest non-severely toxic dose (HNSTD) of 30 mg/kg when dosed once every three weeks for 3 times. Together these results indicate that BAT8006 could potentially provide a therapeutic benefit to treat FR α -positive tumors including breast cancer in clinical trial.

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12/8/2022

7:00 AM - 8:15 AM

P4-01-13

A retrospective study of anlotinib in patients with HER-2 negative metastatic breast cancer after prior two or more lines treatment

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Background: Anlotinib is a novel small molecule antiangiogenic drug that can inhibit multiple tyrosine kinase receptor activities. It has demonstrated antitumor activity in various cancers. This retrospective study explored the efficacy and safety of anlotinib combined chemotherapy in HER-2 negative metastatic breast cancer patients who have disease progressed after prior two or more lines of therapy. Methods: This retrospective study enrolled twenty-two HER-2 negative metastatic breast cancer patients including TNBC and HR+ subtypes. These patients pretreated with at least two lines of chemotherapy and/or endocrine drugs before receiving anlotinib. These patients received anlotinib combination with investigator-selected chemotherapy agents, including docetaxel, vinorelbine, gemcitabine, etoposide, alibrine and so on. Anlotinib was administered 12mg d1-d14 for a 21-day cycle. The primary end point of this study was progression free survival (PFS). Secondary end points included objective response rate (ORR), disease control rate (DCR), overall survival (OS), and toxicity. The treatment continued until disease progression or intolerance or the patient withdraw informed consent. Results: The enrolled breast cancer patients received anlotinib with a median age of 52.5 (rang 30 to 73). The patients with multiple metastases were 59.1% (13/22). All patients were

evaluated and the ORR was 50% (95% CI 0.282-0.718), DCR 95.5% (95% CI 0.772-0.999) and the mPFS was 8 months (95% CI 5.15-10.85). We also analyzed the efficacy of anlotinib combination with chemotherapy in different subtypes. For HR+HER2- metastatic breast cancer patients, the ORR was 77.8% (95% CI 0.4-0.972), DCR 100% (95% CI 0.664-1.0) and the mPFS was 8.5 months (95% CI 7.217-9.783). And for TNBC patients, the ORR was 30.8% (95% CI 0.091-0.614), DCR 92.3% (95% CI 0.640-0.998) and the mPFS was 6 months (95%CI 4.405-7.595). The most common adverse events were grade 1/2 including fatigue, hand-foot syndrome and thrombocytopenia et.al., and no serious adverse events occurred. Conclusion: Anlotinib is safe and effective in patients with HER-2 negative metastatic breast cancer after prior two or more lines treatments, and it is well tolerated.

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Jing Sun, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-01-14

Changes in the Genomic Spectrum of Actionable Alterations in HER2 Negative Metastatic Breast Cancer in Serial Cell Free DNA (cfDNA) Analysis

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Background: Serial cell free DNA (cfDNA) analysis in metastatic breast cancer (MBC) is a noninvasive method for tracking tumor evolution and the emergence of new somatic alterations through the course of the disease. The detection of new actionable alterations may impact treatment selection; thus, serial cfDNA collection is increasingly being performed in the clinic. However, it is not well-understood how often serial cfDNA testing identifies new actionable alterations. We evaluated changes in the genomic spectrum of actionable alterations in serial cfDNA analysis of HER2 negative (HER2-) MBC.

Method: Patients with HER2- MBC who underwent plasma-based cfDNA testing (Guardant360, 74-gene assay) between February 2015 and February 2021 at an academic institution were included. A retrospective review of records was conducted to identify subtype, demographics, lines of therapy, and cfDNA results. At baseline cfDNA testing, all cfDNA alterations were considered new. For patients with serial draws, new cfDNA alterations in each draw, compared to previous draws, were quantified and characterized. The pathogenicity of new alterations was determined using the OncoKB precision oncology database. New pathogenic alterations were further classified as actionable alterations (AA) using the ESMO Scale for Clinical Actionability of Molecular Targets (ESCAT). Alterations that met the ESCAT I (alteration-drug match was associated with improved outcomes in clinical trials) or ESCAT II (alteration-drug match was associated with antitumor activity) criteria were considered as AA.

Results: 344 patients with hormone receptor positive (HR+) MBC and 95 patients with triple negative (TN) MBC had a baseline cfDNA draw. Among the HR+ cohort, 139, 79 and 48 patients had 2nd, 3rd, and 4th serial cfDNA draws, respectively. Among the TN cohort, 33 and 18 patients had 2nd and 3rd serial cfDNA draws, respectively. Table 1 depicts the prevalence of AA found in each of these draws, as well as the median number of prior therapies at each point of collection and the mean time between serial draws. The median number of new genomic alterations was lower in subsequent draws compared to the baseline, regardless of subtype (HR+: 4 vs. 2, TN: 4 vs. 1.5-3, at baseline vs. subsequent draws, respectively). In the HR+ cohort the proportion of patients with new AA (ESCAT I/II) decreased from 63% at baseline to 27-33% in the 2nd-4th draws. While some of the new AA in subsequent draws were new actionable variants in the same genes that were known to be altered in previous draws (in 19%, 68% and 57% of patients with new AA in the 2nd, 3rd and 4th draws, respectively), the remainder were new AA in previously unaltered genes. In the TN cohort 25% of patients had new AA at baseline and this proportion of TN patients with new AA continued to decrease in subsequent draws (9% and 0% in the 2nd and 3rd draws, respectively). PIK3CA and ESR1 were the most frequent genes with new AA in the ER+ cohort, regardless of draw number. In the TN cohort, PIK3CA was the most frequent gene with new AA in the first draw, and in the second draw, new AA in PIK3CA, BRCA2, and ERBB2 were present at an equal frequency.

Conclusion: While the proportion of patients with HER2- MBC identified to have new AA in serial cfDNA decreased with time for both HR+ and TNBC, new alterations continue to emerge, particularly for patients with HR+ MBC. Further research is needed to determine the impact of serial cfDNA testing on the selection of genotype-matched therapy and outcomes.

Table 1.

Test No.	1 (Baseline)	2	3	4
HR+ MBC				
n	344	139	79	48
Median No. of prior therapies (range)	2 (0-14)	3 (1-11)	3 (1-12)	4 (1-9)
Mean time interval from prior draw, months (range)	N/A	7.8 (1-43)	6.3 (1-34)	6.4 (1-29)
% Of Pt. w/ new AA (ESCAT I/II) (95% CI)	63 (58-68)	27 (20-35)	28 (18-38)	33 (20-47)
TN MBC				
n	95	33	18	N/A
Median No. of prior therapies (range)	2 (0-7)	2 (0-7)	3 (1-7)	N/A
Mean time interval from prior draw, months (range)	N/A	5.4 (1-18)	5.1 (1-22)	N/A
% Of Pt. w/ new AA (ESCAT I/II) (95% CI)	25 (17-34)	9 (0-19)	0 (0-0)	N/A

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Jennifer C. Keenan, n/a: No financial relationships to disclose

Lianne Ryan, n/a: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

P4-01-15

Preliminary results from a phase 2 study of praluzatamab ravtansine (CX-2009) in patients with advanced breast cancer (ABC)

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Background: CD166 is broadly expressed in normal epithelium and overexpressed in many types of malignancies, including breast cancer. Probody® therapeutic candidates are masked antibodies, conditionally activated by tumor-associated proteases, which restricts their activity to the tumor microenvironment and minimizes 'off-tumor' toxicity. CX-2009 is a conditionally activated humanized anti-CD166 monoclonal antibody conjugated to DM4 that showed clinical activity in ABC patients in a phase 1 study (Boni et al. Clin Cancer Res. 2022). This phase 2 study (NCT04596150) evaluates CX-2009 as monotherapy in patients with advanced HR+/HER2- BC (Arm A) and TNBC (Arm B), and in combination with pacmilimab (a conditionally activated PD-L1) in TNBC (Arm C). Methods: Key eligibility criteria for all cohorts include: ECOG 0-1, acceptable end-organ function, measurable disease, willingness to receive ocular prophylaxis for DM-4 related toxicity, and available tumor tissue for CD166 evaluation. Eligibility criteria for HR+ BC include: 2-4 prior regimens (excluding single-agent hormonal therapy with up to 2 prior cytotoxic regimens) and a prior CDK 4/6 inhibitor in the metastatic setting; eligibility criteria for TNBC include CD166 by IHC >1% by central assessment, 1-3 prior regimens in the metastatic setting and prior taxane. All patients initially received 7 mg/kg Q3W; the protocol was subsequently amended to enroll patients at 6 mg/kg Q3W. The primary endpoint was overall response rate (ORR) using RECIST v1.1 assessed by central review. Other key endpoints include ORR by investigator assessment, clinical benefit rate at 24 weeks (CBR24; defined as any response, confirmed or unconfirmed, or SD for 24 weeks), duration of response, and progression-free survival by investigator. Archival tumor specimens and blood samples were collected for correlative research including genomic analyses. Results: As of 13 May 2022, 60 patients were enrolled in Arm A (all patients started at 7 mg/kg); 52 were evaluable for efficacy by investigator. Median duration of follow-up was 29.1 weeks (range: 3.6-60.7). Median age was 60.5 years (36, 83); pts received a median of 3.5 (1, 6) prior treatments for ABC. CD166 H-Score > 200 was reported in 53.3% of patients. Arm A met the primary efficacy endpoint with a confirmed ORR by central radiology of 14.9% (n=47); by investigator, ORR was similar at 15.4% (n=52); an additional 9 patients (17.3%) had an unconfirmed response. CBR24 was 40.4%; using only confirmed responses, CBR24 was 23.1%. Median PFS was 11.4 weeks (95% CI 9.0, 13.9). Common treatment-related all-grade adverse events (TRAEs) included blurred vision (42%), nausea (35%), fatigue (35%), diarrhea (25%), peripheral neuropathy (27%), infusion-related reaction (23%) and decreased appetite (20%).

Grade ≥ 3 ocular and neuropathic TRAEs were 15% and 10%, respectively. AEs resulting in treatment discontinuation (AEDC) were 25%. For Arm B and C, 55 and 10 patients were enrolled (the majority received a starting dose of 6 mg/kg). For Arm B, the futility boundary was crossed (ORR < 10%). Grade ≥ 3 ocular and neuropathic TRAEs and AEDC at 7 mg/kg in Arm B were similar to Arm A (11%, 11% and 21% respectively); whereas at 6 mg/kg, they were reduced at 3%, 0% and 0%, respectively. Biomarker data and correlation with outcomes will be presented. Conclusions: Praluzatamab ravtansine demonstrated single-agent activity in unselected heavily pretreated patients with HR+/HER2- ABC. Time to event analyses, such as PFS, were confounded by higher-than-expected toxicity at a starting dose of 7 mg/kg. The toxicity profile was generally consistent with a DM4 payload. The lower dose of 6 mg/kg appears to be better tolerated. Additional clinical studies in HR+ABC, incorporating a starting dose of 6 mg/kg and potentially including a biomarker strategy, are warranted.

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High levels of RSK2 in breast cancer patients is associated with longer PFS in patients treated with PMD-026, a first in class RSK inhibitor

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Background: Breast cancer (BC) is the most common malignancy in women and metastatic triple negative breast cancer (mTNBC) remains one of the most difficult to treat cancers with few targeted treatment options. RSK is recognized as a critical signaling component in the MAPK /PDK-1 pathways, is an important driver for BC and a signature of poor prognosis. PMD-026 is the first RSK inhibitor to enter clinical trials and is being developed alongside an immunohistochemistry (IHC) companion diagnostic to select patients with increased activated RSK2 in tumor tissue. A Phase 1/1b trial of PMD-026 in patients with metastatic breast cancer (mBC) or metastatic triple negative breast cancer (mTNBC) established safety at a dose of 200 mg Q12h. Efficacy signals in patients with heavily pretreated mBC/mTNBC are explored in this analysis along with evaluation of the effect of food (FE) on systemic exposure to treatment. Methods: PMD-026 was administered to 41 patients as a single agent in this phase 1/1b open-label study, with 30 patients evaluable for efficacy. Exploratory objectives were to identify subgroups of patients who may optimally benefit from PMD-026. Subgroup analysis of patients included 1) comparing BC patients who received ≤ 5 vs > 5 prior therapies; 2) comparing TNBC patients (de novo vs secondary subtypes)¹, and 3) comparing patients with low RSK2 H-scores (< 180) vs high (≥ 180). In addition, PMD 026 PK was evaluated at the 200 mg Q12h dose and a FE sub-study enrolled 12 patients administered a single 200 mg dose. Results: PMD-026 monotherapy was generally well-tolerated in the 41 mBC patients who were enrolled and treated. Kaplan-Meier PFS analysis of 30 evaluable BC patients who were dosed with PMD-026 showed that patients with less prior therapy (≤ 5) did significantly better (HR, 0.19; 95% CI [0.06–0.52], $p=0.0014$) than those with > 5 prior therapies. Subgroup analysis of PFS in those with TNBC demonstrated that de novo TNBC ($n=17$) had longer time on treatment with PMD-026 compared with secondary TNBC ($n=9$) (HR, 0.31; 95% CI [0.10-0.99], $p=0.0476$). In those with de novo TNBC with ≤ 5 prior therapies, a high RSK2 H-score was associated with significantly longer PFS at the RP2D (4.2 vs 1.3 months, HR, 0.17; 95% CI [0.03-0.80], $p=0.0254$) than patients with a low RSK2 H-score. In patients with CDK4/6 resistant HR+ BC ($n=3$), PFS was 5.2 (RSK2 high) vs 1.3 months (RSK2 low). Stable disease was observed in 53% (9/17) of patients with de novo TNBC and in 67% (6/9) of de novo TNBC patients with high RSK2. Tumor necrosis or target lesion reduction ($< 30\%$) was observed in 17% of patients (5/30), all of whom had high RSK2 expression. In the FE sub-study, increased interpatient variability in PMD-026 C_{max} and T_{max} but not AUC, was observed when administered with food, favored dosing in a fasted state, which is consistent with the pH dependent solubility of PMD-026. Notably, all FE patients (12/12) achieved the target concentration of 1 μ M (IC₉₀ in preclinical studies) within 4 hours when PMD-026 was taken without food. At the RP2D, PMD-026 taken without food showed relatively consistent exposure among patients over 24 hr timeframe. Conclusions: These findings demonstrate that in patients treated with PMD-026 who had received < 5 prior treatment regimens, had de novo TNBC or CDK4/6 refractory HR+ disease and had high RSK2 scores had longer PFS. Overall, PMD-026 is a well-tolerated, orally available RSK2 inhibitor that will be evaluated further for efficacy in TNBC and CDK4/6i refractory HR+ mBC, in a trial that will prospectively enroll patients based on RSK2 activation as defined by the RSK2 IHC H-scores. Clinical trial information: NCT04115306. 1 Patients diagnosed and treated for TNBC from their initial diagnosis (de novo TNBC) vs patients previously treated for hormone receptor positive (HR+) or human epidermal growth factor 2 receptor positive (HER2+) BC, but became HR or HER2 negative (secondary TNBC)

Disclosure(s):

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7:00 AM - 8:15 AM

P4-01-17

Phase I/II study of pembrolizumab in combination with oral binimetinib in patients with unresectable locally advanced or metastatic triple-negative breast cancer

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Background: Previous studies demonstrated that activation of the RAS/MAPK pathway is associated with reduced tumor-infiltrating lymphocytes and poor response to neoadjuvant chemotherapy in triple-negative breast cancer (TNBC). Further in vivo study showed that inhibition of the MAPK pathway with a MEK inhibitor is synergistic with immune checkpoint inhibitors (ICIs). Methods: Patients with unresectable locally advanced or metastatic TNBC with ≤ 3 prior lines of therapy were treated with pembrolizumab 200 mg every 3 weeks plus an oral MEK inhibitor binimetinib. Treatment was started with a 2-week run-in period with single-agent binimetinib. There were 2 dose levels in phase I, including dose level 0 (DL 0) with binimetinib

at 45 mg orally twice daily continuously and dose level -1 (DL -1) at 30 mg twice daily. A standard 3+3 design was used in phase I to identify the recommended phase II dose (RP2D) and Simon's two-stage Optimal design was used in phase II. Results: A total of 22 patients were enrolled. The median age was 58 years old (range 37-77). 14 (63.6%) patients had no prior systemic therapy in the metastatic setting and 8 (36.4%) patients had 1-2 prior lines of therapy. There were 4 patients treated in DL 0. Dose-limiting toxicity (DLT) was observed in 2 out of 4 patients in DL 0 with grade 3 ALT abnormality in one patient and grade 3 flank pain together with grade 3 nausea and vomiting > 48 hours despite anti-emetic therapy in the other patient. Binimetinib dose was reduced to DL -1. In the next 6 patients, there was 1 DLT observed with grade 3 AST/ALT abnormality. Thus, DL -1 was the RP2D, and an additional 12 patients were treated with DL -1 in phase II. Overall, 18 patients were treated in DL -1 and were included in phase II efficacy evaluation. 17 patients were evaluable for response. Objective responses were observed in 5 patients (29.41%, 95% CI: 10.31 - 55.96) with 1 complete response (CR) and 4 partial responses (PR). The clinical benefit rate (CBR) was 35.29% (95% CI: 14.21 - 61.67) with 6 out of 17 having had CR, PR, or stable disease \geq 24 weeks. Since previous studies showed poor responses to ICIs in patients with liver metastases due to macrophage-mediated T cell elimination, we further conduct exploratory analysis to evaluate responses among patients with and without liver metastases. Among all 5 patients with liver metastases, no response was observed. The objective response rate (ORR) in patients without liver metastases was 55.56% (95% CI: 21.20 - 86.30) and CBR was 66.67% (95% CI: 29.93-92.51), when excluding 3 patients who discontinued treatment due to adverse events prior to follow-up scans. Median progression-free survival in DL 0 was 2.4 (95%CI: 0.5-NE) and in DL -1 was 8.3 (95% CI: 3.9-NE) months. Median overall survival in DL 0 was 7 (95%CI: 0.5-NE) and in DL -1 was 33.2 (95% CI: 10.3-NE) months. Among patients who responded, 3 out of 5 (60%) had a duration of response greater than 12 months and ongoing even after stopping treatment (range: 5.4 - 32.0 months). Adverse events (AEs) were mostly grade 1-2 including anemia, CPK increase, fatigue, diarrhea, nausea, peripheral neuropathy, acneiform rash, AST increase, cardiac troponin increase, and constipation. Additional correlative studies are ongoing and will be presented at the meeting. Conclusions: Pembrolizumab in combination with binimetinib at 30 mg twice daily appears to be safe with manageable toxicities. Promising activity with durable responses was observed with this combination without chemotherapy, particularly in patients without liver metastases. Future studies are warranted to further evaluate the efficacy of this combination.

Disclosure(s):

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7:00 AM - 8:15 AM

P4-01-18

Real-world second-line treatment patterns and associated clinical outcomes for 2795 patients with advanced HR+ HER2- breast cancer treated with first-line CDK4/6 inhibitors

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Background: CDK4/6 inhibitors (CDK4/6i) are standard first-line (1L) regimens for HR+/HER2- advanced breast cancer (aBC). Recent data from the randomized phase II MAINTAIN trial reported a PFS benefit for patients (pts) who received a new endocrine therapy plus ribociclib (ribo) versus new endocrine therapy alone) following progression on CDK4/6i as compared to pts who received endocrine therapy alone. However, second-line (2L) treatment patterns and patient outcomes following 1L CDK4/6i are relatively undescribed. Here we describe real-world 2L treatment patterns following 1L CDK4/6i and associated clinical outcomes from a large clinical genomics database.

Methods: Real-world evidence (RWE) was sourced from the GuardantINFORM (Guardant Health) database which comprises aggregated commercial payer health claims and de-identified records from over 207,000 pts with comprehensive circulating tumor DNA (ctDNA) results via Guardant360 (G360) from 2014 to 2021. Pts with HR+/HER2- aBC with >1 claim of CDK4/6i and >1 claim for treatment after the index G360 test were included. Real-world time to treatment discontinuation (rwTTD) and real-world time to next treatment (rwTTNT) were assessed in months as proxies for progression-free survival. Real-world overall survival (rwOS) was also reported in months.

Results: 2,795 pts met criteria for inclusion; 2,361 (84.5%) were treated with 1L palbociclib (palbo), 271 (9.7%) with 1L abemaciclib (abema) and 163 (5.8%) with 1L ribo. Chemotherapy

(chemo,35.5%) and endocrine-only therapy (32.8%) were the most common 2L therapy regardless of the 1L CDK4/6i agent (Table 1). Other 2L agents included endocrine backbone change (14.7%) or CDK4/6i change (7.7%). Endocrine backbone changes were observed more frequently (15.6%) in pts receiving 1L palbo while CDK4/6i changes were more frequent in pts receiving abema (14.0%) or ribo (22.0%). Pts treated with 2L CDK4/6i had improved rwTTNT, rwTTD and rwOS compared to 2L chemo regardless of 1L agent [rwTTNT: 10.2 (95% CI: 7.2-11.7) vs. 7.2 (6.5-8.1); rwTTD: 6.8 (95% CI: 5.8-8.5) vs. 4.3 (95% CI:3.9-4.7); rwOS: NR (95% CI: 40.0-NR) vs. 34.8 (95% CI: 31.3-37.2)]; improvement in rwTTNT, rwTTD and rwOS were also observed for pts with 2L endocrine backbone changes compared to chemo [rwTTNT: 8.5 (95% CI: 7.2-9.6) vs. 7.2 (6.5-8.1); rwTTD: 6.9 (95% CI: 5.8-7.9) vs. 4.3 (95% CI:3.9-4.7); rwOS: 63.4 (95% CI: 51.2-NR) vs. 34.8 (95% CI: 31.3-37.2)]. Pts treated with 2L alpelisib had the shortest rwOS regardless of 1L CDK4/6i agent used [any 1L: NR (95% CI: 23.6-NR)].

Conclusions: A variety of 2L regimens following 1L CDK4/6i were observed, with an improvement in rwTTNT, rwTTD and rwOS in pts receiving 2L CDK4/6i or 2L endocrine backbone change only relative to 2L chemo. These data are hypothesis generating, and the observed improvement may be secondary to therapy choice versus pts who received 2L chemo having more aggressive disease. Larger randomized trials are ongoing to study sequencing and efficacy of 2L treatments following 1L CDK4/6i.

Table 1. Distribution of 2L therapies by 1L CDK4/6i agent

	ANY 1L CDK4/6i		1L Palbociclib		1L Abemaciclib		1L Ribociclib	
2L Chemotherapy	992	35.5%	845	35.8%	100	36.9%	47	28.8%
2L Endocrine only	917	32.8%	808	34.2%	67	24.7%	42	25.8%
2L Endocrine Backbone change	412	14.7%	369	15.6%	24	8.9%	19	11.7%
2L CDK4/6i	214	7.7%	140	5.9%	38	14.0%	36	22.1%
2L Alpelisib	134	4.8%	105	4.5%	19	7.0%	10	6.1%
2L PARP inhibitor	31	1.1%	24	1.0%	5	1.9%	2	1.2%
2L Anti-HER2	79	2.8%	61	2.6%	13	4.8%	5	3.1%
2L Immunotherapy	16	0.6%	9	0.4%	5	1.9%	2	1.2%
	2795		2361	84.4%	271	9.7%	163	5.8%

Disclosure(s):

Katherine K. Clifton, MD: biotheranostics: Consulting Fees (e.g., advisory boards) (Terminated, March 30, 2022)

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12/8/2022

7:00 AM - 8:15 AM

P4-01-19

Real World Statistics on CDK4/6 Inhibitor Use in Metastatic Hormone Receptor Positive and HER2-Negative Breast Cancer with a Focus on Age

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Background:

Combining CDK 4/6 inhibitors with hormone directed therapy using aromatase inhibitors (AI) or selective estrogen receptor down-regulators (SERD) is considered first line therapy for treatment of hormone receptor positive (HR+) human epidermal receptor 2 negative (HER2-) metastatic breast cancer (mBC). Here we aim to evaluate first line CDK 4/6 inhibitor practice patterns both nationally and locally (Wisconsin) in HR+ HER2- mBC patients and evaluate age as a potential factor impacting practice patterns.

Methods:

A retrospective analysis was performed utilizing IQVIA Anonymized Patient Longitudinal Data. The data base captures 60-85% of cancer patients across all 50 states in the United States and relies on diagnostic coding used in service or treatment claim filing. Patients queried were greater than 18 years old and were identified by a code indicating CDK4/6 inhibitor therapy or a combination of codes indicating mBC, HR+ status and HER- status. First line treatment was

categorized as CDK4/6 inhibitor combination therapy, AI monotherapy, SERD, selective estrogen receptor modulator (SERM) monotherapy, chemotherapy, or other. Patients were further filtered by year, location, practice type (academic vs community), and age.

Results:

A total of 313,978 patients with mBC receiving first-line therapy were identified nationally between 2015 and 2021. The proportion of patients on first line CDK4/6 inhibitor combination therapy nationally significantly improved from 20% in 2015 (N=27,063) when palbociclib was first approved, to 53% in 2021 (N=54,023) (Table 1.) In 2021, first line use of CDK 4/6 inhibitor combination therapy was higher at 59% both in WI and our institution Froedtert Hospital and the Medical College of Wisconsin Cancer Center (Table 2.) At our center in 2021, the use of first line CDK4/6 inhibitor combination therapy in patients greater than age 65 was significantly lower at 35% (N=39) compared to patients less than 65 at 75% (N=64.) Further delineating the age groups at our center (Table 3,) use of CDK4/6 inhibitor combination therapy in patients aged 70-79 was 35% (N=20) and fell to 20% in patients greater than 80 in age (N=8.)

Conclusion:

Despite significant improvement in long-term outcomes with first line CDK4/6 inhibitor combination therapy in HR+ HER2- mBC patients, overall national usage is suboptimal. At our center, this was particularly apparent in patients older than 70. Identifying barriers to optimal use is critical to improve utilization of this important and effective class of drugs.

National Percentages of HR+ HER2- mBC Patients Stratified by First Line Treatment Between 2015-2021

		Year							
		2015	2016	2017	2018	2019	2020	2021	
First Line Treatment Category	CDK4/6 Inhibitor	20%	33%	41%	46%	49%	52%	53%	
	AI Monotherapy	45%	39%	35%	33%	32%	31%	30%	
	Chemotherapy	15%	13%	10%	9%	8%	7%	7%	
	Other	20%	15%	14%	12%	11%	9%	10%	

HR+ HER2- mBC patients Nationally treated with first line therapy (N=313,978.)

National and Local Percentages of HR+ HER2- mBC Patients Stratified by First Line Treatment in 2021

		Location		
		National	Wisconsin	Froedtert Hospital
First Line Treatment Category	CDK4/6 Inhibitor	53%	59%	59%
	AI Monotherapy	30%	26%	34%
	Other	17%	15%	7%

HR+ HER2- mBC patients treated with first line therapy in 2021 Nationally (N=54,026,) in Wisconsin (N=694,) and at Froedtert Hospital and the Medical College of Wisconsin Cancer Center (N=103.)

Local Percentages HR+ HER2+ mBC Patients Stratified by First Line Treatment and Age Group

		Age in Years				
		Age 18-49	Age 50-59	Age 60-69	Age 70-79	Age >80
First Line Treatment Category	CDK4/6 Inhibitor	82%	80%	53%	35%	25%
	AI Monotherapy	11%	13%	41%	55%	75%
	Other	7%	7%	6%	10%	0%

HR+ HER2- mBC patients treated with first line therapy in 2021 at Froedtert Hospital and the Medical College of Wisconsin Cancer Center (N=103.)

Disclosure(s):

Kathleen Monahan, DO: Pfizer: Pfizer helped with data analysis for the abstract, no conflict of interest or publication bias (Ongoing)

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7:00 AM - 8:15 AM

P4-01-20

Phase IV study evaluating talazoparib in patients with locally advanced or metastatic negative HER2 breast cancer and a somatic or germline BRCA1/2 mutation (ViTAL) – Analysis of cohort 1 according to hormonal receptor status

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Background: Talazoparib (TALA) is a highly potent, dual-mechanism PARP inhibitor that has demonstrated clinical benefit in EMBRACA Phase III trial for patients with germline BRCA1/2 mutated locally advanced or metastatic HER2- breast cancer.

Objective: The aim of the study is to ensure the effectiveness and safety of TALA in real-life setting among patients with locally advanced or metastatic HER2- breast cancer, with somatic or germline BRCA1/2 mutation.

Methods: ViTAL is an ambispective, multicentric, longitudinal, phase IV study. It includes two ambispective cohorts:

- Cohort 1: patients treated through the French Early Access Program and inclusion of patients with somatic BRCA1/2 mutation was allowed.
- Cohort 2: patients treated according to the European Marketing Approval granted in 09/21/2021.

Here we present the results of the primary and some secondary endpoints for cohort 1.

Results: From November 2018 to May 2021, 86 patients were included in Cohort 1, with updated results after a median follow-up of 17.3 months (11.2 - 24.4).

Patients' characteristics are 53.5% of ER+ BC / 46.5% of TNBC (refer to the table).

The median Time to Treatment Discontinuation (mTTD) was 9.0 months [range 6.0 ; 11.5] with 37.7% of patients still on treatment at 12 months. Subgroup analysis shows similar mTTD according HR status, germline vs somatic mutation and prior platinum exposure (refer to the table).

The Clinical Benefit Rate assessed by the investigators is 82.4% (Complete Response for 25.7%, Partial response R for 32.4% and stable disease for 24.3%). The median of duration of CNS metastases control was 6.6 months, and 80.0% of patients had control of CNS metastases during TALA.

Out of the 85 treated patients, 69 patients (80.2%) experienced a TALA permanent discontinuation for progressive disease (84.1%), toxicity (10.1%), cancer-related death (1.4%), or other reasons (1.4%).

After discontinuation of TALA, 65.1% of patients received a subsequent treatment with a TTD of 2.3 months [1.7 ; 2.7]. The most common subsequent treatments were non-platinum chemotherapy (64.3%), platinum chemotherapy (19.6%) and others (19.1%).

At least one adverse events (AEs) was recorded in 74.4% of patients. Hematologic AEs (any grade) occurred in 48.8% (anemia 27.9%, thrombocytopenia 12.8%, neutropenia 10.5%).

Most common non-hematologic AEs were alopecia (8.1%) and asthenia (7.0%). Related Serious Hematologic AEs occurred in 10 patients (11.6%) including 7 (8.1%) Anemia.

Related Serious Non-hematologic AEs (vomiting, pyelonephritis and ascitis) were seen in 3 patients (3.6%). AEs associated with temporary drug interruption, dose modification and permanent drug discontinuation occurred in 36 (41.9%), 24 (27.9%), and 7 (10.1%) patients respectively.

The mOS is expected to be reached at the time of the congress, with 51.9% of patients still alive at 24 months.

Conclusions: ViTAL is the largest study that reports real-world data with TALA. Outcomes and safety in Cohort 1 are consistent with the results of EMBRACA study and give additional data on subgroups of interest (ie patients previously treated with carboplatin, presence of CNS). (Litton et al. NEJM 2018)

mTTD on subgroups of interest

mTTD by :		N (%)	Months [95% C.I.]
BRCA mutation	BRCA1	42 (48.8)	6.5 [4.8 ; 9.1]
	BRCA2	44 (51.2)	12.0 [6.1 ; 21.0]
Number of previous lines of chemotherapy	0	14 (16.3)	9.9 [3.9 ; 19.4]
	1	27 (31.4)	10.0 [6.4 ; 21.9]
	≥ 2	45 (52.3)	6.3 [4.7 ; 10.9]
Prior platinum at any setting	Yes	30 (34.9)	10.6 [5.0 ; 14.9]
	No	56 (65.1)	8.2 [5.7 ; 10.9]
Prior platinum at ABC setting	Yes	26 (30.2)	9.1 [5.0 ; 14.9]
	No	60 (69.8)	8.6 [5.7 ; 12.2]
HR status	HR positive	45 (53.5)	9.0 [5.6 ; 12.0]
	HR negative	40 (46.5)	9.0 [5.7 ; 14.3]
De novo ABC	Yes	32 (38.1)	9.1 [6.1 ; 12.5]
	No	51 (61.9)	6.4 [4.8 ; 12.2]
Brain metastasis	Yes	9 (11.6)	5.7 [0.4 ; NE]
	No	76 (88.4)	9.1 [6.1 ; 12.0]
Mutation type	Germline mutation	79 (94.1)	9.0 [6.0 ; 12.0]
	Somatic mutation	5 (5.9)	9.1 [0.7 ; NE]

Patients' characteristics

Patients' characteristics :	ER+ BC	TNBC
Median age (years)	51.0	49.5
BRCA1-mutated / BRCA2-mutated (%)	26.1 / 73.9	75 / 25
gBRCA / sBRCA (%)	95.7 / 4.3	92.3 / 7.7
ECOG at inclusion 0 or 1 or ≥2 (%)	52.2 / 39.1 / 8.7	52.5 / 42.5 / 5.0
De novo mBC (%)	31.8	45.0
Visceral, bones and CNS metastases (%)	65.2 / 65.2 / 10.9	62.5 / 37.5 / 12.5
No breast or ovarian cancer family history at 1 st degree (%)	63.0	57.5
Chemo-naïve (%)	10.9	22.5
Received prior platinum in (neo)adjuvant or metastatic setting (%)	26.1	45.0
Median of previous lines of hormonotherapy	2.0	0
Received CDK4/6 inhibitor as hormonotherapy (%)	73.9	0.0

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12/8/2022

7:00 AM - 8:15 AM

P4-01-21

Phase 2 Study of the CDK4/6 Inhibitor FCN-437c in Combination With Fulvestrant or Letrozole and Goserelin in Patients With HR+, HER2- Advanced Breast Cancer

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Background: FCN-437c is a second-generation CDK4/6 inhibitor. Phase 1b clinical results indicated improved antitumor activity in patients (pts) with HR+, HER2– advanced breast cancer (ABC), treated with FCN-437c + letrozole.

Methods: This Phase 2, multicenter, open-label clinical study evaluated the antitumor activity, pharmacokinetics (PK), and safety of FCN-437c + fulvestrant in post-menopausal pts (Cohort 1, treatment-naïve or 2L), FCN-437c + letrozole + goserelin in pre-menopausal pts (Cohort 2, treatment-naïve). Pts received FCN-437c (200 mg QD) in a 21-day-on and 7-day-off schedule either in combination with fulvestrant (500 mg D1) or letrozole (2.5 mg QD) + goserelin (3.6 mg once per cycle) in 28-day cycles. The primary endpoint was overall response rate (ORR) and secondary endpoints were progression-free survival (PFS), overall survival (OS), PK, and

safety.

Results: At study cutoff (Feb 7, 2022), 36 pts were enrolled in Cohort 1 and 31 pts were in Cohort 2; 42 (62.7%) pts had visceral metastases and 9 (13.4%) pts had bone-only metastases. In Cohort 1, 18 pts were treatment-naïve, 15 pts had received 1L treatment, and 3 pts had received ≥2L treatment. In Cohort 2, 25 pts were treatment-naïve and 6 pts had received 1L treatment. Overall, 27 pts in the per-protocol set achieved partial response (PR), resulting in an ORR of 40.9% (95% CI, 29.0-53.7). Median follow-up was 12.8 months, and median PFS (mPFS), OS, and DOR were not reached. However, at 12 months, the PFS rate was 67.7% (95% CI, 53.2-78.6) and the OS rate was 95.9% (95% CI, 84.5-99.0); the 6-month DOR rate was 96.0% (95% CI, 74.8-99.4). In Cohort 1 (n=35), 11 pts achieved PR: the ORR was 31.4% (16.9-49.3%) and mPFS was 12.9 months (95% CI, 9.2-NR); the 6-month DOR rate was 100%. In Cohort 2 (n=31), 16 pts achieved PR: the ORR was 51.6% (95% CI, 33.1-69.9%). mPFS, OS, and DOR were not reached; the 6-month DOR rate was 92.9% (95% CI, 59.08-98.96) (Table). Treatment-emergent adverse events (TEAEs) were observed in all pts. Majority of AE were G1 or 2 except for hematological TEAE. 58 (86.6%) pts reported grade ≥3 TEAEs, mainly neutropenia (74.6%), leukopenia (49.3%), hypertriglyceridemia (6.0%), lymphocyte count decrease (4.5%), and γ-glutamyltransferase increase (3.0%): most were reversed through dose interruption and symptomatic therapy. Steady-state PK parameters were analyzed after 15-21 days of QD administration: Cohort 1: median Tmax was 3 h, geomean T1/2 was 44.6 h, geomean Cmax was 1650.7 ng/mL, and geomean AUC0-24h was 29,148.08 h*ng/mL; the geomean accumulation ratios of AUC0-24h and RCmax were 2.18 and 1.74, respectively, compared with first dose. Cohort 2: median Tmax was 4 h, geomean T1/2 was 35.7 h, geomean Cmax was 1314.34 ng/mL, and geomean AUC0-24h was 22,889.96 h*ng/mL; the geomean accumulation ratios of AUC0-24h and RCmax were 1.95 and 1.63, respectively, compared with first dose.

Conclusion: FCN-437c in combination with fulvestrant or letrozole + goserelin demonstrates antitumor activity and safety and is well tolerated in pts with HR+, HER2- ABC. This combination therapy will be further investigated in 2 ongoing Phase 3 trials (NCT05438810 and NCT05439499).

Clinical trial number: NCT05004142. Research Sponsor: Avanc Pharmaceutical Co., Ltd

Table. Clinical outcomes for patients in the per-protocol set

	Cohort 1: FCN-437c 200 mg + fulvestrant 500 mg (N=35)	Cohort 2: FCN-437c 200 mg + letrozole 2.5 mg + goserelin 3.6 mg (N=31)	Total (N=66)
ORR, % (95% CI)	31.4 (16.9-49.3)	51.6 (33.1-69.9)	40.9 (29.0-53.7)
Complete response, n (%)	0	0	0
Partial response, n (%)	11 (31.4)	16 (51.6)	27 (40.9)
Stable disease, n (%)	19 (54.3)	14 (45.2)	33 (50.0)
Progressive disease, n (%)	5 (14.3)	1 (3.2)	6 (9.1)
Lesion not evaluable, n	0	0	0
mPFS, m (95% CI)	12.9 (9.2-NR)	NR	NR
12-month PFS rate, % (95% CI)	65.3 (45.7-79.2)	69.4 (44.5-84.9)	67.7 (53.2-78.6)
mOS, m (95% CI)	NR	NR	NR
12-month OS rate, % (95% CI)	92.3 (72.6-98.0)	100	95.9 (84.5-99.0)

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7:00 AM - 8:15 AM

P4-01-22

Clinical outcomes of metastatic breast cancer patients treated with poly (adenosine diphosphate-ribose) polymerase inhibitors (PARPi): the Mayo Clinic experience

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Background: Two poly (adenosine diphosphate-ribose) polymerase inhibitors (PARPi) are currently FDA-approved for the treatment of HER2-negative metastatic breast cancer (MBC) in carriers of germline pathogenic variants (PVs) in BRCA1 or BRCA2 (BRCA1/2). This study explores the clinical outcomes of MBC patients treated with a PARPi. Methods: In this retrospective study, we included MBC patients treated with a PARPi between January 2017 and February 2022 at Mayo Clinic (Minnesota, Arizona, Florida, and Mayo Clinic Health Systems). We used the Kaplan Meier method to estimate the time-to-treatment-failure (TTF) and the log-rank test to compare different subsets. In addition, predictors of TTF were identified in a multivariate cox-proportional hazard regression model, including age at PARPi initiation, race, ethnicity, histology, estrogen receptor (ER), progesterone receptor (PR), and HER2 expression of the tumor, the number of prior therapies, type of PARPi, and PV carrier status (germline BRCA1/2 or PALB2 vs. somatic BRCA1/2 vs. other). Results: Sixty-five patients treated with PARPi (olaparib: 51; talazoparib: 14) were included in the final analysis. Fifty-five patients were carriers of germline PVs in BRCA1 (n=24, 37%), BRCA2 (n=27, 42%) or PALB2 (n=4, 6%), whereas ten patients (15%) had no germline PVs but the tumor had a somatic mutation in the homologous recombination-related (HRR) genes (7 in BRCA1/2, 2 in ATM, and 1 in CDKN2A and CDH1). At the data cutoff, 48 (74%) patients had discontinued PARPi due to progression or death. Fifteen (23%) patients required a dose reduction due to side effects. Occurrence of grade ≥ 3 side effects: anemia in 8, fatigue in 4, neutropenia in 2, and thrombocytopenia in 2 patients. Eight (15.7%) patients in the olaparib group and seven (50%) patients in the talazoparib group required a dose reduction for side effects. No patient on olaparib required drug discontinuation due to side effects, whereas two patients on talazoparib were switched to olaparib due to cytopenias and could tolerate olaparib. Median TTF in the overall population was 8 months (95% confidence interval [CI]: 6.4 – 9.6), and there was no difference ($p=0.64$) in TTF between the olaparib and talazoparib groups. Median TTF in the germline BRCA1, BRCA2, and PALB2 PV carriers were 7, 8, and 11 months, respectively ($p=0.57$). Among patients with somatic BRCA1/2 mutations, the median TTF was 4 months. Numerically, patients with HER2-positive tumors (n=8) had a shorter TTF compared to HER2-negative tumors (Median TTF: 4 vs. 8 months, $p=0.098$). No significant difference in TTF was observed by ER or PR status of the tumor, age at initiation of PARPi, the number of prior therapies, and prior use of platinum-based chemotherapy or CDK4/6 inhibitors. In multivariate analysis, HER2 positivity (hazard ratio [HR]: 8.0, 95% CI: 2.2 – 29.4, $p=0.002$), somatic BRCA1/2 mutations (HR: 7.6, 95% CI: 1.2 – 50.0, $p=0.03$) and somatic mutations in other HRR genes (HR: 19.1, 95% CI: 3.1 – 118.6, $p=0.002$) were associated with worse TTF. Conclusions: In the real world, PARPi were well-tolerated with promising time-to-treatment-failure (TTF) benefits comparable to data from clinical trials. Notably, relatively shorter TTF was observed in

patients with somatic BRCA1/2 and other HRR gene mutations and HER2-positive MBC. These findings improve our understanding of the role of PARPi in MBC and will help to guide treatment decisions with PARPi in the clinical setting.

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-01-23

Updated data from the phase 1 trial of DZD1516, a BBB-penetrant selective HER2 inhibitor, in patients with HER2 positive metastatic breast cancer

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Background: Patients with HER2 positive (+) breast cancer and central nervous system (CNS) metastases often have poor prognoses. DZD1516 is designed as a reversible and selective HER2 tyrosine kinase inhibitor (TKI) with full blood-brain barrier (BBB) penetration. Methods: DZD1516 is being developed in a phase 1 study (NCT04509596) in patients with HER2+ advanced or metastatic breast cancer relapsed from the standard of care. Key overall eligibility criteria were previously presented. DZD1516 was given orally twice daily (BID) in a continuous 21-day cycle (except Cycle 0). The primary objective is to evaluate the safety and tolerability of DZD1516 monotherapy and define the maximum tolerated dose (MTD). Results: As of June 23, 2022, twenty-three patients with HER2+ MBC from the USA and China were enrolled and dosed with DZD1516 monotherapy (25 mg ~ 300 mg, BID). Fifteen patients (65.2%) had baseline CNS metastases. Patients were heavily pre-treated, with a median of 7 lines of prior systemic treatment. All patients had been treated with HER2 large molecules, and 82.6% of patients also received prior HER2 TKI treatment. DZD1516 was well tolerated at doses up to 250 mg BID. Two dose-limiting toxicities were reported in the 300 mg cohort. As a result, 250 mg was defined as the MTD. Treatment-emergent adverse events (TEAEs) were reported in 91.3% of patients. Grade 3 drug-related TEAEs were reported in two patients. No grade 4 or 5 TEAEs were reported. The most common TEAEs included headache, vomiting, and hemoglobin decreased. The majority of the TEAEs could be managed and were reversible. The longest treatment duration was > 3 months. Following single oral dosing, DZD1516 was eliminated with a mean half-life of 13.4 – 22.5 hrs. After twice-daily dosing for 15 days, moderate accumulation of DZD1516 systemic exposure was observed at doses ≤ 200 mg BID and negligible accumulation at 250 mg BID. The combined molar exposure of DZD1516 and its active metabolite DZ2678 increased with dose between 50 mg to 250 mg dose range. In patients (n = 6), mean K_{puu},CSF was 2.1 for DZD1516 and 0.76 for DZ2678 across the dose range, indicating full penetration of DZD1516 and DZ2678 into human CNS. Nineteen patients (82.6%) had at least one post-treatment RECIST assessment. With a median of 7 lines of prior systemic treatment, the best antitumor efficacy in intracranial, extracranial, and overall lesions

was stable disease. Conclusion: DZD1516 is a full BBB-penetrant HER2 inhibitor. Consistent with its high selectivity, no wild-type EGFR-related AEs have been reported. The updated data will be presented at the meeting.

Disclosure(s):

Nicholas P. McAndrew, MD, MSCE: Biotheranostics: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Travel accommodation (Ongoing); Dizal: Contracted Research (Ongoing); Genomic Health: Consulting Fees (e.g., advisory boards) (Ongoing); GoodRx: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Speaking honorarium (Ongoing); Roche: Travel accommodation (Ongoing); Seattle Genetics: Contracted Research (Ongoing); TRIO: Travel accommodation (Ongoing)

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12/8/2022

7:00 AM - 8:15 AM

P4-01-24

Targeting receptor tyrosine kinases in overcoming tamoxifen resistance and dormancy in invasive lobular cancer

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Objective: The molecular hallmark of invasive lobular cancer (ILC) is the loss of E-cadherin, resulting in the unique morphology, low mitotic index and unusual metastatic spread to ovaries, gut, and peritoneum. Patients with ILC face delayed, and higher stage at diagnosis, worse disease-free and overall survival¹. The most frustrating challenge is the delayed recurrence, likely due to resistance and induction of dormancy². Despite these unique features, ILC is lumped with hormone receptor-positive invasive ductal cancers (IDC); consequently, management strategies are based on data from IDC. Hence there is an unmet need to address the unique challenges of ILC. We generated Tamoxifen-resistant (TAMR) ILC cell lines with the aim to study the distinct characteristics, dormancy, differentially activated pathways, and response to drugs targeting such pathways in the resistant cells. Methods: We used MDA-MB-134-VI and SUM44-PE cells to study the effect of tamoxifen in combination with multi-targeted receptor tyrosine kinase inhibitor, Lenvatinib. TAMR cells from both MB-134 and SUM44PE cells were generated by growing them in increasing concentrations of 4-hydroxy tamoxifen (4-HT) up to 500nM, for 6 months. Total RNA from parental and TAMR cells were subjected to RNA-seq. Whole cell extracts were analyzed for specific phospho proteins by Western Blot analysis. Growth kinetics and effect of drugs on cell viability was measured using MTT assay (Roche). Cell migration was measured using Transwell migration assay. Novel engineered 2D and 3D cultures were used to study dormancy and the effect of the drug combination. Orthotopic tumor induction in NSG mice is ongoing to determine the effect of drug combination in vivo. Results: The TAMR cell lines show distinct morphological features, small but significant increase in growth rate ($p=0.05$) and remarkably higher migration (MB-134TAMR:11.5-fold, $p<0.005$ and SUM44TAMR:>100-fold, $p<0.005$). The IC₅₀ for tamoxifen increased from 8.1 μ M (MB-134) to 16.8 μ M (MB-134TAMR) and from 11.3 μ M (SUM44) to 26.6 μ M (SUM44TAMR). RNA seq analysis revealed enrichment of PI3K-AKT, MAPK, cAMP, Rap1 signaling pathways, ECM-receptor interaction, Focal adhesion, and steroid hormone biosynthesis pathways in the

TAMR cells. Upon stimulation by endothelial growth factor, the MB-134TAMR but not the parental cells showed dose dependent increase in phospho-AKT and phospho-MAPK levels. Using novel 2D/3D cultures, we show differential morphologies between IDC (MCF7) cells, MB-134TAMR, and the parental cells. MCF7 and MB-134TAMR cells are more adherent to fibronectin ($p < 0.0001$), whereas the parental ILC cells are more adherent to COL3A1 ($p < 0.0001$), a feature observed in dormancy³. Further, the administration of 5 μ M 4-HT induced a cessation of growth in the parental cell line, with a sub-population of apparent dormant cells. The combination of Lenvatinib (5 μ M) and 4-HT (7.5 μ M) synergistically inhibited both the parental cell lines by ~60%. Lenvatinib (5 μ M) and 4-HT (15 μ M) inhibited the MB-134TAMR and SUM44TAMR cell lines synergistically by 65% and 45% respectively. In vivo, the growth of MB-134 induced tumors were completely suppressed when 5mg sustained release pellet of TAM citrate was injected in the subscapular region of tumor bearing mice (tumor @100cm³). The results of the combination using in vivo models and 2D/3D cultures will be reported. Conclusion and significance: Lenvatinib with tamoxifen is active and synergistic against parental and TAMR ILC cell lines. Our novel 2D/3D cultures show distinct pattern of growth for ILC cells and a possible induction of a dormant subpopulation upon 4-HT treatment. Overcoming resistance to conventional therapies and preventing induction of dormancy will improve long-term outcomes of patients with ILC. 1. PMID:33641217 2. PMID: 34388695 3. PMID: 35121989

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P4-01-25

Safety analysis after 11 years of follow-up of the randomized phase III trial SAKK22/99: upfront chemotherapy in advanced HER2 positive breast cancer

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Background: The SAKK 22/99 is a phase III randomized clinical trial launched by the Swiss Group for Clinical Cancer Research and the European Institute of Oncology in Milan in 99 for women with HER2-positive advanced breast cancer (ABC). 175 patients were randomized 1:1 from Sept 99 to Jan 2013 to receive first-line trastuzumab (T) alone followed at disease progression by the combination with chemo (Arm A) vs the upfront combination of T and chemo (Arm B). The results were published in 2017 (O. Pagani et al Ann Onc 28: 305–312, 2017). The outcome was similar for sequential T-chemo or upfront combination

The patients' treatment and FU continued until March 2022 and we now report the safety data after 135.2 months of median FU.

Patients and methods: at the time of study termination 1 patient with SD was still receiving T alone in the study and T was continued after trial closure. The safety analyses include 86 pts allocated to arm A and 88 to arm B. 1 pt did not receive any trial treatment and was excluded from this analyses.

19 of the 86 patients in arm A stopped trial treatment after T alone, 67 continued with T+chemo. Baseline characteristics were well balanced and are summarized in Table 1.

Treatment

The T loading dose of 4 mg/kg/iv was followed by 2 mg/kg/iv weekly. In the 1st-line population (84) chemo was weekly paclitaxel (90 mg/m²/iv-3/4 weeks). After amendment 1 chemo was at investigator's choice (taxanes, vinorelbine, platin) according to label indications and could be stopped after 24 weeks (6–8 cycles) in responding patients or after unacceptable toxicity.

Results:

7 patients in arm A (8%) and 11 in arm B (13%) stopped trial treatment due to toxicities (Fisher's exact test, p=0.46). 3 of the 7 patients in arm A stopped under T alone and 4 under T+chemo (all paclitaxel weekly)

Treatment durations of these 7 and 11 patients were 7.7 months (range 0.5 – 49) in arm A and 5.5 months (range 0.6 – 31 months) in arm B, respectively.

Cardiovascular toxicities: The most common toxicities were thromboembolic events, blood pressure disorders and arrhythmia. 6 patients (7%) in arm A and 10 (11%) in arm B had cardiac

events (Fisher's exact test, $p=0.43$). G1-3 toxicities occurred in 2 (2%), 2 (2%) and 2 (2%) patients of arm A and in 5 (7%), 2 (2%) and 3 (3%) of arm B. We observed no grade 4 events. Split by treatment phase in arm A, G1-3 toxicities were seen in 1 (1%), 2 (2%) and 1 (1%) patient under T alone (N=86) and in 1 (1%), 0 (0%) and 2 (3%) under T+chemo (N=67). LVEF-decline: 78 patients in arm A and 74 in arm B had sequential LVEF measurements. A decline $\geq 10\%$ was found in 35 patients (45%) in arm A and in 20 (27%) in arm B (Fisher's exact test, $p=0.028$). Among the 35 patients in arm A, 12 had the decline under T alone, 14 under T+chemo, and 9 under both T alone and T+chemo. A decline $\geq 20\%$ was found in 10 patients (13%) in arm A and in 3 (4%) in arm B (Fisher's exact test, $p=0.08$). Among the 10 patients in arm A, 7 had the decline under T alone, 3 under T+chemo.

Sensory neuropathy

43 patients (50%) in arm A and 48 (54%) in arm B had neuropathy (Fisher's exact test, $p=0.65$). G1-3 toxicity in arm A was developed by 26 (30%), 11 (13%) and 6 (7%) patients, respectively; in arm B 30 (34%), 12 (14%) and 6 (7%). No grades 4 events occurred.

Conclusion: After more than 11 years of follow-up, no relevant toxicities were found in these patients receiving T for ABC. In particular, the incidence and grade of cardiac toxicity was low. The decline in LVEF was numerically higher in the arm A and in particular in the T alone group, but was not clinically relevant. Our data potentially suggest that T+chemo followed by T maintenance could have less cardiotoxicity than T followed by T+chemo. The possible causes for the difference in LVEF decline between the two arms are unclear, but could be related to treatment duration. The women in Arm A shows a trend to longer therapy: Median treatment duration (months) in Arm A was 7.92 (0.46 - 135.98) vs 6.62 (0.56 - 71.28) in Arm B. This long-term analysis confirms the favorable safety and good tolerability of the reported regimes.

	Arm A (N=86)	Arm B (N=88)	Both arms (N=174)
Age (years)			
Median (range)	53 (33-79)	57 (33-79)	55 (33-79)
ECOG PS (%)			
0-1	85 (99%)	88 (100%)	173 (99%)
HER2/neu overexpression (%)			
2+	11 (13%)	13 (15%)	24 (14%)
3+	75 (87%)	75 (85%)	150 (86%)
N° CT regimens (%)			
1 st line	63 (73%)	63 (72%)	126 (72%)
2 nd -3 rd line	23 (27%)	25 (28%)	48 (28%)
ER status (%)			
Positive	51 (59%)	52 (59%)	103 (59%)
Negative	35 (41%)	36 (41%)	71 (41%)
PR status (%)			
Positive	36 (42%)	35 (40%)	71 (41%)
Negative	48 (56%)	47 (53%)	95 (55%)
Unknown	2 (2%)	6 (7%)	8 (5%)
ER and/or PR positive (%)	53 (62%)	56 (64%)	109 (63%)
Neo/adjuvant chemotherapy (%)	38 (44%)	40 (45%)	78 (45%)
Adjuvant Anthracyclines (%)	34 (40%)	34 (39%)	68 (39%)
Radiotherapy (%)	48 (56%)	55 (63%)	103 (59%)
Palliative radiotherapy (%)	13 (15%)	11 (13%)	24 (14%)
Endocrine therapy (%)			
No	49 (57%)	43 (49%)	92 (53%)
Adjuvant	25 (29%)	11 (35%)	56 (32%)
Palliative	12 (14%)	14 (16%)	26 (15%)
Disease sites (%)			
Bone only	7 (8%)	13 (15%)	20 (11%)
Visceral only	32 (37%)	38 (43%)	70 (40%)
Visceral + bone	26 (30%)	18 (20%)	44 (25%)
Other	21 (24%)	19 (22%)	40 (23%)
Number of disease sites (%)			
<3	22 (26%)	27 (31%)	49 (28%)
≥3	64 (74%)	61 (69%)	125 (72%)
Advanced disease at diagnosis (%)	25 (29%)	29 (33%)	54 (31%)

Table 2 Treatment duration

	Median (range)
Arm A (N = 86)	7.92 (0.46 - 135.98)
Arm B (N = 88)	6.62 (0.56 - 71.28)
Total (N = 174)	7.33 (0.46 - 135.98)

Disclosure(s):

Manuela Rabaglio, MD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-01-26

Real-world treatment duration of subsequent therapy after palbociclib (PAL) in patients with hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (ABC) in Japan

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Background: PAL is a first-in-class cyclin-dependent kinase 4/6 inhibitor (CDK4/6i) for the treatment of HR+/HER2- ABC. Two CDK4/6is are currently available in Japan; PAL and abemaciclib (ABE). CDK4/6i+endocrine therapy (ET) has shown significant clinical benefits compared to ET alone in clinical trials. CDK4/6i combination therapy is strongly recommended as a first-line (1L) treatment in global and Japanese treatment guidelines. However, no optimal subsequent treatment has been established after discontinuing treatment with CDK4/6i+ET. Substantial data are required to determine whether the available treatment options remain effective after CDK4/6i treatment. Here, we report the treatment pattern of subsequent therapy after PAL in a real-world setting in Japan to provide insights into the optimal subsequent therapy.

Methods: This retrospective, observational study utilized a nationwide hospital-based medical claims database managed by Medical Data Vision (MDV). The MDV database, one of the largest medical databases in Japan, covers 26% of acute-care hospitals across Japan, including 226 cancer therapeutic facilities. We evaluated the data of patients who received PAL from September 2017 to June 2021 and subsequently received therapy. Any treatment for ABC initiated within 30 days was considered part of one regimen. The median time-to-treatment failure (TTF) of subsequent therapy was estimated using the Kaplan–Meier method.

Results: From the database, we identified 1,170 patients with HR+/HER2- ABC who received PAL, among which 398 (34%) received combination therapy as 1L treatment. The median age at PAL initiation was 64 years (range 53–72), and 13.0% of the patients were pre-/peri-menopausal. Among the 398 patients, 224 (56.3%) received therapy after PAL+ET. Endocrine-based therapy was commonly used as the first subsequent therapy (n=136; 60.7%), including CDK4/6i+ET (n=70; 31.2%), ET alone (n=39; 17.4%), and everolimus+ET (n=27; 12.1%). Among the 81 (36.2%) patients who received chemotherapy as the first subsequent therapy, 27 (12.1%) received bevacizumab+chemotherapy. The median TTF (95% confidence interval [CI])

of the first subsequent therapy was 7.5 months (6.5–8.4), and that of each subsequent regimen is listed in Table 1. The median TTF (95% CI) for patients received CDK4/6i+ET as first subsequent therapy after PAL+ET was the longest among the regimens, 10.9 months (6.5–15.6). Among the 70 patients, 36 changed only CDK4/6i type, 17 changed only ET type, and 12 changed both CDK4/6i and ET types. The median TTF (95% CI) was 20.1 months (6.5–not reached [NR]), 8.7 months (2.9–11.2), and 7.7 months (2.6–NR), respectively. No obvious trend was observed between the TTF of PAL+ET as a 1L treatment and the TTF of subsequent ABE after the PAL+ET treatment.

Conclusion: More than half the patients received endocrine-based therapy after PAL+ET as a 1L treatment, and the observed treatment duration was comparable to the results of clinical trials reported to date, even after PAL treatment. ET+targeted therapy and chemotherapy represent acceptable treatment options after PAL+ET. One-third of patients received CDK4/6i+ET after PAL+ET in Japanese clinical practice; however, further investigation is warranted to confirm that this treatment strategy is effective.

Table 1. Median TTF of each subsequent therapy after PAL+ET

First subsequent therapy	Median TTF (95% CI), months
ET alone	4.4 (2.8–13.7)
CDK4/6i+ET	10.9 (6.5–15.6)
changed only CDK4/6i type	20.1 (6.5–NR)
changed only ET type	8.7 (2.9–11.2)
changed both CDK4/6i and ET types	7.7 (2.6–NR)
Everolimus+ET	6.1 (5.1–7.2)
Chemotherapy alone	7.2 (4.9–8.5)
Chemotherapy plus bevacizumab	9.4 (6.1–12.1)
Chemotherapy plus ET	8.4 (5.6–NR)

Disclosure(s):

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P4-01-27

Prognosis and treatment landscape of HER2-positive metastatic breast cancer (MBC) before the availability of tucatinib and trastuzumab-deruxtecan: Results from the Austrian AGMT_MBC-Registry

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Background: New anti-HER2 drugs such as tucatinib and trastuzumab deruxtecan (T-DXd) have shown to improve survival of HER2+ MBC in clinical phase III trials. To allow a future confirmation of this survival advantage in real world, we evaluated the prognosis of HER2+ MBC patients before the availability of tucatinib and T-DXd in Austria. Furthermore, we analyzed the treatment landscape and the drop-out rate between subsequent lines of therapy as documented in the MBC-Registry of the Austrian Study Group of Medical Tumor Therapy (AGMT).

Patients and methods: The AGMT-MBC-Registry is a multicenter nationwide ongoing retrospective and prospective registry for MBC patients in Austria. In this analysis, patients with known HER2 status, available survival data, at least one treatment line and diagnosis of metastatic disease after 01/04/2013 (pertuzumab available) were included. Follow-up was censored at Dec 31, 2020, when tucatinib und T-DXd became available.

Results: As of 04/05/2022, 2,235 patients have been included in the registry. Out of 2,000 evaluable patients, 362 (18.1%) were HER2+, of which 171 (47.2%) fulfilled the inclusion criteria. Out of them 69.0% were hormone-receptor positive. In patients with metachronous metastatic disease (53.2%), 61.5% had received trastuzumab-based treatment for early breast cancer. Median overall survival (OS) for all patients was 50.1 months (95%CI 40.7-73.0), and 66.1 months (95%CI 50.1-NA) for those who received a pertuzumab combination as first-line treatment. The drop-out rate from 1st- to 5th-line was 26.9%, 24.4%, 28.3% and 36.7%, respectively. This yields an estimated percentage of patients that received at least 3, 4, and 5 treatment lines for advanced disease of 55.2%, 39.6% and 25.1%, respectively. In first line, 50.9% received trastuzumab plus pertuzumab and 11.1% T- DM1. In second line, 38.9% were treated with T-DM1 and 35.6% with trastuzumab-based chemotherapy or endocrine therapy. In third line, 11.3%, 17.0% and 49.1% received T-DM1, lapatinib-based and trastuzumab-based therapy, respectively. Outcomes according to treatment line are shown in Table 1.

Table 1: Outcome according to treatment line

Conclusion: Median overall survival of HER2+ MBC in Austria who received a pertuzumab combination treatment is comparable to the results reported in the registration CLEOPATRA trial. In this analysis, only ~40% of patients are estimated to receive more than three treatment lines and treatment benefit diminished from line to line. This underlines the importance of investigating and ultimately using the most effective compounds in early treatment lines in order to allow more patients to benefit from these life prolonging drugs.

Table 1: Outcome according to treatment line

Table 1: Outcome according to treatment line

Line	Median PFS* (95%-CI)	ORR*	CBR*
1 st (n=171)	14.60 (10.90-18.80)	50%	71%
2 nd (n=90)	7.70 (5.70-12.40)	31%	62%
3 rd (n=53)	5.80 (4.90-10.10)	22%	49%
4 th (n=30)	4.00 (3.00-7.70)	23%	43%
5 th (n=16)	3.60 (2.70-5.90)	0%	15%
≥6 th (n=26)	3.00 (1.80-4.90)	6%	25%

* calculated in patients with available data

PFS=progression-free survival; ORR=overall response rate; CBR=clinical benefit rate

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PALBOSPAIN: OBSERVATIONAL ANALYSIS OF FIRST-LINE THERAPY WITH PALBOCICLIB IN PATIENTS WITH HR+/HER2- METASTATIC BREAST CANCER (MBC) IN REAL-LIFE CONDITIONS

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INTRODUCTION AND OBJECTIVES

Palbociclib associated with hormone therapy (HT) has shown significant benefit in progression-free survival (PFS) and response rate versus HT alone in patients with HR+, HER2- MBC. The PALBOSPAIN study evaluates the efficacy and safety of palbociclib treatment under real-life conditions. The main objective of the study was to assess PFS, and secondary objectives were overall survival (OS), response rate, time to next line of treatment, percentage of dose reduction and safety.

MATERIAL AND METHODS

This is an observational, ambispective, multicenter, nation-wide study. Patients diagnosed with

HR+/HER2- MBC who had started first-line treatment with palbociclib between November 2017 and November 2019 were included. Patients treated within a clinical trial were excluded, as were those who had received any previous systemic treatment for advanced disease.

RESULTS

762 patients from 35 centers were included. 79% (n=600) were postmenopausal, 54.9% (n=418) had visceral disease, and 30.6% (n=233) had de-novo metastatic disease. Palbociclib was combined with an aromatase inhibitor in 69.6% of patients and fulvestrant in 30.2%. Four groups were established to assess efficacy (table 1): overall population; patients with de-novo metastatic disease (cohort A); patients relapsing >12 months after the end of adjuvant hormonal therapy (cohort B); and patients relapsing within 12 months after the end of adjuvant hormonal therapy (cohort C). Median PFS was 24 months (CI 95%; 25-27) overall and 28 (IC 95%; 23-39), 29 (IC 95% ;25-35) and 14 months (IC 95% ;11-17) for cohorts a, B and C, respectively. Median overall survival was 42 months (40-NA).

The most common side effects were neutropenia (71.3%, grade 3-4 in 52.5%, no episodes of febrile neutropenia), fatigue (38.6%), leucopenia (29.8%), anemia (28.9%), articular pain (19%), and thrombocytopenia (2,2%). 49% (n=385) of patients required dose reduction of palbociclib (one level in 27.6% and two levels in 21.4%).

CONCLUSION

In the first two years after its approval in Spain, palbociclib in first line of HR+/HER2- MBC in real-life conditions yielded PFS and safety results comparable to those of PALOMA 2 and PALOMA 3 clinical trials. OS results were poorer, although the population included in this retrospective study is heterogeneous and median survival values have not been reached in some subgroups.

Table 1. Efficacy results of palbociclib in real world

	Overall population (n=762)	Cohort A (n=233)	Cohort B (n=220)	Cohort C (n= 309)
Response (%)				
Complete remission	(6.5)	(5.5)	(9.6)	(4.5)
Partial remission	(37.1)	(52.5)	(35.6)	(27.1)
Stable disease	(37.5)	(32.2)	(42)	(35.6)
Progression	(13.8)	(5.9)	(8.7)	(25.9)
Not evaluated	(5)	(3.8)	(4.1)	(6.9)
PFS months (CI 95%)	24 (21-27)	28 (23-39)	29 (25-35)	14 (11-17)
OS months (CI 95%)	42 (40-NA)			

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P4-01-29

Ribociclib plus letrozole alters the immune subset composition in older (≥70 yrs.) patients with HR+/HER2- metastatic breast cancer

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Background The combination of CDK4/6 inhibitors and endocrine therapy is the current standard first-line therapy for patients with HR+/HER2- metastatic breast cancer (mBC). Preliminary data suggest that CDK4/6 inhibitors not only induce tumor response by blocking CDK-dependent cell growth but that they can also alter the host immune function and stimulate tumor cell-directed immunity. However, clinical data are scarce, and no data exist about the impact of age and frailty, which are known to impact host immunity (immunosenescence). **Materials and methods** This prospective ongoing study is evaluating the efficacy and toxicity of the CDK4/6 inhibitor ribociclib and letrozole in older (≥ 70 years) patients with HR+/HER2- mBC (RIBOB, NCT03956654). In the associated blood biomarker sub-study, we investigate the impact of ribociclib and letrozole on the immune subset composition. Immune cell subsets were analyzed using flowcytometry (BD FACSVerserTM) of peripheral blood mononuclear cells isolated at baseline (before ribociclib administration) and after three months of ribociclib treatment. In total, six multicolor flow cytometry staining panels were set up to investigate the changes in the immune cell subsets (CD4+ T-cell subsets, CD8+ T-cell subsets, general immune cell subsets, T-regulatory cell subsets, T-cell activation status subsets, and myeloid-derived suppressor cells subsets). Frailty status was assessed at baseline using the G8 screening tool (range score: 0-17) as a proxy. The paired t-test and matched-pairs Wilcoxon signed-rank test are used to evaluate changes in immune subset composition between baseline and after three months. The unpaired t-test and Mann-Whitney U test are used to evaluate differences in immune subset composition between frail and fit patients. **Results** Immune cell subset distribution and evolution were available for 15 older patients (median age: 77 yrs.; IQR 74-83), 4 considered fit (G8-score >14), and 11 frail (G8-score ≤ 14). Firstly, we analyzed the difference in immune subset composition between baseline and three months for the whole cohort. There was a significant increase of naïve T-regulatory cells ($p=0.0012$) and a significant increase in CD8+ T-cell activation indicated by an upregulation of HLA-DR+ ($p=0.0055$) and CD38+ ($p=0.0203$). Secondly, the difference in immune subset composition between fit and frail persons was assessed showing a lower activation status of CD4+ and CD8+ T-cell subsets in frail persons at baseline, as assessed by several activation markers: CD4+PD1+ ($p=0.0051$), CD4+PD1+CD69+ ($p=0.0013$), CD8+PD1+ ($p=0.0073$), and CD8+PD1+CD69+ ($p=0.0339$). These significant differences between fit and frail disappeared after three months, largely because of increased T-cell activation in the frail subset. **Conclusion** Ribociclib plus letrozole treatment for three months results in an upregulation of the T-regulatory cells' naïve subset, suggesting an expansion of the T-cell repertoire, which is compatible with immune cell activation. Furthermore, the activation status of the CD8+ T-cells was upregulated. These observations confirm recent findings reported by Scirocchi F. et al. (Lancet, 2022). In addition, frail older patients show a lower baseline T-cell activation status compared to fit older patients but seem to have increased T-cell activation after treatment exposure. In the future, correlations with treatment response will be evaluated when follow-up data matures. Our data encourage

the further assessment of immune cell modulation in combination with CDK4/6 inhibitors in the treatment of patients with metastatic breast cancer.

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-01-30

Real-world treatment patterns and survival among adults with metastatic breast cancer with BRCA1/2 mutations

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Background: Limited information is available about real-world treatment patterns and survival among patients with metastatic breast cancer (mBC) with BRCA1/2 mutations. BRCA1/2 mutations, which are involved in the repair of DNA double-strand breaks, are rare. Since 2018, PARP inhibitors (olaparib and talazoparib) have been approved for the treatment of patients with germline BRCA-mutated HER2-negative locally advanced and/or mBC.

Methods: This retrospective chart review study included adults diagnosed with mBC with ≥ 1 oncogenic somatic BRCA1/2 mutation detected by tumor comprehensive genomic profiling who began a line of therapy on or after July 1, 2014, at 3 oncology centers in the American Association for Cancer Research (AACR) Project Genomics Evidence Neoplasia Information Exchange (GENIE) consortium. The index date was the first initiation of a new therapy for mBC in this period (which could be first-line [1L] or subsequent line of therapy). Data on all available lines of therapy post-index were collected. Treatments received in different lines of therapy for mBC and overall survival (OS) were described separately for patients with HR-positive/HER2-negative (HR+/HER2-) mBC, triple negative mBC (TNBC), and HER2-positive (HER2+) mBC. OS from the start of each line of therapy was assessed using Kaplan-Meier analysis.

Results: A total of 48 women with mBC met the inclusion criteria. The mean age at index was 58 years; 73% of women were White. Common sites of metastases included lymph nodes (56%), bone (52%), and lungs (31%). Somatic BRCA1 mutation was detected in 48% and BRCA2 mutation was detected in 54% of women. Assessment of germline BRCA mutations was conducted in 25 (52%) women; 2 (8%) of assessed women tested positive for germline BRCA mutations. 29 (60%) of women had HR+/HER2- mBC, 9 (19%) had TNBC, 9 (19%) had HER2+ mBC, and 1 woman had unknown HER2 status. Treatments received in different lines of therapy for mBC and OS from start of each line of therapy by HR and HER2 status are reported in Table 1. Common treatments for women with HR+/HER2- mBC included endocrine-based therapy, and chemotherapy. Women with TNBC were most often treated with chemotherapy. Women with HER2+ mBC most often received endocrine-based therapy in 1L; chemotherapy or HER2-targeted combination therapy in second-line (2L); and chemotherapy or HER2-targeted monotherapy in third-line (3L). Median OS from the start of 1L therapy was 37.5

months among women with HR+/HER2- disease; 20.0 months for women with TNBC; and 51.7 months for women with HER2+ disease.

Conclusions: These findings provide real-world insights about treatment patterns and survival among women with mBC and BRCA1/2 mutations. Further studies with larger sample sizes are needed to confirm these findings.

Table 1. Treatment patterns and survival by line of therapy, HR, and HER2 status among patients with BRCA1/2 mutated mBC

	HR+/HER2- mBC			TNBC			HER2+ mBC		
	1L	2L	3L	1L	2L	3L	1L	2L	3L
Treatment category, n (%)	N = 21	N = 22	N = 17	N = 8	N = 7	N = 5	N = 5	N = 8	N = 7
Chemotherapy	9 (43%)	11 (50%)	6 (35%)	7 (88%)	5 (71%)	4 (80%)	1 (20%)	4 (50%)	3 (43%)
Endocrine-based therapy	11 (52%)	8 (36%)	5 (29%)	0	1 (14%)	0 (0%)	3 (60%)	1 (13%)	1 (14%)
HER2-targeted therapy, combination therapy	0	0	0	0	0	0	1 (20.0)	3 (38%)	0
HER2-targeted therapy, monotherapy	0	0	0	0	0	0	0	0	3 (43%)
Immunotherapy, combination therapy	0	0	2 (12%)	1 (13%)	0	0	0	0	0
Immunotherapy, monotherapy	0	0	1 (6%)	0	0	0	0	0	0
PARP inhibitor	1 (5%)	1 (5%)	2 (12%)	0	1 (14%)	1 (20%)	0	0	0
Other	0 (0.0)	2 (9%)	1 (6%)	0	0	0	0	0	0
Overall survival (months)									
Median	37.5	21.2	22.0	20.0	11.3	4.8	51.7	41.0	34.7
95% CI of median	(15.6, 58.6)	(10.3, 33.1)	(4.5, 44.4)	(13.5, NR)	(5.2, NR)	(3.1, NR)	(21.6, NR)	(3.3, NR)	(19.5, NR)
Number of patients with event	15	16	13	5	5	5	3	6	5

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-01-31

High Incidence of Palbociclib Related Neutropenia in Asian Patients Associated with Genetic Polymorphisms

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CDK4/6 inhibitors (CDK4/6i) is well established as the current standard of care for hormone positive (HR(+)) metastatic breast cancer (mBC), in combination with endocrine therapy. CDK4/6i extend a chemotherapy-free, progression free survival (PFS) that preserves quality of life in patients. The most common side effect of CDK4/6i is myelosuppression, with neutropenia the most prevalent adverse effect, especially for palbociclib and ribociclib. In PALOMA-2 and MONALEESA-2, where neutropenia was prevalent (any grade neutropenia 79.5%, grade 3/4 neutropenia 66.5% in PALOMA-2, and any grade neutropenia: 74.3%, grade 3/4 55.3% in MONALEESA-2), although febrile neutropenia seldom occurred (1.8%). Several studies have proposed different genetic factors predisposing to CDK4/6 inhibitor induced neutropenia, including Duffy antigen polymorphisms, ABCB1 and ERCC1 polymorphisms (ABCB1_rs1128503, ABCB1_rs1045642, ERCC1_rs11615, ERCC1_rs3212986), CDK6 polymorphisms, and others. Subgroup studies from the PALOMA trials have suggested that Asian patients receiving palbociclib have higher rates of neutropenia, although the exact

explanation is unknown.

We conducted a retrospective analysis of 102 Taiwanese patients who received palbociclib for HR(+) mBC at the Taipei Veterans General Hospital for the clinical features, incidence and time course of neutropenia were analyzed. Significant neutropenia incidence was observed (> 95% of all grade neutropenia, 74.5% grade 3/4 neutropenia). In addition, in our clinical cohort, one of the patients was a long term peritoneal dialysis patient newly diagnosed of HR(+) mBC and started on Palbociclib, initially 125mg, later decreased dosage to 100mg after neutropenia occurrence. By Liquid chromatography–mass spectrometry (LC–MS), we quantified the levels of palbociclib in her serum and peritoneal fluid at various time points, while on different dosage use. To our knowledge, this is the first pharmacokinetics analysis on a peritoneal dialysis patient receiving CDK4/6i. To investigate a possible genetic association for the high prevalence of neutropenia, we queried the Taiwan biobank, a nationwide biospecimen repository with 129,586 healthy individual genome wide DNA sequencing data deposited. We investigated the prevalence of the 4 SNPs previously reported to be related to neutropenia in the PALOMA studies. By comparing the Taiwan biobank data to SNP databases from different ethnicities, we observed interesting findings on ethnicity differences of SNP distribution and higher prevalence of neutropenia SNPs. Collectively, in this study we report real world data, biobank genome wide analysis, and a novel report of pharmacokinetic study in a peritoneal dialysis patient, providing novel insights into the real world use of palbociclib and CDKi.

Characteristics of the clinical cohort treated with palbociclib at TVGH

	number	percentage
Patients, n	102	
Median Age, y	56.9	
Female, %	100	
premenopausal	22	21.5%
Median BMI	23.72	
Median height (cm)	155.8	
Median weight (kg)	57.5	
Menopausal	10	9.8%
Lung metastasis	69	67.6%
Liver metastasis	50	49.2%
No. of metastasis sites	2	
Median PFS	509 (28-1317)	
Median OS	Not reached	
Death events	32	31.37%
1L	53	51.96%
2L	15	14.7%
≥3L	34	33.3%
Response		
CR	0	
PR	37	36.27%
SD	55	53.92%
PD	10	9.8%
In 1 st line patients		
Median follow up time	737 days (24.5 months)	
Median PFS	Not reached	
Median OS	Not reached	
Progression/death events	14	13.72%
Death events	9	8.82%
In 2 nd line patients		
Median follow up time	870 days (29 months)	
Median PFS	318 days (10.6 months)	
Median OS	Not reached	
Progression/death events	13	86.67%
Death events	5	33.3%
All grade neutropenia	99	97.1%
Grade 3/4 neutropenia	76	74.5%

Disclosure(s):

Kuan-Jung Huang, n/a: No financial relationships to disclose

Ting-Hao Kuo, n/a: No financial relationships to disclose

Ta-Chung Chao, n/a: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

P4-01-32

BAT8008, a novel Trop-2 ADC with strong bystander effect, for the treatment of Trop-2 positive cancer

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Trophoblast cell surface antigen 2 (Trop-2) is overexpressed on many epithelial carcinomas, yet is expressed at much lower level on normal tissue. Elevated expression of TROP-2 is often associated with tumor invasion/aggression, progression, and metastasis. Efficacy of anti-TROP2 ADC have been demonstrated in clinical trials for both TNBC (triple negative breast cancer) and HR+/HER2- breast cancer. We have developed a novel Trop-2 ADC with strong bystander killing effect, BAT8008, which consists of an enzymatically cleavable linker and a topoisomerase I inhibitor as the payload, with DAR of 6. BAT8008 demonstrated potent in vitro cell growth inhibitory activity to Trop2-positive cells with IC50 values of < 1 nM. In an in vitro bystander killing assay, proliferation of Trop-2-negative cells was potently inhibited by

addition/transfer of culture medium of BAT8008-treated Trop-2-positive cells, but not that of BAT8008-treated Trop-2-negative cells, indicating the bystander killing effect of the released payload in the culture medium. Less than 0.1% of the payload was released from BAT8008 when incubated with human or monkey plasma for 7 days in 37°C, suggesting the stability of BAT8008 in blood circulation. Single dose of BAT8008 at 1 and 2.5 mg/kg could inhibit 73% and 81% tumor growth in the Trop-2-positive MDA-MB-468 and MX-1 xenograft mice model, respectively. BAT8008 also demonstrated superior tumor inhibition activity than a modified ADC using Daiichi's ADC technology or Trodelvy in a pancreatic BxPC-3 xenograft mice model. In addition, BAT8008 showed favorable pharmacokinetic and safety profiles in cynomolgus monkeys with the highest non-severely toxic dose (HNSTD) of at least 25 mg/kg when dosed once every two weeks for 3 times. Together these results indicate that BAT8008 could potentially provide a therapeutic benefit to treat TROP2-positive breast cancers in clinical trial.

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12/8/2022

7:00 AM - 8:15 AM

P4-01-34

Benefits Provided by Antibody Drug Conjugates in Overall Survival Outweighs those in Progression-free Survival for Metastatic Breast Cancer: A Class Effect

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Background:

In metastatic breast cancer (MBC), the benefits of progression-free survival (PFS) and overall survival (OS) is not always proportional. This dissociation is related to the multiple other treatment options such as chemotherapy after disease progression and these treatments would contribute to the long post-progression survival. A constant improvement of PFS that translates into OS has been reported in anti-HER2 antibody containing treatments. In the era of antibody drug conjugates (ADC), we aim to examine the relationship between the increments of PFS and OS in MBC.

Methods: We have used “metastatic breast cancer” and “antibody drug conjugate” to search for clinical trials that report both PFS and OS. Hazard ratios (HR) and median survival were analyzed. Increments in PFS (delta PFS) and increments in OS (delta OS) were compared between studies.

Results: A total of 5 trials were identified and summarized in table 1. The target of ADC is HER2 (N=4) or Trop2 (N=1). In DESTINY-Breast 03 trial, the control arm is another ADC (T-DM1). The control arms in all the other 4 trials are chemotherapy. The HR of PFS ranged from 0.28 to 0.65 and the HR of OS ranged from 0.48 to 0.68. The HR of PFS is smaller than HR of OS in all of the 5 trials. The median OS was not reached in 1 of the trials (DB-03) and was thus removed from the analysis for delta PFS and delta OS. In the comparison of delta PFS, the increments of median PFS fell between 2.9 and 4.8 months. The increments of median OS were between 5.4 and 6.6 months. All the delta OS are larger than the delta PFS in the four trials.**Conclusion:** Regardless of the antibody drug targets, ADC provides consistent improvements in median OS that surpasses the improvements in median PFS in metastatic breast cancer. The mechanism warrants further investigation.

Table 1

Table 1

Trial	EMILIA		DESTINY		DESTINY	
	HER2	Th3resa	Breast-03	ASCENT	Breast-04	
Antibody Target	HER2	HER2	HER2	Trop 2	HER2	
Year of Publication	2012	2015	2021	2021	2022	
HR PFS	0.65	0.53	0.28	0.41	0.5	
HR OS	0.68	0.68	0.55	0.48	0.64	
Median PFS Control (M)	6.4	3.3	6.8	1.7	5.1	
Median PFS Exper. (M)	9.6	6.2	NR	5.6	9.9	
Delta PFS	3.2	2.9		3.9	4.8	
Median OS Control (M)	25.1	15.8	NR	6.7	16.8	
Median OS Exper. (M)	30.9	22.7	NR	12.1	23.4	
Delta OS	5.8	6.9		5.4	6.6	

Disclosure(s):

I-Chun Chen, M.D., Ph.D.: No financial relationships to disclose

Ching-Hung Lin, M.D., Ph.D.: No financial relationships to disclose

Yen-Shen Lu, MD, PhD: AstraZeneca: Clinical Trial, Speaker (Ongoing); Daichii Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Speaker (Ongoing); Eisai: Speaker (Ongoing); Eli Lilly: Speaker (Ongoing); Merck Sharp & Dohme: Contracted Research (Ongoing), Speaker (Ongoing); Novartis: Clinical Trial Study Fee (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Grant for clinical study for ESR1 mutation detected by cell free DNA; Advisory board consultation fee; Speaker fee (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Speaker (Ongoing); Roche: Contracted Research (Ongoing), Speaker (Ongoing)

12/8/2022

7:00 AM - 8:15 AM

P4-01-35

A Phase 1 Study of the Oral CDK7 Inhibitor XL102 as a Single Agent and in Combination Therapy in Patients With Advanced Solid Tumors (QUARTZ-101): Initial Results From the Dose-Escalation Stage

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Background: Cyclin-dependent kinase 7 (CDK7) plays a significant role in the cell cycle via activation of CDKs 1, 2, 4, and 6, and regulates transcription via phosphorylation of RNA polymerase II and the estrogen receptor. CDK7 overexpression has been reported in several tumor types, including hormone receptor-positive breast cancer (HR+ BC), triple-negative BC (TNBC), small-cell lung cancer, and epithelial ovarian cancer (EOC). In all major BC subtypes, CDK7 overexpression is associated with poor prognosis. XL102 is a potent, orally bioavailable, highly selective covalent CDK7 inhibitor. QUARTZ-101 is a first-in-human, open-label trial (NCT04726332) evaluating the safety, tolerability, and optimal dose of XL102 as a single agent and in combination regimens in patients with solid tumors, with expansion in subsequent tumor cohorts of advanced HR+ BC, TNBC, EOC, and metastatic castration-resistant prostate cancer

(mCRPC). Presented here are initial results from the dose-escalation stage for single-agent XL102 (cohort A). Methods: In the single-agent dose-escalation stage, patients received XL102 orally at multiple dose levels (DLs) using a modified interval 3+3 design: once daily at 20 mg (DL A1), 40 mg (DL A2), 80 mg (DL A3), and 120 mg (DL A4); and twice daily at 40 mg (DL A5). Eligible patients had confirmed inoperable, locally advanced, metastatic, or recurrent solid tumors and ECOG performance status (PS) of 0 or 1; any CNS disease must have been adequately treated and stable for ≥ 4 weeks. Patients with previous exposure to XL102 or other selective CDK7 inhibitors were excluded, as were patients with uncontrolled, significant intercurrent or recent illness. Prior use of CDK4/6 inhibitors was allowed. The primary objective of dose escalation was to determine the maximum tolerated dose (MTD) and/or recommended dose (RD) of XL102; secondary objectives included safety and tolerability, pharmacokinetics (PK), and drug-drug interactions. Results: At data cutoff of May 13, 2022, twenty patients with various advanced solid tumors (100% stage IV) were enrolled in dose-escalation stage cohort A and treated with single-agent XL102 (DL A1 n=3; A2 n=3; A3 n=7; A4 n=4; A5 n=3). Median age was 67 (range 43–84) years, 85% were female, and 75% had an ECOG PS of 1. Six patients remained on XL102 including 2 treated for >6 months with stable disease, both had received prior CDK4/6 inhibitors (HR+BC and liposarcoma). There were no dose-limiting toxicities at any DL, and MTD/RD has not been determined. Treatment-emergent adverse events (TEAEs) occurred in 95% of patients, with 4 (20%) grade 3 and 0 grade 4 TEAEs; there were no grade 5 treatment-related AEs. Treatment discontinuations were mostly due to radiographic progression (n=8); longest treatment duration was 6.7+ months and ongoing. XL102 demonstrated rapid absorption with a T_{max} of approximately 1–2 h and elimination half-life of 5–8 h. Target occupancy was exposure-dependent and prolonged relative to XL102 PK, consistent with covalent binding to CDK7. Conclusions: Single-agent XL102 was well tolerated at the DLs tested. Updated data, as well as PK results, will be presented. Expansion cohorts in HR+BC, TNBC, EOC, and mCRPC will be initiated once a recommended dose for the expansion-cohort stage is determined.

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-01-36

Real World Data for Trastuzumab Deruxtecan in HER2-Positive Metastatic Breast Cancer Patients with Brain Metastases.

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Background: Trastuzumab deruxtecan (T-DXd) improves outcomes in HER2-positive metastatic breast cancer (MBC) patients, including patients with previously treated stable brain metastases (BMs). Our objective was to examine the characteristics of HER2-positive MBC patients with BMs prior to T-DXd use. Methods: We performed a retrospective cross-sectional study of T-DXd prior authorization (PA) approvals by OncoHealth for HER2-positive MBC patients between 1/17/2020 – 6/21/2022. Using medical records and utilization management data, we assessed the characteristics of PA approvals for 145 patients requesting T-DXd in Stage 4, HER2-positive, female MBC with BMs. Results: Brain metastases were identified in 41/145 patients with HER2-positive MBC prior to T-DXd authorization. Among the 41 patients The mean age was within the range of 50-59 years, 72% were hormone receptor-positive, and all were HER2 positive. 19/41(46%) had symptomatic BMs, 5/41(12%) had asymptomatic BMs. Prior local therapies for the BMs included craniotomy in 19.5% and brain radiotherapy in 87.8% prior to T-DXd. The median number of prior MBC therapies was 2 (range: 0-8) and 73% (30/41) did not receive tucatinib-based therapy prior to T-DXd. Tucatinib-based therapy was the most

common subsequent line of therapy among T-DXd patients with further therapy (5/8). For available data (13 metastatic patients), 8 metastatic patients received tucatinib for an average of 149 days before receiving T-DXd for an average of 238 days, compared to 5 metastatic patients who received T-DXd for an average of 295 days before receiving tucatinib for 240 days, implying improved disease management in the T-DXd-to-tucatinib sequence. Conclusions: In the real world, patients with symptomatic, progressing BMs are more likely to receive T-DXd prior to tucatinib or potential tucatinib-based therapy, with longer duration of stability and treatment. Appropriate sequencing of available treatments with activity on brain metastases such as T-DXd and tucatinib-based therapy needs to be further studied.

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7:00 AM - 8:15 AM

P4-01-37

Discontinuation of HER2+ targeted therapy among cancer survivors with metastatic HER2+ breast cancer: A case report

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Abstract Title: Discontinuation of HER2+ targeted therapy among cancer survivors with metastatic HER2+ breast cancer: A case report

Background: Anti-HER2 directed therapy (aHER2tx) has significantly improved survival outcomes in patients with HER2-positive metastatic breast cancer (HMBC). Current United States (US) and European oncology practice guidelines recommend continuing aHER2tx until intolerable side effects or disease progression. It is estimated that 10-15% of treated patients (pts) may achieve prolonged complete remission (CR). Currently, the optimal duration of aHER2tx in patients achieving a CR is unknown. A PubMed literature search identified 7 case reports outside of the US that describe pts who remain in CR after discontinuation of aHER2tx. To our knowledge, this is the first analysis of similar cases in the US.

Method: We identified pts with a diagnosis of HMBC who discontinued aHER2tx between January 1, 2010, to June 30, 2021, at a large integrated healthcare system in the US. Pts were included if they had discontinued aHER2tx for at least one year. Data collection included demographics, histology, confirmed sites of metastatic disease (mets), local and systemic treatment (tx) before and after aHER2tx discontinuation, documented radiographic response, and reason to discontinue aHER2tx. Data collection ended on June 30, 2022.

Results: Our case report identified 15 pts (mean age at diagnosis 53.0 ± 13.2) based on inclusion criteria. Baseline demographics and characteristics are listed in Table 1. Common clinical characteristics of the cohort include mean age at mets diagnosis is 56 years, postmenopausal status (67%), invasive ductal carcinoma (87%), ER-negative (60%), HER2-positive 3+ by IHC (93%), de-novo mets (60%), multiple sites (93%) and multi-organ mets (87%).

Among the cohort, 6 pts (40%) received prior adjuvant therapy, then later recurred, and of these only one had received HER2-based adjuvant tx. In all pts, first line therapy for mets included chemotherapy and aHER2tx, except one pt received endocrine therapy (ET) and aHER2tx. A CR was achieved in all but one pt (93%) with one line of aHER2tx consisting of trastuzumab (H) ± pertuzumab (P). One pt (7%) received local tx to all metastatic sites. In 13 pts, the median time to first radiologic complete response (RCR) after first line therapy for mets was 4 months (Interquartile (IQR) 3-15). Two cases were not included as we were unable to determine time to initial response after tx. All pts had confirmed RCR at the time of aHER2tx discontinuation. Median duration of aHER2tx was 8.3 years (IQR 4.8-9.5), including a median of 6.3 years (IQR 2.8-8.8) on maintenance aHER2tx. Twelve pts (80%) were off all therapy, and 3 pts (20%) continued ET for ER+ disease at the last follow-up (f/u). Patient preference (47%) was the most common reason for stopping aHER2tx. The median disease-free survival off aHER2tx was 4.8 years (IQR 3.1-6.2) and all pts were alive without evidence of disease at last f/u.

Conclusion: A subset of HMBC pts successfully discontinued aHER2tx without experiencing recurrence with a median of 4.8 years off therapy in a US cohort. In this case report, common clinical features like strong HER2 overexpression, no prior aHER2tx, and achieving RCR while on first line aHER2tx with H ± P are potential indicators for prolonged CR after discontinuing aHER2tx. Future studies with a comparator group are needed to fully understand the pt population who may safely stop aHER2tx after a CR.

Table 1: Baseline Demographics and Clinical Characteristics

Table 1: Baseline Demographics and Clinical Characteristics		n = 15
Age at diagnosis in years - mean ± SD		53.0 ± 13.2
Age at diagnosis of mets in years - mean ± SD		56.2 ± 11.9
Female sex - n (%)		15 (100)
Menopausal status at mets		
Premenopausal - n (%)		4 (26)
Postmenopausal - n (%)		10 (67)
Unknown - n (%)		1 (7)
Histology		
Invasive ductal carcinoma - n (%)		13 (87)
Mammary carcinoma - n (%)		2 (13)
ER-receptor status		
Negative - n (%)		9 (60)
Positive - n (%)		6 (40)
HER2-overexpression		
3+ by IHC - n (%)		14 (93)
2+ confirmed by FISH - n (%)		1 (7)
Metastatic diagnosis		
De-novo - n (%)		9 (60)
Recurrence - n (%)		6 (40)
via Biopsy - n (%)		10 (67)
via Radiographic changes - n (%)		5 (33)
Metastasis		
Number of sites		
Single site- n (%)		1 (7)
Multiple sites - n (%)		14 (93)
Location		
Bone only - n (%)		2 (13)
Multi-organ - n (%)		13 (87)
Treatment		
Prior HER2 tx		
Yes - adjuvant tx - n (%)		1 (7)
No - adjuvant or mets tx - n (%)		14 (93)
Lines of HER2 tx for mets		
1 - n (%)		14 (93)
2 - n (%)		0
3 - n (%)		1 (7)
HER2 tx for mets		
trastuzumab - n (%)		10 (67)
trastuzumab + pertuzumab - n (%)		4 (26)
trastuzumab + lapatinib followed by TDM1 - n (%)		1 (7)
Local tx - all metastatic sites		1 (7)
Reason to discontinue HER2 tx		
Patient Preference		7 (46)
MD Advice		6 (40)
Patient Preference & MD Advice		1 (7)
Side Effects		1 (7)
mets = metastatic disease; ER = estrogen receptor; IHC = immunohistochemistry test; tx = treatment FISH = Fluorescence in Situ Hybridization test; HER2 = human epidermal growth factor receptor 2		

Disclosure(s):

Lai Fong Hui, M.D.: No financial relationships to disclose

Nina N. Shah, PharmD, BCOP: No financial relationships to disclose

Rita L. Hui, PharmD, MS: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-01-38

A single arm phase II trial of Palbociclib in combination with Tamoxifen as first line therapy for metastatic hormone receptor positive breast cancer

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Background: Palbociclib is a CDK4/6 inhibitor used to treat metastatic hormone receptor-positive (HR+) breast cancer (MBC) in combination with endocrine therapy. Tamoxifen is an effective treatment for HR+ MBC, with different toxicity profile compared with aromatase inhibitors (AI) and fulvestrant. Preclinical data demonstrated synergy for the combination of tamoxifen and palbociclib, being effective in a model of acquired tamoxifen resistance.

Methods: We conducted a non-randomized, open-label, single-arm, multicenter, phase II trial of palbociclib in combination with tamoxifen in patients with HR+/HER2 - advanced BC, with no prior therapy for MBC. Ovarian suppression was recommended for pre-menopausal women.

Primary objective was progression free survival, PFS. **Secondary objectives:** objective response rate, ORR (CR or PR) based on RECIST 1.1 or MDA Criteria (for patients with bone only disease); safety and tolerability (using CTCAE v4); clinical benefit rate, CBR (CR, PR or SD lasting min 24 weeks); 2-year overall survival. **Correlative objectives:** proteomic analysis of plasma exosomes to identify mechanisms of primary and secondary resistance to tamoxifen/palbociclib.

Results: Between 6/30/2016 and 7/02/2019, we enrolled 49 patients (47 evaluable): 23 pts with de-novo metastatic disease and 24 pts with recurrent BC (12 pts were on adjuvant treatment with AI at time of recurrence and 12 pts on surveillance). As of 6/30/2022 data cut-off, 2 pts were still on treatment. This is an updated analysis with median follow-up time of 24 months (range 8-51). Median age was 60 (range 39-82). The median PFS was 19.8 months with 95% CI (8-41) for pts with de-novo MBC and 7 months (2-12) for pts with recurrent BC. The ORR was 30% overall, 39% for pts with de novo MBC, 21% for pts with recurrent BC. CBR was 64% overall, 77% for pts with de novo MBC and 50% for pts with recurrent BC. CBR was 65% for white pts and 55% for AA pts. Best response per RECIST1.1: 14 pts (34%) had PR, 18 pts (44%) had SD, 9 pts (22%) had PD. All 6 pts with bone only disease had SD. The most common drug related grade ≥ 3 AE was neutropenia (51%), transient and manageable by dose modifications, no cases of febrile neutropenia. Four patients (8%) developed thromboembolic events (grades 2, 3, 4) and discontinued treatment. One patient died while on treatment from PD. More than 800 exosome proteins were detected in the samples analyzed so far. Exosomal protein networks in pretreatment samples predicted treatment response with 89% sensitivity and 95% specificity in unsupervised clustering. Data on correlative objectives will be presented in a separate abstract.

Conclusions:

The combination of palbociclib and tamoxifen showed tolerable, expected safety profile. This may be an alternative approach for selected patients in first line treatment of HR+ MBC, especially those who present with de-novo metastatic disease and are intolerant to AI; although this small study indicates a lower PFS.

Baseline Demographics

Parameter	N	%
Sex		
Female	47	100
Race		
White	31	66
Black or African American	11	23
Asian	1	2
American Indian or Alaska Native	1	2
Unknown	3	6
Ethnicity		
Hispanic or Latino	3	6
Non-Hispanic	44	94
ECOG Performance status		
0	31	66
1	15	32
2	1	2
Menopausal status		
Post-menopausal	38	81
Pre-menopausal	9	19

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-01-39

Real-world efficacy of dual antiHER2 therapy in first line metastatic HER2-positive breast cancer and the possibility of prediction of long-term response

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Real-world efficacy of dual antiHER2 therapy in first line metastatic HER2-positive breast cancer and possible predictors of long-term treatment response

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Background: Although huge progress has been made in treating HER2-positive metastatic breast cancer in the last decade, it remains an incurable disease. Dual anti-HER2 therapy with pertuzumab and trastuzumab combined with chemotherapy represents the standard first line treatment of metastatic HER2-positive breast cancer, in view of the impressive CLEOPATRA study results. The aim of this study was to analyze the efficacy of dual antiHER2 therapy in real-world clinical practice and determine the differences in the clinicopathological characteristics of the long-term responders in comparison with short-term responders.

Methods: Retrospective analysis of dual antiHER2 therapy efficacy was done and correlated to clinical and pathological characteristics of patients with different duration of response (DoR) in the first line metastatic HER2-positive breast cancer. The study was conducted at the UHC Zagreb, Croatia and approved by the Ethics Committee. Long-term responders were defined as patients with a duration of response (DoR) to dual antiHER2 therapy ≥ 36 months, and short-term responders were defined as patients with DoR ≤ 12 months. Progression-free survival was estimated using the Kaplan-Meier method. The reverse Kaplan-Meier method was used to estimate median follow-up duration. The non-parametric Chi-Square test (between categorical variables) and Mann-Whitney U-test (between continuous variables) were used to determine the differences between long-term and short-term responders groups. The significance level was set at $p < 0.05$.

Results: Altogether, 128 patients treated with dual antiHER2 therapy for HER2-positive metastatic breast cancer from October 2015 to May 2022 were included in the study. By data cut-off, 50.8 % (N=63) of patients had progressed or died. The median follow-up time was 36 months. The median PFS was 31 months for the total cohort (95% CI 22.6 -39.3). Overall, 29

patients among the long-term responders and 32 patients in the short-term responders group were identified. A comparison of clinical and pathological characteristics between the two groups is shown in Table 1. Even though patients in the group of long-term responders were younger (54.5 years vs. 56.5 years), had less visceral involvement (69 % vs. 81.3%), and were more often trastuzumab "naive" (75.9% vs. 68.7%), no statistically significant differences were found between the two groups.

Conclusion: In this real-life study, the median PFS was 31 months for the total cohort, even longer than in the referent CLEOPATRA trial, which confirms the effectiveness of dual antiHER2 therapy in a real-world setting. No possible clinical or pathological predictors of long-term response were identified, but larger studies may be able to distinguish patients' characteristics associated with long-term response.

Table 1: A comparison of clinical and pathological characteristics between the group of long-term responders and short-term responders

Total cohort N=128	Long-term responders (DoR \geq 36months)	Short-term responders (DoR \leq 12months)	P-VALUE
	N= 29/128	N= 32/128	
Median age (years)	54.5	56.5	0.1055
Visceral involvement	N=20 (69.0 %)	N=26 (81.3%)	0.7198
>3 metastatic sites at initial diagnosis	N= 9 (31.0%)	N=16 (50%)	1.0
Trastuzumab "naive"	N =22 (75.9 %)	N=22 (68.7%)	0.9373
HR positivity	N=21 (72.4%)	N= 23 (71.9%)	0.3775
Brain metastasis at baseline	N=3 (10.3 %)	N= 4 (12.5%)	0.8788
De novo metastatic disease	N=16 (55.2 %)	N= 12 (37.5%)	0.4242
Recurrent disease	N= 13 (44.8%)	N= 20 (62.5%)	0.4242
Adjuvant trastuzumab	N=7 (53.8%)	N=10 (50.0 %)	0.1566

Disclosure(s):

Marija Križić, n/a: Novartis: Contracted Research (Ongoing); Roche: Contracted Research (Ongoing)

Tajana Silovski, n/a: Eli Lilly: speaker (Ongoing); Novartis: Contracted Research (Ongoing), speaker (Ongoing); Pfizer: speaker (Ongoing); Roche: Contracted Research (Ongoing), speaker (Ongoing)

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12/8/2022

7:00 AM - 8:15 AM

P4-01-40

Real World Data with Off-Label Insurance Approval of Trastuzumab Deruxtecan in Metastatic Breast Cancer

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Background: Trastuzumab deruxtecan (T-DXd) improves outcomes in HER2-positive, and recently in HER2-low (IHC 1+ or IHC 2+/ISH-) previously treated metastatic breast cancer (MBC) patients. OncoHealth is a digital health care company that leverages managed care-trained, board-certified oncologists and oncology pharmacists to review the appropriateness of prior authorization (PA) requests for cancer treatment regimens. Our objective was to examine the rate of off-label PA approvals for T-DXd in MBC.

Methods: We performed a retrospective cross-sectional study of T-DXd PA approvals by OncoHealth for MBC patients between 1/17/2020 – 6/21/2022. Using medical records and utilization management data, we assessed the prevalence of PA approvals for T-DXd in HER2-low and HER2-positive MBC patients according to PA support at the time of approval, whether on-label, off-label NCCN compendium supported, off-label acceptable scientific literature-only (LIT) supported, or approved by clinical justification if off-label/off-NCCN or LIT.

Results: We identified 156 patients with MBC with a PA approval for T-DXd. The median patient age range was 60-69 years, 85% had visceral disease, 28% had brain metastases, 93.6% had

HER2-positive MBC and remaining were HER2-low MBC. The median line of T-DXd therapy was 6 (range, 1-15) for HER2-low and 3 (range, 1-10) for HER2-positive MBC. All HER2-low T-DXd cases were supported by LIT and approved prior to NCCN guidelines incorporation in 6/21/2022. Among HER2-positive MBC patients, 25% (37/146) of PA approvals were off-label. Of these, 57% (21/37) were supported by NCCN, and the remaining 43% (16/37) were approved off-label/off-NCCN or LIT. The majority of the off-label/off-NCCN or LIT cases (10/16) were approved by clinical judgement based on 2nd line HER2-positive MBC abstract data from DESTINY-Breast03 presented at ESMO on 9/19/21.

Conclusions: All off-label PA approvals for T-DXd in HER2-low MBC occurred prior to NCCN's incorporation, expanding access. One quarter of all T-DXd approvals in HER2-positive MBC were off-label. Leveraging managed care, board-certified oncology clinicians with knowledge of the latest cancer therapies and use of additional coverage determination resources such as NCCN and acceptable scientific literature can help expedite and expand access to off-label anti-cancer drugs that may be beneficial for cancer patients.

T-DXd Authorization Approvals

Approval Support	HER2-positive (n=146)	HER2-low (n=10)
On-Label, n (%)	109 (75%)	NA
Off-Label, NCCN, n (%)	21 (14%)	NA
Off-Label, Acceptable Scientific Literature-Only, n (%)	0	10 (100%)
Off-Label/Off-NCCN or Literature, n (%)	16 (11%)	0

Disclosure(s):

Laura R. Bobolts, PharmD, BCOP: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-01-41

Clinical outcome and toxicity profile of Cyclin-dependent kinase 4/6 inhibitors in combination with hormonal treatment in management of metastatic breast cancer patients: A Middle-East Real World Experience.

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Background: Cyclin-dependent kinase 4/6 (CDK4/6) inhibitors in combination with hormonal treatment is the standard of care in the management of hormone receptor positive, human epidermal growth factor receptor-2 (Her2) negative metastatic breast cancer (MBC) patients. Data coming from the Middle east region is very rare and our patients' population were poorly represented in the CDK4/6 inhibitors landmark clinical trials, This retrospective study is to evaluate our real-world experience with this treatment combination in our patients' population. Patients and methods: A retrospective study was conducted in a middle eastern tertiary institution, where the clinical data of treatment outcome and toxicity were collected from the electronic medical records of 164 patients with hormone receptor positive, Her2 negative MBC who were managed with CDK4/6 inhibitors in combination with hormonal treatment, at and beyond first line of treatment. Progression free survival (PFS) was the study primary objective, Objective response rate (OR), Overall survival (OS), and toxicity profile were the secondary objectives. Results: From January 2017 to April 2021, 164 patients (5 men and 159 women) were managed with CDK4/6 inhibitors in combination with hormonal treatment for MBC, median age was 52 years (IQR: 45-59), 63% of patients were postmenopausal, 60% had luminal type B tumors, 22% had Her2 expression of 2+ by IHC, 55% had de Novo metastases, 67% had visceral metastases, 61% defined to have endocrine resistant disease (13% primary and 48% secondary resistance), CDK inhibitors (46% Palbociclib, 54% Ribociclib) were given as 1st, 2nd and beyond 2nd line in (48%, 28% and 24% respectively), at a median duration of follow up of 25.3 months (IQR: 13.8-33.9 months), the median PFS for the overall group was 14.2 months (CI 09.8-18.7), it was highest for 1st line treatment 19 months vs 15 and 5 months for the 2nd and beyond 2nd line treatment respectively. The median overall survival was 51.6 months (CI

35.8-67.5) for the whole group, 50.3 and 51.6 months for 1st and 2nd line vs 33.1 months for beyond 2nd line treatment. 5% of patients had achieved complete response, 37% partial response, and 24% had stable disease, with a clinical benefit rate of 74%. A body mass index (BMI) < 30, KI67 < 20%, luminal type A, de Novo metastases, Ribociclib as a CDKi, Aromatase inhibitor (AI) as the hormonal partner, and introducing the treatment combination in early treatment lines (1st and 2nd lines) were all associated with significantly higher PFS in univariate analysis. BMI and AI were the only factors associated with significantly higher PFS in multivariate analysis. Efficacy was consistent regardless of the menopausal status, type of endocrine resistance, and site of metastases. The most common toxicities were neutropenia, fatigue, vomiting, diarrhea, QTC prolongation and hepatic toxicity, the most common G3&4 toxicity were Neutropenia 56%, hepatic toxicity 5.4% and QTC prolongation in 4.3%. Treatment was permanently stopped because of toxicity in 12 patients (7.3%). Conclusion: Our real-life data came consistent with the pivotal clinical trials' results, encouraging and supporting the use of CDK 4/6 inhibitors in combination with hormonal treatment in our patient population with metastatic breast cancer, especially in the early treatment lines, deferring the start of more toxic therapies to a later stage.

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Ahmed Mostafa Gad, MD: No financial relationships to disclose

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P4-01-42

Pooled analysis of post-progression treatments after first-line ribociclib + endocrine therapy in patients with HR+/HER2- advanced breast cancer in the MONALEESA-2, -3, and -7 studies

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Background: The MONALEESA (ML) studies showed significant PFS & OS benefits for 1L ribociclib (RIB) + endocrine therapy (ET) in patients (pts) with pre/peri & postmenopausal advanced breast cancer. The benefit of RIB beyond study treatment (tx) was also observed, with improvements in PFS2 & delays in time to 1st subsequent chemotherapy (CT). While there is currently no preferred tx for the next line post-progression on a CDK4/6 inhibitor (CDK4/6i), except alpelisib in pts with a PIK3CA mutation, guidelines encourage multiple lines of ET or ET-based therapies before switching to CT (except for visceral crisis). This pooled exploratory analysis of the ML studies examined outcomes of various tx strategies post progression on RIB + ET.

Methods: Data from pts receiving 1L therapy in ML-2, -3, & -7 (NSAI cohort only & excluding pts with early relapse \leq 12 mo after end of (neo)adjuvant ET] whose prognosis is closer to that of 2L pts) were pooled & pts receiving 1st subsequent therapies after progression were analyzed. Three groups of subsequent therapies were assessed: ET only, CT, & targeted therapy. Subsequent CT comprises CT +/- any other therapy; targeted therapy includes CDK4/6i, mTORi, PI3Ki, AKTi, etc, +/- ET. Subsequent CT & targeted therapy groups are mutually exclusive. Median duration of study tx, 1st subsequent therapy, & OS (from randomization to death) were analyzed by KM methods. Weighted Cox regressions were performed using inversed propensity scoring matching method (inverse probability tx weighting [IPTW]) to ensure compatible pt characteristics between tx arms. These are not randomized comparisons; only baseline characteristics were used for the estimation of propensity scores in the IPTW, imbalance of prognostic factors at progression may exist.

Results: Median follow-up time was 74 mo. 461 pts treated with RIB (81%) & 440 (86%) with PBO discontinued study tx & received a subsequent therapy. In the RIB arms, the most common 1st subsequent therapies were ET only (40%), CT (29%), combination with targeted therapy (28%), & other (4%); for the PBO arms, 34% received CT as a 1st subsequent therapy & 31% each received ET only or combination with targeted therapy (5% received other). In 14% & 20% of pts in the RIB & PBO arms, the 1st subsequent therapy was a CDK4/6i, of these 31% & 12% were RIB. In general, regardless of type of 1st subsequent therapy, the duration of both the study tx & the 1st subsequent therapy was longer for pts treated with RIB vs PBO (Table). In both RIB & PBO arms, pts who received subsequent CT had the shortest duration on study tx, whereas those who received subsequent targeted therapy combination had the longest. Among pts on 1L RIB + ET, after matching pre-randomization baseline characteristics, subsequent CDK4/6i use was associated with the longest mOS (84 [84-NE] mo), followed by ET only (60 [51-68] mo), then a non-CDK4/6i targeted therapy (52 [43-72] mo); post-progression CT was associated with the shortest mOS (37 [32-48] mo).

Conclusions: This large, pooled analysis of the ML studies shows that, in general, duration of any subsequent therapy was numerically longer post-1L RIB + ET vs PBO + ET, & subsequent CT was used less frequently for pts on RIB vs PBO. Both findings confirm that upfront tx with RIB does not worsen pt outcomes. This trend in enhancement of outcomes of subsequent therapies seen with 1L RIB suggests a post-tx effect that merits further exploration.

Table.

Median Duration, mo	All	CT	ET Only	Any Targeted Therapy	Any CDK4/6i	RIB
RIB + ET, n	461	132	184	128	65	20
1L RIB + ET	19.3	13.5	17.4	24.8	29.4	47.4
First subsequent therapy	10.5	7.6	8.3	15.0	22.8	34.2
PBO + ET, n	440	150	136	134	86	10
1L PBO + ET	14.7	9.2	14.9	22.5	28.0	29.9
First subsequent therapy	8.9	9.0	7.4	9.4	14.7	21.1

Disclosure(s):

Erika Hamilton, MD: Abbvie: Research Funding - Paid to Institution (Ongoing); Accutar Biotechnology: Research Funding - Paid to Institution (Ongoing); Acerta Pharma: Research Funding - Paid to Institution (Ongoing); ADC Therapeutics: Research Funding - Paid to Institution (Ongoing); AKESOBIO Australia: Research Funding - Paid to Institution (Ongoing); Amgen: Research Funding - Paid to Institution (Ongoing); Aravive: Research Funding - Paid to Institution (Ongoing); Arcus: Consulting Fees to Institution (Ongoing); ArQule: Research Funding - Paid to Institution (Ongoing); Artios: Research Funding - Paid to Institution (Ongoing); Arvinas: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); AstraZeneca: Study sponsor, consulting fees and research grant paid to institution (Ongoing); AtlasMedx: Research Funding - Paid to Institution (Ongoing); Black Diamond: Consulting and Research Funding - Paid to Institution (Ongoing); Bliss BioPharmaceuticals: Research Funding - Paid to Institution (Ongoing); Boehringer Ingelheim: Consulting and Research Funding - Paid to Institution (Ongoing); Cascadian Therapeutics: Research Funding to Institution (Ongoing); Clovis: Research Funding to Institution (Ongoing); Compugen: Research Funding to Institution (Ongoing); Cullen-Florentine: Research Funding to Institution (Ongoing); Curis: Research Funding to Institution (Ongoing); CytomX: Consulting Fees and Research Funding to Institution (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Dana Farber Cancer Inst: Research Funding to Institution (Ongoing); Dantari: Consulting Fees and Research Funding to Institution (Ongoing); Deciphera: Consulting Fees and Research Funding to Institution (Ongoing); Duality Biologics: Research Funding to Institution (Ongoing); eFFECTOR Therapeutics: Research Funding to Institution (Ongoing); Eisai: Consulting Fees to Institution (Ongoing); Ellipses Pharma: Research Funding to Institution (Ongoing); Elucida Oncology: Research Funding to Institution (Ongoing); EMD Serono: Research Funding to Institution (Ongoing); Fochon: Research Funding to Institution (Ongoing); FujiFilm: Research Funding to Institution (Ongoing); G1 Therapeutics: Research Funding to Institution (Ongoing); Greenwich Lifesciences: Consulting Fees to Institution (Ongoing); H3 Biomedicine: Consulting Fees and Research Funding to Institution (Ongoing); Harpoon: Research Funding to Institution (Ongoing); Hutchinson MediPharma: Research Funding to Institution (Ongoing); Immunogen: Research Funding to Institution (Ongoing); Immunomedics: Research Funding to Institution (Ongoing); Incyte: Research Funding to Institution (Ongoing); Infinity Pharmaceuticals: Research Funding to Institution (Ongoing); InvestisBio: Research Funding to Institution (Ongoing); iTeos: Consulting Fees to Institution (Ongoing); Jacobio: Research Funding to Institution (Ongoing); Janssen: Consulting Fees to Institution (Ongoing); Karyopharm: Research Funding to Institution (Ongoing); Leap Therapeutics: Research Funding to Institution (Ongoing); Lilly: Consulting Fees and Research Funding to Institution (Ongoing); Loxo: Consulting Fees to Institution (Ongoing); Lycera: Research Funding to Institution (Ongoing); Mabspace Biosciences: Research Funding to Institution (Ongoing); MacroGenics: Research Funding to Institution (Ongoing); MedImmune: Research Funding to Institution (Ongoing); Merck: Consulting Fees and Research Funding to Institution (Ongoing); Mersana: Consulting Fees and Research Funding to Institution (Ongoing); Merus: Research Funding to Institution (Ongoing); Millennium: Research Funding to Institution

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12/8/2022

7:00 AM - 8:15 AM

P4-01-43

Pyrotinib in combination with Capecitabine for trastuzumab-Resistant, HER2-positive advanced breast cancer (PICTURE): a multicenter phase 2 trial

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Background: Approximately 10% of patients with HER2-positive breast cancer have primary resistance to trastuzumab, leading to poor prognosis. Although several trials enrolled those hard-to-treat patients, there has been no strong evidence available for the clinical decision making. This multicenter phase 2 trial aimed to investigate the activity and safety of pyrotinib plus capecitabine only in those patients with trastuzumab-resistant, HER2-positive advanced breast cancer. Methods: Patients from 17 sites in China received pyrotinib 400 mg once a day and capecitabine 1000 mg/m² twice a day on days 1-14 every 21 days until disease progression or intolerable toxicity. Based on the definitions used in prior clinical trials, primary trastuzumab resistance was defined as progression during trastuzumab treatment (Group 1) or within 12 months after completing trastuzumab treatment in the (neo)adjuvant setting (trastuzumab should have been for ≥ 9 weeks, Group 2), or progression within 6 months after the initiation of trastuzumab treatment in the advanced setting (treatment should have been for ≥ 6 weeks, Group 3). The primary endpoint was progression-free survival (PFS). The study is registered with ClinicalTrials.gov, NCT04001621. Results: Between June 2019 and September

2021, a total of 100 patients enrolled; 35 (35.0%) patients had hormone receptor (HR)-positive disease, and 65 (65.0%) had HR-negative disease. Prior use of trastuzumab, pertuzumab and antibody-drug conjugate was reported in 100%, 21.0% and 2.0% of patients, respectively. By the data cutoff on July 10, 2022, the median follow-up duration was 23.4 months (95%CI, 20.5-25.6) with 66 PFS events documented. Median PFS was 11.8 months (95%CI, 8.4-15.1) in the overall population. Patients in Group 2 (n=49) had the longest median PFS of 17.8 months (95%CI, 13.8-not reached), which was significantly different from either 8.2 months (95%CI, 3.0-20.7; p = 0.001) in Group 1 (n=21) or 5.6 months (95%CI, 4.1-6.9; p < 0.001) in Group 3 (n=30). No significant difference in median PFS was observed in subgroup by HR status (HR-positive: 9.7 months [95%CI, 6.4-18.4]; HR-negative: 12.3 months [95%CI, 8.2-17.8]; p = 0.764). Objective response rate was 70.0% (95%CI, 60.0%-78.8%). Overall survival data was immature. The most common grade ≥3 treatment-emergent adverse events included diarrhea (24.0%), palmar-plantar erythrodysesthesia syndrome (9.0%), neutrophil count decreased (7.0%), hypokalemia (5.0%), and decreased appetite (5.0%). No treatment-related deaths occurred. Conclusions: Pyrotinib plus capecitabine resulted in a promising PFS that crossed the pre-specified efficacy boundary in patients with HER2-positive advanced breast cancer who met the traditional definition of primary trastuzumab resistance. Patients in Group 2 had a significant longer PFS than those in either Group 1 or Group 3, highlighting the need to re-define primary trastuzumab resistance and to clarify efficacy of new anti-HER2 biologicals for each subpopulation.

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P4-02-01

Efficacy of HER2 ADCs against HER2 inhibitor resistance alterations in the PI3K and MAPK pathways in HER2-positive breast cancer

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Background: HER2 positive (HER2+) breast cancers harboring downstream MAPK or PI3K pathway alterations manifest persistent downstream signaling on anti-HER2 inhibitors with metastatic patients having worse outcomes on first line trastuzumab and pertuzumab (HP) therapy. However, HER2 antibody-drug conjugates (ADCs) are not as dependent upon potent signal transduction inhibition to exert their antitumor effects. To further investigate, we sought to determine whether MAPK and/or PI3K alterations affect the biologic or clinical outcomes of patients and models receiving HER2 ADCs. Methods: We performed prospective genomic sequencing using MSK-IMPACT on patients with advanced HER2+ breast cancer who received trastuzumab emtansine (T-DM1) in the metastatic setting between March 2013 and July 2021. We collected detailed information on clinical outcomes and correlates through our institutional IRB-approved retrieval process. HER2/ER/PR status at the time of metastatic recurrence were defined as per ASCO/CAP guidelines. Cox proportional hazard models were used to determine the association between MAPK and PI3K pathways alterations and progression-free survival (PFS) on T-DM1. Common mutations associated with outcomes were modeled in HER2+ breast cancer cell lines using short hairpin RNAs and CRISPR/Cas9, and the sensitivity to HER2 ADC was evaluated via cell proliferation and xenograft assays. Results: We identified 185 HER2+ breast cancer patients treated with T-DM1 at any line (median: 5) whose primary (N=65) or metastatic (N=120) tumor samples were sequenced. Median age was 55 (range: 20-87). The majority of the patients received T-DM1 in 2nd or 3rd line (52%) and received prior trastuzumab or HER2 TKI in metastatic setting (96%). 74/185 (40%) had de novo metastatic breast cancer and 119/185 (64%) had ER/PR+ /HER2+ disease. Pathogenic activating alterations involving the MAPK pathway were observed in 14% of patients with the most frequent alterations being ERBB2 activating mutations (42%) and NF1 loss (34%). PI3K pathway alterations were identified in 42% of the patients, the majority being activating mutations of PIK3CA (87%). MAPK alterations were significantly enriched in the metastatic tumors compared to the treatment-naïve primaries (20% vs 3%, $p=0.001$), while PI3K alterations were not (44% vs 40%, $p=0.6$). To reduce the possible confounding resistance mechanisms induced by prior treatment, we restricted the survival analyses to patients who received T-DM1 up to 3rd line of therapy (N=100). On multivariable analysis adjusted for ER/PR status (positive vs negative), stage at the presentation of metastatic disease (de novo metastatic vs recurrence), treatment line and type of sequenced sample (primary vs metastatic), patients with MAPK (N=14) and PI3K (N= 38) alterations had similar PFS compared to wild type (HR 1.20, 95%CI 0.62-2.30, $p=0.6$ and HR 1.23, 95%CI 0.77-1.95, $p=0.4$, respectively). Similar results were found in the combined analysis including alterations in either pathway (N=48, HR 1.28, 95%CI 0.81-2.04, $p=0.3$). To verify the antiproliferative effect of HER2 ADCs on breast cancer cells with MAPK pathway activation, we depleted NF1 in a panel of HER2+ breast cancer cell lines. Consistently, MAPK-altered cell lines were sensitive to FDA-approved HER2 ADCs including trastuzumab deruxtecan (T-DXd). Conclusions: In contrast to H/P therapy, T-DM1 therapy was equally effective in tumors with downstream PI3K or MAPK alterations and wild type tumors. Expanded analysis on a larger cohort, including a subgroup of patients treated with novel HER2 ADCs such as T-DXd will be presented. The characterization of PI3K and MAPK pathways status in metastatic HER2+ breast cancer may inform prioritization of treatment options.

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12/8/2022

7:00 AM - 8:15 AM

P4-02-02

Changes in treatment recommendation for patients with Ductal Carcinoma In Situ using a 7-gene predictive biosignature: Analysis of the PREDICT Study

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Background: The role of adjuvant radiotherapy (RT) following breast conserving surgery (BCS) for women with ductal carcinoma in situ (DCIS) remains controversial. Although there is Level 1 evidence supporting the use of RT in reducing the risk of local recurrence, prognostic and predictive tools are needed to better stratify individual risks and benefits of RT. The DCISionRT® Test (PreludeDx, Laguna Hills, CA) is a 7-gene predictive biosignature that uses tumor biology in conjunction with clinicopathologic factors. The test provides a validated score (DS) for women receiving BCS that assesses 10-year risk of DCIS recurrence and development of invasive breast cancer with and without adjuvant RT. We established a registry to evaluate the decision impact of the 7-gene predictive biosignature on DCIS treatment recommendations.

Methods: The PREDICT study is a prospective, multi-institutional registry for patients who received DCISionRT testing as part of their routine care. The registry includes females 26 and older who are diagnosed with DCIS and are candidates for BCS and eligible for RT or systemic therapy. Treating physicians completed treatment recommendation forms before and after receiving test reports to capture surgical, radiation and hormonal treatment (HT) recommendations and patient preferences. The primary endpoint is to identify the proportion of

patients where testing led to a change in RT recommendation. Additional analyses include changes in recommendations in patient subgroups based on clinicopathologic factors or clinician specialty.

Results: Analysis was performed in 2,308 patients treated at 63 clinical sites. The median age of patients was 62 years, 18% were 50 or younger, nuclear grade was high in 33%, and tumor size was 2.5 cm or greater in 11%. Test results were DS Low Risk (DS ≤ 3) for 63% of women and 37% were DS Elevated Risk (DS > 3). Overall, RT recommendation (yes/no) was changed for 38% of women after the 7-gene biosignature testing and HT recommendation was changed for 11%. There was a net decrease in RT recommendation from 71% pre-assay to 53% post-assay (p< 0.001), where RT recommendations decreased 53% in DS Low Risk patients but increased 25% in DS Elevated Risk patients. Surgeons were more likely to change their RT recommendation (47%) than radiation oncologists (35%). When test results indicated DS Elevated Risk, both surgeons (79%) and radiation oncologists (88%) were likely to recommend RT, but when the results were DS Low risk, surgeons were more likely than radiation oncologists to recommend omitting RT (82% vs. 60%, respectively). Compared to traditional clinicopathologic features, the factor most strongly associated with RT recommendation was the biosignature result with other factors of importance being patient preference, tumor size and grade.

Conclusions: This analysis demonstrates significant changes in recommendations to add or omit RT based on the 7-gene predictive biosignature in 2,308 patients. The integration of DCISionRT into clinical decision processes has substantial impact on recommendations aimed at optimal management to prevent over- or under-treatment.

TABLE 1. Impact of the 7-gene predictive biosignature on adjuvant radiation recommended by clinicopathologic features.

Clinical Factor	N	RT Recommended			Pre- to post-test change in RT recommended		Total change in RT recommended		
		Pre-test (%)	Post-test (%)	Net change (%)	Yes, % to no (%)	No, % to yes (%)	Overall change (%)	Overall change (95% CI)	p-Value
Overall	2308	71	53	-18	40	34	38	36, 40	<0.001
Age, years									
≤ 50	422	80	47	-33	45	15	39	35, 44	<0.001
> 50	1886	69	54	-15	38	37	38	36, 40	<0.001
Nuclear Grade									
1 or 2	1553	64	48	-16	45	34	41	39, 44	<0.001
3	755	86	64	-22	27	31	34	29, 35	<0.001
Tumor Size									
≤ 2.5 cm	1534	65	48	-17	43	31	39	37, 41	<0.001
> 2.5 cm	218	90	71	-20	26	38	27	22, 33	<0.001
RTOG 9804-like Criteria*									
'Good Risk'	1125	61	44	-17	49	33	43	40, 46	<0.001
Not 'Good Risk'	1183	81	62	-19	33	37	34	31, 36	<0.001

*RTOG 9804-like criteria (Nuclear Grade 1 or 2, non-Palpable, Screening Detected, Negative Margins)

Disclosure(s):

Pat Whitworth, MD: Agendia: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Biotheranostics: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Genomic Health: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Impedimed: Consulting Fees (e.g., advisory boards) (Ongoing); Medneon: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Myriad: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Prelude: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Veracyte: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing)

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12/8/2022

7:00 AM - 8:15 AM

P4-02-03

Transcriptomic signature score of Epithelial-Mesenchymal Transition (EMT) of a bulk tumor may not reflect that of cancer cells

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Background: Epithelial-mesenchymal transition (EMT) is a well-known multistep process of cancer cell invasion and metastasis, as well as treatment resistance. Our group has been reporting the predictive role of scores generated using Gene Set Variation Analysis (GSVA) of Hallmark pathways in breast cancer. In this study, we hypothesized that EMT score high breast cancer is aggressive and is associated with poor clinical outcome. Material and Methods: The clinicopathological data and transcriptome data of breast cancer patients from three independent large publicly available databases, The Cancer Genome Atlas (TCGA, n = 1077), The Molecular Taxonomy of Breast Cancer International Consortium (METABRIC, n = 1904), and GSE96058 (n=3069) were utilized. Survival analyses; Overall survival (OS), Disease-specific survival (DSS) and Disease-free survival (DFS) were performed by comparing the high and low score groups. Tumor immune microenvironment was analyzed utilizing the values reported by Thorsson et al. Also, single sample Gene Set Enrichment analysis (ssGSEA) was performed between EMT high and low expression groups utilizing single cell sequence cohorts. Results: EMT score was generated by Gene Set Variation Analysis of a Hallmark gene set and we divided each cohort into EMT score high and low groups by utilizing median as the cutoff. To our surprise, EMT score of the primary tumor was not associated with metastasis (N and M categories of cancer staging), Nottingham histological grade, nor MKI67 expression levels consistently in TCGA, METABRIC, and GSE96058. EMT score high tumors were not associated with worse DFS, DSS, OS in TCGA and METABRIC and OS in GSE96058.

Analyses using xCell demonstrated that EMT score high tumors were associated with high infiltration of stromal cells such as adipocyte ($p < 0.001$, $p < 0.001$ and $p < 0.001$, respectively) and fibroblasts ($p < 0.001$, $p < 0.001$ and $p < 0.001$, respectively) in all three cohorts, TCGA, METABRIC, and GSE96058. Also, myeloid cells such as macrophages ($p < 0.001$, $p < 0.001$ and $p < 0.001$, respectively) and dendritic cells ($p < 0.001$, $p < 0.001$ and $p < 0.001$, respectively) were highly infiltrated with EMT score high tumors. Result of ssGSEA of single cell sequence cohorts revealed that cancer associated fibroblasts demonstrated highest EMT scores compared with the other cell types such as cancer cells, T-cells, B-cells, or myeloid cells. In other words, EMT score of a bulk tumor may reflect the signature from fibroblasts rather than cancer cells. Conclusion: We found that cancer associated fibroblasts rather than cancer cells are the major source of the transcriptomic signatures of EMT in the bulk tumor, which cautions us to be careful with the interpretation of the results of EMT signature from a bulk tumor.

Disclosure(s):

Yoshihisa Tokumaru, n/a: No financial relationships to disclose

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Manabu Futamura, n/a: Chugai: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Daiichi Sankyo: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Eli Lilly: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Nihonkayaku: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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7:00 AM - 8:15 AM

P4-02-04

Serial monitoring of circulating tumor cells and circulating tumor DNA in metastatic lobular breast cancer identifies intra-tumor heterogeneity and precision and immunology biomarkers of therapeutic importance

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Clinical decisions on precision and immuno-oncology therapies are based on predictive biomarkers commonly obtained from a single metastatic biopsy or archived primary tumor tissue. Circulating genomic biomarkers offer a minimally invasive approach to monitor intra-patient tumor heterogeneity and detect in real-time the clinically-relevant evolving clonal architecture. Although currently underutilized, we hypothesize that single-cell DNA next generation sequencing (scNGS) of circulating tumor cells (CTC) is a particularly well-suited method to complement biomarker information obtained from tissue and cell-free circulating tumor DNA (ctDNA). In this study we analyzed 113 individual CTC, 21 ctDNA, and 15 white blood cells (WBC) samples, from 15 CTC-positive lobular breast cancer patients, four of whom had CTC available at both metastatic baseline and after progression on a variety of therapies chosen at their physician's discretion. Clinical NGS data from 15 tumor tissue biopsies obtained using a ~1700-gene DNA panel and whole transcriptome sequencing were available for comparison. CTC were enriched with the CellSearch® system and isolated as single cells with the DEPArray™ system. Whole genome amplified CTC and WBC, as well as ctDNA underwent scNGS with the OncoPrint Comprehensive Assay covering ~500 genes and 1.1Mb of genomic space to detect mutations, copy number alterations, tumor mutation burden (TMB) and microsatellite instability (MSI). 99.1% of single cells and 95.2% of ctDNA samples were informative, with a mean sequencing depth of 664x. Using our previously developed, CTC-based precision medicine reporting platform, MI-CTCSeq, CTC in 9 of 15 patients (60%) had mutations that were actionable by FDA-approved targeted therapies including in the oncogenes PIK3CA and FGFR2 and HER2. 3 of these 9 patients (33%) harbored actionable alterations not shared between all 3 analyte types (tissue, CTC and ctDNA). These included 3 actionable mutations found in CTC and ctDNA only, 1 in tissue and ctDNA only, and 1 in ctDNA only. However, 2 of those ctDNA mutations were identified near the limit of detection and with a priori knowledge of their presence from tissue or CTC. Further, 1 patient with plentiful CTC had no detectable ctDNA and one patient's tissue biopsy was inadequate for sequencing while both liquid biopsy analytes were abundant. 13 patients (87%) displayed intra-patient, inter-CTC genomic heterogeneity of putative driver mutations. 1 of 4 (25%) patients with CTC available in >1 timepoint displayed fluctuations in their CTC subclonal makeup between timepoints. Data from this patient's 2 tissue biopsies, 3 ctDNA samples, and 27 individual CTC over 4 timepoints combined to reveal in unprecedented detail inter-metastatic lesion and inter-CTC heterogeneity and tumor evolution in response to endocrine and immunotherapy selective pressures. ScNGS of CTC helped provide an additional level of detail not appreciated by sequencing of the other two analyte types. In another patient, CTC were composed of 2 subclones which were indistinguishable by ctDNA, 1 of which appears to have not been sampled by the tissue biopsy. Using a novel method, we enabled detection of single-cell CTC TMB and MSI. CTC TMB scores (dichotomized as above/below 10 mutations/Mb) were 100% concordant with those measured in the corresponding tissue biopsies. Further, in a novel observation, we detected intra patient, inter-CTC heterogeneity of TMB and MSI, which has potential implications for immunotherapy response and development of resistance. Taken together, these data support the non-invasive biomarker interrogation and monitoring by liquid biopsy that incorporates CTC scNGS and complements tissue in informing precision and immuno-oncology approaches. This may have important implications for appropriate treatment selection and identification of therapeutic resistance mechanisms.

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Andi Cani, n/a: No financial relationships to disclose
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12/8/2022

7:00 AM - 8:15 AM

P4-02-05

Predictors of long-term durable response in de novo HER2 positive metastatic breast cancer and the real world treatment experience at two institutions

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Purpose

Modern HER2-directed therapies enable some patients with de novo HER2+ metastatic breast cancer (MBC) to achieve long-term, durable responses (DR), which can be defined as no progression of disease since initial diagnosis. Clinical and pathologic factors that predict DR continue to be elucidated. Expert opinion dictates indefinite HER2-directed therapies for patients who achieve DRs, but real-world examples of this practice are lacking in the literature.

Methods

This is a retrospective study of all patients with de novo HER2+ MBC at two major academic institutions who received at least one dose of trastuzumab between 2012-2019. DR is defined as absence of progression/death at any point after diagnosis. Controls are patients with evidence of progression/death. Age, ER/PR status, sites of metastasis, surgical resection of primary tumor and initial treatment were analyzed as predictors of DR using an unpaired T test, with $p < 0.05$ chosen as threshold for significance. For patients with DR, time to complete (CR) and partial response (PR) according to RECIST 1.1 were recorded, as was the duration and treatment patterns surrounding trastuzumab and pertuzumab. Patients were defined as having cardiotoxicity if they experienced a decline in cardiac ejection fraction at any point while on trastuzumab therapy leading to treatment delays or discontinuation.

Results

96 patients with de novo HER2+ MBC, 28 with DR and 68 with progression, were identified. The average follow up of patients with DR was 90 months (range 27-224), compared to 58 months (range 1-208) in controls. The entire cohort of 96 patients had a median PFS of 23.5 months and a median OS of 88 months. Among the 28 patients with DR, 2 achieved stable disease, 10 patients had documented PR at 4 months on average (range 2-6 months), and 26 patients had CR at 7.7 months on average (range 2-19 months). Among patients with DR, nine patients have been receiving trastuzumab for over ten years with no evidence of disease and one patient opted to discontinue trastuzumab. 75% of patients with DR had a single metastatic site, compared with 47% of patients with progression (OR 3.7, $p=0.01$). 64% of patients with DR received a regimen containing trastuzumab, pertuzumab, and a taxane, while 28% of patients who progressed did (OR 4.5, $p < 0.001$). 57% of patients with DR underwent surgical removal of breast primary, compared with 24% of patients who progressed (OR 4.3, $p=0.002$.) Age, and ER/PR status did not predict DR. (Table 1) Six patients (6.3%) developed reduced ejection

fraction requiring treatment interruption or cessation, five in the group who progressed, one in the DR group.

Conclusion

Nearly a third of patients with de novo HER2+ MBC achieved DR. Factors that correlate with DR include single metastatic site, initial trastuzumab, pertuzumab and taxane therapy, and surgical resection of primary tumor. This suggests that in selected patients, a more aggressive up front approach including surgical resection, and agents such as carboplatin, and trastuzumab deruxtecan deserves further study. Among patients with DR, indefinite trastuzumab administration is the norm with minimal cardiotoxicity but the impact of this on quality of life and financial toxicity are not well described.

Table 1: Clinical characteristics of de novo HER2 positive metastatic breast cancer that predict durable response

Table 1: Clinical characteristics of de novo HER2 positive metastatic breast cancer that predict durable response

	Durable Response No. (%)	Progression No. (%)	
No. Patients	28	68	
Age (years)	54 (range 33-77)	52 (range 28-80)	p=0.6
ER/PR status			
ER and/or PR positive	15 (54%)	46 (68%)	OR 0.55 95% CI (0.24-1.3) p=0.25
ER and PR negative	13 (46%)	22 (32%)	
1 organ involved			
Bone only	9 (32%)	20 (29%)	OR 3.7 95% CI (1.4-10.3) p=0.01
Liver only	9 (32%)	8 (12%)	
Lung only	3 (11%)	4 (6%)	
≥2 organs involved	6 (21%)	34 (50%)	
Any brain	0	5 (7%)	
Initial Chemotherapy			
TCHP or THP	18 (64%)	19 (28%)	OR 5.4 95% CI (1.6-16) p<0.001
Other (*)	10 (36%)	43 (63%)	
Surgery			
Surgical resection of primary	16 (57%)	16 (24%)	OR 4.3 95% CI (1.7-11.5) p=0.002
Surgical resection of metastasis	1 (4%)	4 (6%) all brain	
(*) Other therapies included trastuzumab + taxol, trastuzumab + endocrine therapy, trastuzumab + carboplatin + taxol, trastuzumab + other cytotoxic chemotherapy, lapatinib + taxol. 6 patients in this group did not receive any initial therapy as they opted for hospice or were deceased prior to therapy initiation.			

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-02-06

Clinical and biological predictors of lymph node involvement in patients with early breast cancer for adjuvant treatment personalization

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Background: Over the last years, the management of patients with node positive early breast cancer has gone through important innovations. On the medical side, new targeted therapies such as olaparib and abemaciclib have been introduced, with promising results on the invasive disease-free survival. Moreover, sparing axillary lymph node dissection has proven to be noninferior in terms of overall survival. However, no tools are currently available to predict lymph node involvement before definitive surgical evaluation. The aim of the study was to analyze clinical and pathological characteristics of patients with node positive early breast cancer to explore potential risk profiles associated with a ≥ 3 nodal involvement. Methods: The study retrospectively analyzed 335 node-positive breast cancer patients treated at the Breast Unit of the CRO Aviano National Cancer Institute, between 2017 and 2021. Data regarding primary tumor biological features, lymph node involvement and surgical approach were collected. Associations between clinico-pathological characteristics and ≥ 3 lymph node involvement were tested through stepwise logistic regression and the gradient boosting machine learning algorithm (GBM). Results: Among the 335 analyzed patients, 87.0% had a primary tumor < 5 cm, with a single positive lymph node in 73.3% of cases. Hormone receptors were mainly positive (respectively 93.5% and 83.4% for estrogen and progesterone receptors). Tumor grade was most frequently well differentiated (Grade 1 in 60.7%), with a Ki67 $< 20\%$ (59.5%). After multivariable logistic regression, a tumor size ≥ 3 cm (OR 3.24, CI95% 1.47-7.17, $p = 0.004$), the presence of massive lymphovascular stromal invasion (OR 2.50, CI95% 1.02-6.14, $p = 0.045$) and 2 or more positive sentinel lymph nodes at surgical evaluation (OR 6.08, CI95% 3.34-11.05, $p < 0.001$) were associated with a higher risk of identifying ≥ 3 positive lymph nodes after subsequent axillary dissection. Similar results were observed in the luminal-like cohort. A GBM machine learning model was then developed with a 0.77 Area Under the Curve. Features with the highest relative importance (RI) were single sentinel node involvement (RI 16.1873), followed by tumor size ≥ 3 cm (RI 10.2024), ≥ 2 positive sentinel lymph nodes (RI 8.5050) and lymphovascular stromal invasion (4.0217). Consistently, number of positive sentinel lymph nodes and tumor size were the predominant features in all top 20 GBM models. Conclusions: The present study explored the definition of risk profiles linked to 3 or more positive lymph nodes based on clinical and pathological features. It, moreover, tested the

feasibility of developing machine learning classifiers to support future clinical decision-making. Due to the growing complexity of the adjuvant setting, finding a balance between minimally invasive surgical and staging approaches and risk definition for treatment personalization will become increasingly critical.

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12/8/2022

7:00 AM - 8:15 AM

P4-02-07

A large real-world study of circulating tumor DNA in early breast cancer patients

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Background

Around 30-40% of early breast cancer (EBC) patients relapse after curative surgery and systemic treatment. However, it is very difficult to identify the patients with high risks of relapse. Recently, circulating tumor DNA (ctDNA) is shown to be a sensitive method to evaluate the minimal residual disease (MRD) of solid tumors after surgery. Here, we explored the prognostic value of ctDNA in a large real-world study of EBC patients.

Method

346 invasive EBC patients from three hospitals in China were enrolled in this study. All patients received radical surgery and were followed up for a median of 13.1 months from surgery. 17 patients developed local and/or distant relapse during the follow-up. Primary breast cancer samples (n=346) and plasma samples (n=1059) were subjected to deep targeted sequencing using a large next-generation sequencing panel that covers 1,021 cancer-related genes.

Results

Among the 346 patients, 153 patients had detectable ctDNA in at least one of the plasma samples and 15 of them relapsed. Only two of the 193 patients with consistent negative ctDNA

relapsed, demonstrating the value of positive ctDNA in predicting RFS ($p < 0.0001$; HR=13.09; 95%CI: 2.98-57.45).

Of 334 patients who had postoperative plasma samples tested, 108 patients with positive ctDNA in at least one of the postoperative plasma samples had 11 relapse during follow-up, which had a significantly worse RFS than the 226 patients with negative postoperative ctDNA and 4 relapse ($p < 0.0005$; HR=5.98; 95%CI: 1.90-18.79).

In this study, 176 patients received neoadjuvant therapy (NAT) and 59 of them had twice or more ctDNA tests before surgery. Among them, 12 patients with negative ctDNA before NAT remained negative before surgery and had no relapse, 36 patients with positive ctDNA before NAT turned negative before surgery and had 4 relapse, while 11 patients kept positive ctDNA before surgery and had 2 relapse.

165 patients received NAT and had postoperative ctDNA tests. Of the 31 patients achieved pCR, 21 patients with negative postoperative ctDNA did not relapse and 10 patients with positive postoperative ctDNA had 1 relapse. Of the 134 non-pCR patients, 90 patients with negative postoperative ctDNA had 4 (4.4%) relapse, which is significantly better than the 44 patients with positive postoperative ctDNA and 8 (18.2%) relapse ($p < 0.05$), indicating the feasibility to further distinguish the real high-risk patients among the patients with non-pCR after NAT.

Among the 17 patients with relapse or metastasis, 11 patients had positive ctDNA after surgery before relapse and the median lead time was 74 days and a maximum of 526 days. Four patients had negative ctDNA before relapse and two patients did not test after surgery.

Conclusions

Circulating tumor DNA is a sensitive assay to predict the relapse in early breast cancer, especially in the patients who received NAT and did not achieve pCR. This may provide a window of opportunity to personalize the escalated adjuvant treatment in patients with high relapse risk.

Table1. The association between patients' characteristics and ctDNA positivity

	ctDNA +		ctDNA -		Positive Percentage (%)
	N=153	Percentage(%)	N=193	Percentage(%)	
Age					
age<40	40	26.1	50	25.9	44.4%
age>=40	113	73.9	143	74.1	44.1%
NAT					
Yes	98	64.1	78	40.4	55.7%
No	55	35.9	115	59.6	32.4%
Type					
HR+HER2-	48	31.4	64	33.2	42.9%
HR+HER2+	17	11.1	26	13.5	39.5%
HR-HER2+	17	11.1	17	8.8	50.0%
TNBC	71	46.4	86	44.6	45.2%
ER					
Positive	59	38.6	86	44.6	40.7%
Negative	94	61.4	107	55.4	46.8%
PR					
Positive	42	27.5	70	36.3	37.5%
Negative	111	72.5	123	63.7	47.4%
HER2					
Positive	34	22.2	43	22.3	44.2%
Negative	119	77.8	150	77.7	44.2%
Ki67					
Ki67<20	33	21.6	45	23.3	42.3%
Ki67>=20	113	73.9	139	72.0	44.8%
unknown	7	4.6	9	4.7	43.8%
Stage					
I	16	10.5	34	17.6	32.0%
II	85	55.6	124	64.2	40.7%
III	47	30.7	29	15.0	61.8%
unknown	5	3.3	6	3.1	45.5%
Grade					
1	1	0.7	8	4.1	11.1%
2	41	26.8	72	37.3	36.3%
3	73	47.7	85	44.0	46.2%
unknown	38	24.8	28	14.5	57.6%
Initial T					
T1	27	17.6	65	33.7	29.3%
T2	97	63.4	116	60.1	45.5%
T3	24	15.7	6	3.1	80.0%
Tx	5	3.3	6	3.1	45.5%
Initial N					
N0	68	44.4	99	51.3	40.7%
N1	52	34.0	69	35.8	43.0%
N2	12	7.8	14	7.3	46.2%
N3	20	13.1	11	5.7	64.5%
Nx	1	0.7	0	0.0	100.0%
Family history of breast cancer					
Yes	11	7.2	20	10.4	35.5%
No	142	92.8	173	89.6	45.1%

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7:00 AM - 8:15 AM

P4-02-08

Towards Precision Radiation Oncology: Endocrine Therapy Resistance as a Biomarker for Radiation Resistance in ER-Positive Breast Cancer

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Pre-operative endocrine therapy use in post-menopausal women with localized, ER-positive breast cancer affords comparable rates of response and breast preservation, but lower toxicity relative to chemotherapy. Pre-operative endocrine therapy exerts selective pressure on cancer cells and promote evolution and/or enrichment of pathogenic alternations such as ESR1 mutations and other cellular adaptations. How such endocrine therapy-induced adaptations alter response to radiation therapy remains poorly defined. In this study, we show that diverse mechanisms that confer endocrine therapy resistance also drive radiation resistance by reprogramming of DNA repair pathways. We also show that BRD4, a member of bromodomain and extraterminal domain (BET) family of proteins, mediates such DNA repair reprogramming. BRD4 also plays a key role in transcriptional reprogramming in ER-positive breast cancer cells that confers endocrine therapy resistance. Thus, OTX015, a BET inhibitor with a favorable safety profile in early stage clinical trials, reverses both endocrine therapy resistance and radiation resistance in ER-positive breast cancer cells and tumors. Our findings are also consistent with reports that tamoxifen-resistant breast cancer cells are resistant to DNA damaging chemotherapeutic agents such as adriamycin and cisplatin. Overall, our findings suggest that endocrine therapy resistance in the pre-operative setting serves as a biomarker for reduced response to adjuvant radiation therapy, and that pharmacological BET inhibition reverses radiation resistance in such patients. The increasing use of “window of opportunity” studies to assess response to endocrine therapy in the pre-operative setting will further facilitate personalization of radiation treatments in these patients based on their response to endocrine therapy. Thus, we provides a therapeutic rationale for personalization of radiation treatments in breast cancer patients based on their response to endocrine therapy. We also provide a molecularly targeted approach for reversing radiation resistance in such patients. Thus, our study provides a framework for advancing Precision Radiation Oncology in breast cancer patients.

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-02-09

Evaluation of the Automated Liquid Biopsy-Breast Cancer Methylation (LBx-BCM) Cartridge Assay for Predicting Early Disease Progression and Survival: TBCRC-005 Prospective Trial

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Purpose: We previously demonstrated that high levels of circulating methylated DNA are associated with subsequent disease progression in women with metastatic breast cancer (MBC). In this study, we validated the clinical utility of a Liquid Biopsy-Breast Cancer Methylation (LBx-BCM) prototype assay using the GeneXpert® cartridge system for early assessment of disease progression in MBC. Study Design: The 9-marker, LBx-BCM prototype assay was evaluated in TBCRC-005, a prospective biomarker study, using plasma collected at baseline, week 4 and week 8 from 144 MBC patients. Results: At week 4 MBC patients with high cumulative methylation (CM) had a significantly shorter median PFS (2.88 months v 6.60 months, $p = 0.001$) and OS (14.52 months v 22.44 months, $p = 0.005$) compared to those with low CM. In a multivariable model, high versus low CM was also associated with shorter PFS (HR = 1.90, 95%CI 1.20-3.01; $p = 0.006$). Change in CM from baseline to week 4 (OR = 4.60, 95%CI 1.77, 11.93; $p = 0.002$) and high levels of CM at week 4 (OR = 2.78, 95%CI 1.29, 5.99; $p = 0.009$) were associated with progressive disease at the time of first restaging. A robust risk model (AUC = 0.733) based on week 4 circulating CM levels was developed to predict disease progression as early as 3 months after initiating a new treatment. Conclusion: The easy to perform and automated LBx-BCM prototype assay is a promising clinical tool for detecting disease progression early after initiating treatment in women with MBC. Further validation in larger clinical datasets is needed.

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12/8/2022

7:00 AM - 8:15 AM

P4-02-10

MRI models by response predictive subtype for predicting pathologic complete response

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Background: MRI predictive modeling is used in the I-SPY 2 neoadjuvant clinical trial as a key component of the pre-RCB (Predicted Residual Cancer Burden) clinical workflow for re-directing “good responders” to skip AC (anthracycline) and proceed to surgery early. The current MRI model is hormone receptor (HR)- and human epidermal growth factor receptor 2 (HER2)-specific, and was trained retrospectively using data from 990 patients in I-SPY 2. Recently, new breast cancer subtypes based on gene expression and pathologic response were proposed by Wolf et al [1]. Their study predicted that drug allocation by the new response-predictive subtype (RPS) would lead to a higher pathologic complete response (pCR) rate than allocation based on HR/HER2 subtypes. In this project, we evaluated the MRI model optimized by RPS and compared it with the HR/HER2 optimized model.

Methods: A total of 990 patients enrolled in I-SPY 2 and randomized to one of 9 drug arms or control were evaluated in this analysis. Functional tumor volume (FTV) was calculated from dynamic-contrast enhanced MRI [2] performed pretreatment (T0), after 3 weeks of treatment (T1), and between sequential drug regimens (T2). pCR was assessed at surgery after treatment was completed. HR/HER2 subtype was defined by HR and HER2 +/-, which resulted in four subtypes: HR+/HER2-, HR+/HER2+, HR-/HER2+, and HR-/HER2- (triple negative). RPS subtype was defined by immune, DNA repair deficiency (DRD), HER2, and BluePrint (BP) subtype (Agendia) biomarkers to define five subtypes: HER2-/Immune-/DRD-, HER2-/Immune+, HER2-/Immune-/DRD+, HER2+/BP-HER2_or_Basal, and HER2+/BP-Luminal. A logistic regression model using at least 1 FTV variable (value at T0, percent change at T1 or T2) was analyzed for predicting pCR. AUC (area under the receiver operating characteristic curve) was used to identify the optimal logistic regression model (highest AUC) in each biomarker-defined subset. For multi-predictor analysis, 10-fold cross validation was used.

Results: 854 patients (301 pCRs, 35%) with FTV evaluations at T0, T1, and T2, HR/HER2 and RPS subtypes, and pCR outcomes were included. Numbers of patients and pCR rates in individual subtypes are listed in Table 1. Of FTV variables, percent change at T2 was selected for inclusion in almost all subtype specific optimal models except HR+/HER2+. FTV at T0 (pretreatment tumor volume) was included in triple negative, HER2-/Immune+, and HER2+/BP-HER2_or_Basal models. Using the current HR/HER2-specific model, the highest AUC (0.74) was found in triple negatives and the lowest AUC (0.68) was in HR+/HER2+. Using the proposed RPS-specific model, the highest AUC (0.84) was found in HER2-/Immune-/DRD+ and the lowest AUC (0.59) was found in HER2+/BP-Luminal cohorts. Table 1 shows AUCs estimated using predictions generated by HR/HER2- versus RPS-specific models, in the full cohort and in individual HR/HER2 sub-cohorts. AUCs were improved when RPS-specific models were used in full and in HR+/HER2-, HR+/HER2+, and triple negative cohorts. No improvement was observed in the HR-/HER2+ cohort where 97% (72/74) were HER2+/BP-HER2_or_Basal.

Conclusion: Improved prediction of pCR was observed using the RPS-specific MRI model compared to the current HR/HER2-specific model. A new preRCB workflow is being developed to combine MRI-based prediction with core biopsy assessment to re-direct “good responders” to surgery earlier and more precisely based on a patient’s biological subtype.

	N	pCR rate	AUC by HR/HER2	AUC by RPS
Full	854	35% (n=301)	0.77	0.80
HR+/HER2-	336	19% (n=65)	0.71	0.82
HER2-/Immune-/DRD-	177	5% (n=9)		
HER2-/Immune-/DRD+	29	31% (n=9)		
HER2-/Immune+	130	36% (n=47)		
HR+/HER2+	141	38% (n=54)	0.68	0.77
HER2+/BP-HER2_or_Basal	87	55% (n=48)		
HER2+/BP-Luminal	54	11% (n=6)		
HR-/HER2+	74	66% (n=49)	0.73	0.69
HER2+/BP-HER2_or_Basal	72	65% (n=47)		
HER2+/BP-Luminal	2	100% (n=2)		
Triple negative	303	44% (n=133)	0.75	0.76
HER2-/Immune-/DRD-	75	23% (n=17)		
HER2-/Immune-/DRD+	36	50% (n=18)		
HER2-/Immune+	192	51% (n=98)		

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P4-02-12

Validation of Profile for the Omission of Local Adjuvant Radiotherapy (POLAR) in early-stage invasive breast cancer patients of the Scottish Conservation Trial

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Background: Adjuvant whole breast radiotherapy (RT) is provided to almost all women with early-stage invasive breast cancer after breast conserving surgery and appropriate systemic therapy. While there is increasing interest to personalize the use of RT based on molecular profiling, to date, there is no molecular signature available to reliably assess the benefit of radiotherapy after surgical resection. Here we assess the ability of a 16-gene signature named Profile for the Omission of Local Adjuvant Radiotherapy (POLAR) to identify who may be suitable candidates for radiotherapy omission in patients of the Scottish Conservation Trial. Methods: The POLAR signature was applied to archival tissue from the Scottish Conservation Trial, which randomized 585 patients with stage I-II breast cancer, tumor size < 4 cm, and age ≤70 years old to receive RT or not. The archival tissue was measured for ER (ER+ >10%), PgR (PgR+ ≥20%), Ki67 (Ki67 high ≥14%), and HER2 (HER2+ defined as HER2 over-expressed or amplified). 26% received adjuvant chemotherapy, the remainder received tamoxifen 20 mg/daily for 5 years. Cox models for the locoregional recurrence (LRR) endpoint tested the association between treatment arms separately for patients with a low and high POLAR score using a pre-specified cut point. Cumulative incidences were computed, with distant metastasis and death without recurrence considered competing events. Results: 224 patients had tissue available and complete clinical data for analysis, 40 (18%) were node-positive. The distribution of clinicopathologic variables between the RT and no RT arms remained balanced. 43% were ER+/PgR+/Ki67 low/HER2-, 31% were ER+/HER2-/Ki67 high or PgR-, 5% were HER2+, and 13% were triple negative. The continuous standardized POLAR score was prognostic for LRR in the no RT arm after adjusting for relevant covariates (HR=1.78 [1.20-2.64], p=0.003). For patients with a POLAR-high score, the 10-year LRR rate was 31% [21%-42%] for patients not receiving RT and 8% [3%-15%] for patients receiving RT (HR 0.36 [0.19-0.69], p=0.0022). For

patients with a POLAR low score, the 10-year LRR rates were 20% [10%-33%] for patients not receiving RT and 6% [1%-18%] for patients receiving RT; HR=0.28 [0.08-0.98], p=0.046). In the subgroup of node-negative patients with ER+/HER2-negative tumors (N=137), there was a statistically significant RT benefit for patients with a POLAR high score (HR=0.31 [0.11-0.88], p=0.028) but not for patients with a POLAR low score (HR=0.5 [0.1-2.4], p=0.39). Conclusions: For patients with early-stage invasive breast cancer treated with breast-conserving surgery without RT, POLAR is prognostic for LRR and may refine the selection of “low risk” for omission of RT.

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Homologous recombination deficiency, RB-loss gene signatures, intrinsic subtype and response to neoadjuvant treatment in HR+/HER2- early breast cancer: a correlative analysis of two phase II trials

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Background: Hormone-receptor (HR)+/HER2- breast cancer (BC) is a biologically heterogeneous disease. Homologous recombination deficiency (HRD) and BRCA mutations have been previously reported to be associated with worse outcomes in HR+/HER2- metastatic BC patients receiving CDK4/6 inhibitors and endocrine therapy. Here, we assess the relation between HRD and RB-loss signatures, intrinsic subtyping, the PAM50-based chemo-endocrine score, and response to chemotherapy-based therapy and endocrine treatment in HR+/HER2- early BC. Methods: GIADA is a multicentric neoadjuvant phase II trial that treated premenopausal patients with Luminal B (LumB)-like BC (HR-positive, HER2-negative, with Ki67>20% and/or histologic Grade 3) with a combination of chemotherapy, immunotherapy and endocrine treatment. Expression of 758 genes on baseline tumor samples from all 43 patients was quantified by nCounter platform. The LETLOB phase II trial randomized postmenopausal women with clinical stage II-IIIa HR+/HER2- BC to neoadjuvant letrozole + lapatinib or letrozole + placebo for 6 months (Guarneri, JCO 2014). Gene-expression data (Affymetrix platform) from pre-treatment frozen core-biopsies was available from 66 out of 92 pts enrolled. Intrinsic subtype was assigned using a research-based PAM50 subtype predictor. A published HRD signature (Peng, Nat Commun 2014) and a signature of RB loss (RBSig), previously reported to potentially predict resistance to CDK4/6 inhibitors in HR+/HER2- BC (Malorni, Oncotarget 2016) were computed. The PAM50 based chemo-endocrine score (CES) was calculated using published definition (Prat, CCR 2017). Higher values of CES indicate increased endocrine sensitivity, while lower values indicate chemosensitivity. Association between genomic

signatures was assessed through Pearson's correlation coefficient. Association of genomic signatures with pCR was assessed through logistic regression and association with PEPI scores was assessed through Kruskal-Wallis test. Results: HRD signature levels were significantly higher in non-luminal (Basal-like and HER2-enriched) tumors as compared to Luminal (A or B) tumors ($p > 0.001$ in the GIADA trial, $p = 0.021$ in the LETLOB trial). Moreover, higher levels of HRD signature were associated with higher levels of RB-loss signature (Pearson correlation 0.355, $p = 0.020$ in the GIADA trial; Pearson correlation 0.942, $p < 0.001$ in the LETLOB trial), higher levels of Basal-like signature (Pearson correlation 0.502, $p < 0.001$ in the GIADA trial; Pearson correlation 0.373, $p = 0.002$ in the LETLOB trial) and lower levels of CES (Pearson correlation -0.422, $p = 0.005$ in the GIADA trial; Pearson correlation -0.763, $p < 0.001$ in the LETLOB trial), indicative of higher chemosensitivity. In the GIADA trial, higher levels of HRD signature ($p = 0.018$) and RBloss signature ($p = 0.073$) and lower levels of CES ($p = 0.007$) were associated with higher pCR rates after chemo, endocrine and immunotherapy. In the LETLOB trial, lower levels of HRD signature ($p = 0.068$) and RBloss signature ($p = 0.042$) and higher levels of CES ($p = 0.050$) were associated with higher sensitivity to endocrine treatment (lower PEPI scores, 0 vs 1-3 vs 4 or more, after neoadjuvant letrozole). Conclusions: In HR+/HER2- early BC, HRD gene signatures, RB-loss gene signatures and non-luminal (especially Basal-like) intrinsic subtyping are associated with each other and associated with higher sensitivity to chemotherapy-based therapy and lower sensitivity to endocrine treatment. These observations might help correctly tailor systemic therapy, including biologic agents, in patients with HR+/HER2- early and advanced BC.

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12/8/2022

7:00 AM - 8:15 AM

P4-02-14

Gain of HER2 Amplification in Patients with HR+/HER2- and Triple Negative Early Breast Cancer Treated with Neoadjuvant Chemotherapy

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Background: Neoadjuvant chemotherapy (NAC) is standard of care for the majority of patients with clinical stage II-III triple negative breast cancer (TNBC) and is considered in high-risk patients with hormone receptor positive (HR+)/ human epidermal growth factor receptor 2 (HER2) negative (-) tumors, with expected pathological complete response (pCR) rates of 40-60% and 10-12%, respectively. In HER2- patients with residual disease (RD) after NAC, there is limited data on rates of gain of HER2 amplification. The biological and clinical significance of this phenomenon is unknown and determining the best adjuvant therapy for these patients

remains a challenge. We sought to determine the rate of HER2 gain in a cohort of consecutive patients with HER2- breast cancer (BC) treated with NAC.

Methods: From 01/2021 to 12/2021, we identified patients with HER2- breast cancer treated with NAC followed by surgery at our institution. Patients who received neoadjuvant endocrine therapy were excluded. The rates of pCR (ypT0/is ypN0) and HER2 status pre- and post-NAC were assessed. Estrogen receptor (ER), progesterone receptor (PR) and HER2 status on surgery specimens were internally determined for all patients using ASCO/CAP 2020 guidelines. ER-low was defined as ER expression by immunohistochemistry (IHC) 1-10%.

Results: We included 256 patients, 130 (51%) HR+/HER2- [13/130(10%) ER-low] and 126 (49%) TNBC. Median age was 48 years (range 25-82) and the majority presented with clinical T2 (57%) and N1 (59%). Of 130 patients with HR+/HER2-tumors, 120 (92%) received dose-dense (dd) doxorubicin/cyclophosphamide-paclitaxel (AC-T). Of 126 TNBC patients, 46 (37%) received ddAC followed by carboplatin in combination with paclitaxel +/- pembrolizumab. Centralized HER2 status assessment on the core biopsy was performed in 22% of samples. Overall, pCR was achieved in 40% of TNBC and 11% of HR+/HER2-. Among the 192 patients with RD, the rate of HER2 gain was 8/192 (4%), including 3% (2/76) of TNBC and 5% (6/116) of HR+/HER2- patients. 7 of the 8 patients (88%) converted from IHC 1+ or 2+ fluorescence in situ hybridization (FISH) not amplified on core biopsy to IHC 2+ FISH amplified on the surgical specimen. In only 1 case, the HER2 status converted from IHC2+ FISH not amplified to IHC3+. 3/8 patients had multifocal disease. All 6 patients with HR+/HER2- BC and HER2 gain had high (>90%) ER expression (Table 1). All but one patient with HER2 gain received adjuvant anti-HER2 therapy. After a median follow-up of 10 months, no recurrence events occurred in this group. 12 of the remaining 184 patients experienced a recurrence [11 distant recurrences (8 and 3, in the TNBC and HR+/HER2- groups, respectively), and there was 1 local event (localized chest wall recurrence) in the HR+/HER2- group].

Conclusions: At a single center, we found that in patients with HER2- BC treated with NAC, HER2 gain in patients with RD was uncommon and occurred more frequently in those with HR+ tumors. Analysis of a larger cohort is ongoing to corroborate these results. It remains to be determined if this phenomenon represents a true HER2 status conversion or tumor heterogeneity.

Table 1

Pts	Age at dx	NAC	ER/PR bx %	HER2 IHC bx	FISH Ratio bx	FISH CN bx	Internal HER2 on bx (Yes/No)	ER/PR surg %	HER2 IHC surg	FISH Ratio surg	FISH CN surg	Final path	Post-NAC therapy
1	45	ddAC-T	95/94	1+	-	-	Yes	95/35	2+	3.35	8.4	ypT2y pN1	V/HP, AI
2	63	ddAC-T	100/15	2+	1.2	3.3	No	99/5	2+	1.94	7.7	ypT1 ypN1	AI alone
3	44	ddAC-TCb/Pembro	0/0	1+	-	-	No	0/0	2+	3.36	7.6	ypT1b ypN1mi	Pembro-HP
4	36	ddAC-T	100/90	1+	-	-	No	95/95	2+	2.6	5.4	ypT1 ypN1	V/HP, AI
5	64	ddAC-T	95/100	1+	-	-	Yes	NA	2+	3.1	6.1	ypT2 ypN2a	HP + AI
6	53	TCx4	99/90	2+	1.5	3.3	No	95/65	2+	2.04	7.49	ypT2 ypN1	THP
7	67	ddAC-T	95/95	1+	-	-	No	99/70	2+	2.58	5.6	ypT2 ypN1	T-DM1
8	82	TCx4	0/0	2+	1.6	5.6	Yes	0/0	3+	-	-	ypT2 ypN1	TH

Abbreviations: Pts: patients; NAC: neoadjuvant chemotherapy; Bx: biopsy; Surg: dx diagnosis; FISH: fluorescence in situ hybridization; CN: copy number; path: pathology; Pembro: pembrolizumab; HP: trastuzumab and pertuzumab; V: Vinorelbine; AI: aromatase inhibitor; TC: Taxotere/cyclophosphamide; Cb: carboplatin; ddAC-T: dose dense anthracycline, cyclophosphamide followed by paclitaxel; TH: paclitaxel and trastuzumab; NA: not available.

Clinico-pathological characteristics of patients with HER2 gain on residual disease

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12/8/2022

7:00 AM - 8:15 AM

P4-02-16

Prognostic and Predictive Capacity of Tumor Infiltrating Lymphocytes in the MA.20 regional radiotherapy trial

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Background: The benefit of regional nodal irradiation (RNI) in patients with low burden metastatic axillary disease was established in MA.20 showing that patients randomized to receive adjuvant whole breast irradiation (WBI) plus RNI experienced a significantly better disease free survival (DFS) and distant disease free survival (DDFS) compared to those who received WBI alone and this advantage was maintained in the hormone receptor negative subgroup. Stromal tumor infiltrating lymphocytes (sTILs) have shown prognostic and predictive value in HER2 positive and triple negative breast cancers. To date, clinical importance of immune infiltrates as prognostic and predictive biomarkers in the context of benefit from RNI has not been shown. Methods: 1064 full-face hematoxylin and eosin (H&E) stained sections and formalin fixed paraffin embedded primary tumor blocks assembled into 16 tissue microarrays (TMAs) in quadruplicates linked with clinical data were accessible from the original 1832 patients in the MA.20 trial for this retrospective-prospective translational study conducted according to the REMARK guidelines. sTILs were assessed on scanned images of H&E sections according to the International Immuno-Oncology Working Group method, and on TMAs by CD8 immunohistochemistry (IHC) using a validated assay. Biomarkers were scored by pathologists blinded to the clinical data and analyzed as continuous and categorical variables using prespecified median cutpoints. The median follow-up was 9.5 years. Cox proportional regression modelling was used after adjusting for clinicopathological factors and treatments. Hazard ratios (HR) with 95% confidence intervals (CI) were reported for the primary endpoint of DFS and secondary endpoint of DDFS. Predictive value was assessed by the interaction test between the treatment arm and the biomarkers in the full cohort and an IHC defined non-luminal A subgroup. Results: 1035 cases were evaluable for sTILs on H&E sections. Of these 52.6% (n=544) cases with $\geq 10\%$ sTILs displayed a significant correlation with age < 50 years, grade III, tumor size >2cm, hormone receptor negative status, and non-luminal A subgroup ($p < 0.05$). Of the 857 evaluable cases on TMAs, CD8+sTILs (≥ 16) were observed in 49.8% (n=427) cases and showed a significant association with grade III, ER negativity and non-luminal A status ($p < 0.05$). For the full cohort, H&E sTILs assessed as a continuous parameter, were not prognostic for DFS (HR 0.993; 95% CI 0.984-1.003; $p=0.18$) but provided prognostic information for DDFS (HR 0.988; 95% CI 0.977-0.999; $p=0.04$) in multivariate analyses. H&E sTILs did not show predictive value as a continuous variable. Similarly, using the prespecified cutpoint ($\geq 10\%$), H&E sTILs were neither prognostic nor predictive. Increasing level of CD8+sTILs was associated with significantly improved DFS (HR 0.99; 95% CI 0.983-0.998; $p=0.02$) and DDFS (HR 0.98; 95% CI 0.97-0.99; $p=0.002$) in multivariate analyses. For the full cohort, CD8+sTILs as a continuous variable, showed a significant improvement in DDFS for patients randomized to WBI and RNI (HR 0.979; 95%CI 0.959-0.999; $p(\text{interaction}) = 0.04$) compared to WBI alone and a trend (HR 0.977; 95%CI 0.954-1.001; $p(\text{interaction}) = 0.06$) for better outcome was observed for the non-luminal A subgroup. CD8+sTILs at the prespecified cutpoint (≥ 16) were not prognostic or predictive. Conclusions: Pre-treatment tumoral infiltration with stromal lymphocytes provided positive prognostic information for DFS (CD8+sTILs) and DDFS (H&E sTILs and CD8+sTILs) when examined as a continuous variable but failed to do so at prespecified cutpoints. While CD8+sTILs as a continuous variable predicted benefit from RNI, significant prediction results were not seen for prespecified cutpoint or related biomarker H&E sTIL. These results require further validation.

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12/8/2022

7:00 AM - 8:15 AM

P4-02-17

Impact of low hormone receptor expression on neoadjuvant chemotherapy response and patterns of care in early-stage HER2-negative breast cancer: a US National Cancer Database analysis

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Background: Hormone receptor (HR) low (1-10%) HER2-negative breast cancer (BC) is emerging as a distinct subtype with similarities in clinical outcomes to triple-negative BC. However, there is a lack of consensus on treatment recommendations for chemo-immunotherapy and endocrine therapy in this subset. Here, we present results from a US National Cancer Database (NCDB) analyses of patients with HER2-negative BC evaluating response to neoadjuvant chemotherapy (NAC) and patterns of care by HR expression.

Methods: Patients with stage I-III HER2-negative BC diagnosed in 2018 were identified in NCDB, a nationwide oncology outcomes database in the US. Quantitative HR expression was unavailable prior to 2018. Data were categorized into four groups by estrogen receptor (ER) and progesterone receptor (PR) expression: ER < 1% & PR < 1% (HR-Neg), ER 1-10% and/or PR 1-10% (HR-Low), ER > 11-30% and/or PR > 11-30% (HR-Int), ER > 30% and/or PR > 30% (HR-High). Those with undocumented HR status (3%) or without curative intent surgery (5%) were excluded. The primary outcome was pathologic complete response (pCR) by HR expression in those undergoing neoadjuvant chemotherapy. Key secondary objectives included

assessment of clinicopathologic characteristics and practice patterns. The categorical variables were compared between the four groups using a Chi-square test. Age was compared using a Kruskal-Wallis test.

Results: Out of 104,205 incident cases, 2541 (2.4%) were HR-Low and 1241 (1.2%) were HR-Int. Significant differences were found between HR groups with higher grade, clinical stage, and Ki-67 in HR-Low vs. HR-Int or HR-High groups (Table 1). Patients with HR-Low and HR-Int BC were more likely to receive chemotherapy than HR-High (74%, 70% vs. 20%; $p < 0.001$) and the use of adjuvant endocrine therapy correlated with HR expression. Only half of patients in the HR-Low group received any endocrine therapy compared to higher rates in the HR-Int and HR-High groups (52% vs. 74%, 92%; $p < 0.001$). pCR rates in those receiving neoadjuvant chemotherapy were significantly different by HR status, with higher pCR rates in HR-Low vs. HR-High groups ($p < 0.001$) (Table 2). NAC utilization significantly differed between groups. A higher proportion of patients with HR-Low BC received NAC than other HR-positive groups ($p < 0.001$). Additionally, there was an increased use of NAC in patients with HR-Low BC treated at academic vs. community cancer centers ($p < 0.001$).

Conclusions: This is one of the largest real-world analyses comparing key differences in biology and practice patterns of HR-Low, HER2-negative BC. Consistent with prior studies, we report HR-Low BC to be a rare and distinct subtype with higher pCR rates compared to HR-High BC. Practice patterns show wide variability in utilization of neoadjuvant chemotherapy and endocrine therapy for these patients. Future studies should address this disparity and enhance representation of patients with HR-Low BC in clinical trials to improve long-term outcomes.

Table 1: Patient demographics

Variable		HR-Neg (n=13776)	HR-Low (n=2541)	HR-Int (n=1241)	HR-High (n=86647)	Total (n=104205)
Age at Diagnosis	Median [IQR] (min, max)	60 [49, 69] (19, 90)	59 [49, 70] (18, 90)	59 [49, 69] (19, 90)	64 [54, 72] (19, 90)	63 [53, 71] (18, 90)
	Sex	Female 13737 (100%)	2530 (100%)	1239 (100%)	85837 (99%)	103343 (99%)
	Male	39 (0%)	11 (0%)	2 (0%)	810 (1%)	862 (1%)
Race	White	9936 (72%)	1831 (72%)	878 (71%)	73240 (85%)	85885 (82%)
	Black	3036 (22%)	533 (21%)	246 (20%)	7680 (9%)	11495 (11%)
	Other	697 (5%)	158 (6%)	104 (8%)	5063 (6%)	6022 (6%)
	Unknown	107 (1%)	19 (1%)	13 (1%)	664 (1%)	803 (1%)
Facility Type	Academic/Research Program	4061 (29%)	641 (25%)	351 (28%)	25388 (29%)	30441 (29%)
	Community Cancer Program	891 (6%)	189 (7%)	70 (6%)	6114 (7%)	7264 (7%)
	Comprehensive Community Cancer Program	4985 (36%)	1012 (40%)	487 (39%)	35293 (41%)	41777 (40%)
	Integrated Network Cancer Program	2595 (19%)	435 (17%)	208 (17%)	17270 (20%)	20508 (20%)
	Unknown	1244 (9%)	264 (10%)	125 (10%)	2582 (3%)	4215 (4%)
Clinical Stage	Stage 1	5730 (42%)	1158 (46%)	562 (45%)	73657 (85%)	81107 (78%)
	Stage 2/3	8046 (58%)	1383 (54%)	679 (55%)	12990 (15%)	23098 (22%)
Tumor grade	1	259 (2%)	122 (5%)	78 (6%)	29814 (34%)	30273 (29%)
	2	2634 (19%)	484 (19%)	289 (23%)	40652 (47%)	44059 (42%)
	3	9863 (72%)	1746 (69%)	785 (63%)	8739 (10%)	21133 (20%)
	Unknown	1020 (7%)	189 (7%)	89 (7%)	7442 (9%)	8740 (8%)
Ki-67 (%)	<10	498 (4%)	135 (5%)	84 (7%)	15561 (18%)	16278 (16%)
	10-50	1759 (13%)	374 (15%)	206 (17%)	23932 (28%)	26271 (25%)
	>50	4075 (30%)	725 (29%)	351 (28%)	3200 (4%)	8351 (8%)
	Missing/Unknown	7444 (54%)	1307 (51%)	600 (48%)	43954 (51%)	53305 (51%)
Breast surgery	Partial mastectomy (lumpectomy)	7488 (54%)	1363 (54%)	693 (56%)	57759 (67%)	67303 (65%)
	Mastectomy	6245 (45%)	1170 (46%)	547 (44%)	28683 (33%)	36645 (35%)
	Other/Unknown	43 (0%)	8 (0%)	1 (0%)	205 (0%)	257 (0%)
Chemotherapy use	Yes	11175 (81%)	1883 (74%)	866 (70%)	17304 (20%)	31228 (30%)
	No	2485 (18%)	628 (25%)	368 (30%)	68671 (79%)	72152 (69%)
	Unknown	116 (1%)	30 (1%)	7 (1%)	672 (1%)	825 (1%)
Hormone therapy recommended or given	Yes	532 (4%)	1313 (52%)	921 (74%)	79718 (92%)	82484 (79%)
	No	13183 (96%)	1203 (47%)	308 (25%)	6381 (7%)	21075 (20%)
	Unknown	61 (0%)	25 (1%)	12 (1%)	548 (1%)	646 (1%)

Table 2: Neoadjuvant chemotherapy response amongst differing HR expression levels

Neoadjuvant chemotherapy response	HR-Neg (n=6220)	HR-Low (n=1051)	HR-Int (n=409)	HR-High (n=9383)	Total (n=17063)	p-value
Pathologic complete response	2003 (32%)	332 (32%)	105 (26%)	452 (5%)	2892 (17%)	<0.001
Partial response	1318 (21%)	219 (21%)	61 (15%)	1844 (20%)	3442 (20%)	
No response	371 (6%)	58 (6%)	34 (8%)	756 (8%)	1219 (7%)	
Unknown/Not documented	2528 (41%)	442 (42%)	209 (51%)	6331 (67%)	9510 (56%)	

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7:00 AM - 8:15 AM

P4-02-18

Impact of clonal hematopoiesis on disease progression following CDK4/6 inhibitor therapy

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Background Clonal Hematopoiesis (CH) is a well-established risk factor for adverse clinical outcomes including all-cause mortality, cardiovascular disease, and progression to hematologic malignancies. The presence of CH has been shown to adversely impact overall survival in non-hematologic cancers, however whether CH modulates response to specific therapies in breast cancer is not known. Here we investigate the impact of CH mutations on disease progression in patients with metastatic estrogen receptor (ER) positive breast cancer undergoing treatment with first line CDK4/6 inhibitors and endocrine therapy (CDK4/6i+ET). Methods We analyzed data from a well annotated cohort of patients with ER+ breast cancer who received endocrine therapy and CDK4/6 inhibitors. All patients underwent prospective tumor and matched WBC sequencing utilizing the MSK-IMPACT assay. CH variants were detected in blood samples utilizing the well-validated variant detection and filtration pipeline of MSK-IMPACT. CH mutations were defined as putative drivers (CH-PD) or non-putative drivers (CH) as previously described. To ensure the presence of CH at the time of therapy initiation, only patients who had CH sampling performed from 6 months before through 4 months after initiation of CDK4/6i+ET were included. We compared progression free survival (PFS) in patients with and without CH, as well as by CH-PD status and DNMT3A CH mutations. We investigated clinical covariates including type of endocrine therapy, receipt of prior neoadjuvant or adjuvant chemotherapy, and age at start of CDK4/6i+ET. Results The final cohort was comprised of 378 patients, of whom 135 (35.7%) had CH. The median time between sample collection and CDK4/6i+ET initiation was 0 (IQR -0.79 to 0.47 months). Patients with CH were older at time of therapy initiation (median 63.0 versus 54.7 years, $p < 0.001$). There were no significant differences between groups in terms of endocrine therapy (aromatase inhibitor or fulvestrant), prior chemotherapy, and time from CH sample collection to CDK4/6i+ET start. Univariate Cox-proportional hazard analysis did not reveal a difference between progression free survival and overall CH (HR 0.96, 95% CI 0.75 – 1.23, $p = 0.76$), CH-PD (HR 1.05, 0.77 – 1.43, $p = 0.77$), or DNMT3A mutations (HR 1.12, 0.80 – 1.60, $p = 0.52$) compared to patients without CH. Interestingly, age less than 60 years was found to be associated with PFS outcome (univariate HR 1.57, 1.22 – 2.01, $p = 0.0004$). Multivariate analysis adjusted for endocrine therapy partner and age at CDK4/6i+ET therapy did not reveal an association between outcome and overall CH (HR 1.07, 0.83 – 1.39, $p = 0.59$). In patients younger than age 60, presence of overall CH did not confer a significant PFS difference (HR 0.90, 0.63 – 1.29, $p = 0.57$). In the subset of patients older than 60 ($n = 168$) presence of CH conferred numerically, but not statistically, significant shorter PFS (HR 1.41 [0.96 – 2.09], $p = 0.08$). In this population, CH-PD conferred a shorter PFS (HR 1.75, 1.12 – 2.72, $p = 0.02$). Conclusion We found that CH, CH-PD and DNMT3A CH mutations did not affect PFS among metastatic ER+ breast cancer patients treated with first line CDK4/6 inhibitors. Younger age was associated with increased risk of progression, warranting further investigation. In the subset of patients with age older than 60, CH-PD conferred a shorter PFS. Further data, incorporating records of dose reductions, will be presented at the meeting.

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Jacqueline Tao, MD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-02-19

Development of a Novel Imaging Biomarker to Ascertain Responsiveness to Immunotherapy

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Background: Immunotherapy has emerged as an essential treatment modality for enhancing survival in triple negative breast cancer (TNBC). Despite demonstrated improvements in pathologic complete response (pCR), both toxicity and adverse events from immuno-oncology (IO) drugs remain a significant limitation. Currently, a lack of tests to differentiate patients likely to respond to IO vs. poor responders precludes a tailored approach to immunotherapy. Here we describe an imaging biomarker that allows physicians to target breast cancer patients with the highest likelihood of response to immunotherapies. Methods: We identified a rapidly assessable, non-invasive biomarker of tumor response to immunotherapy. This biomarker uses

radiological imaging (DCE-MRIs) coupled with the biophysical simulation platform TumorScope® to predict a patient's likelihood of pCR following treatment with immunotherapy and backbone chemotherapy. While this biomarker does not depend on transcriptomic data, it was designed by matching biological function (transcriptomics) to tumor microenvironmental features (as observed in biophysical simulations) derived from the SimBioSys TumorBank®. With this simulation-derived biomarker in hand, we validated our methods in a small, independent cohort. We additionally applied the SimbIOScope IO-prediction analysis to assess a large immunotherapy-naïve cohort, in order to validate if an increase in pCR rates in the presence of immunotherapy correlated with the anticipated rate of response to immunotherapy. Results: In TNBC tumors prior to neoadjuvant therapy, we found that a high immune evasive capability was associated with low nutrient utilization. Tumor immune evasion (including the PD-1/PDL-1 axis) is strongly correlated with tumor hypoxia ($r = 0.45$, $p < 1 \times 10^{-6}$). Similarly, in HR+/HER2- tumors prior to neoadjuvant therapy, we found that immune evasion was negatively correlated with angiogenesis ($r = -0.40$, $p = 0.006$), suggesting that low tumor vascularization is associated with immune evasion capability. As these associations were identified from available transcriptomic data obtained from a single biopsy site within each patient's tumor, they were unable to account for tumor heterogeneity. We therefore sought to identify a spatially-resolved biomarker for immune evasive potential in TNBC and HR+/HER2- tumors. We used publicly available DCE-MRIs of patients treated with the immunotherapy drug pembrolizumab and paclitaxel from the ISPY2 trial ($n=63$) to train a model to predict pCR in IO-treated tumors. Critically, the resulting model's predictive power matched that obtained from transcriptomics data. SimbIOScope was then tested on IO-treated patients in a small, independent cohort and correctly predicted pCR in >91% ($n=12$). We further validated SimbIOScope by predicting the expected pCR rate in 292 patients from our virtual TumorBank in response to immunotherapy. Consistent with empirical increase (13.6% in TNBC, Keynote522) anticipated as seen from clinical trials, we found that SimbIOScope predicted a 14% increase in pCR rate in TNBC patients (and 9% increase in HR+ patients) with addition of immunotherapy versus chemotherapy backbone alone. Conclusions: The SimbIOScope platform offers physicians a rapid, non-invasive biomarker to differentiate patients likely to respond to immunotherapy from non-responders. This innovative technology thereby personalizes oncologic care and mitigates the potential for adverse effects by helping to optimize selection of patients best suited for immunotherapy.

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-02-20

Utility of the 70-gene signature and 10 year follow up in patients with early-stage breast cancer in a single institution study

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Introduction: Genomic tests are routinely used by clinicians to guide treatment decisions in early-stage breast cancer (EBC). The 70-gene MammaPrint assay (MP) assesses the risk of distant recurrence in untreated patients with EBC and categorizes the tumors as High Risk (HR, MP index: -1 to ≤ 0) or Low Risk (LR, >0 to $+1$). The LR category is further divided into Low but non-UltraLow (LNUL; >0 to ≤ 0.355) and UltraLow Risk (UL; >0.355 to 1). Here, we report the risk of distant recurrence by MP and 10-year outcomes in patients with EBC diagnosed at Magee Women's Hospital of the University of Pittsburgh Medical Center.

Methods: In this retrospective analysis, 259 women diagnosed with EBC between 2005 and

2008, who received a MP result, were included. Patient clinical and tumor characteristics were collected. The median FU was 13.1 year among patients with clinical data. Treatment received, 10-year Distant Metastasis Free Interval (DMFI) and 10-year Breast Cancer Specific Survival (BCSS) are reported according to the MP groups. Differences in DMFI and BCSS between MP risk groups were assessed by log-rank. Patients were treated at the physician's discretion. Treatment was started prior to obtaining MammaPrint results.

Results: Among the 259 patients, 69% were post-menopausal women (mean [range] age: 58 [31-81] years) and diagnosed with hormone receptor-positive HER2-negative tumors (90%), grade 1 or 2 (64%), and without lymph node invasion (93%). In this cohort, 69% (n = 159) had a MP LR result and 31% (n = 100) had a MP HR result. Overall, 14% (n = 35) of patients had a MP UL risk of recurrence of whom 74% (n = 26 / 35) were post-menopausal women. Substantially more patients received chemotherapy in the HR group (57%, n = 57) compared with the LR group (15%, n = 24) (table). Considering that treatment was initiated before MammaPrint results were known, MP results might have allowed chemotherapy de-escalation in 15% (n = 24) of patients with a MP LR. Similarly, in the 39% (n = 39) of women with a MP HR treated with endocrine therapy only, knowledge of MP results could have provided important information to add chemotherapy to the treatment plan.. In the MP UL group, 74 % (n = 26) of patients were treated with endocrine therapy only compared with those who received chemotherapy (9%, n = 3) and no adjuvant treatment (9%, n = 3). The 10-year DMFI and 10-year BCSS were higher in the LR compared with the HR group (table). When further stratifying the MP LR group in LNUL and UL, the 10y DMFI was 0.97 (95% CI; 0.94 – 1.00) and 1.00 for the MP LNUL and UL groups, respectively. Within the first 10 years, 8 of the 10 distant recurrences observed were in the MP HR group, and 2 were in the MP LNUL group. Among the 18 recorded deaths, 5 were breast cancer-related, 4 in the MP HR and 1 in the MP LR (LNUL) groups.

Discussion: In this single-institution retrospective analysis, all patients showed excellent BCSS and DMFI outcomes confirming the ability of MP to correctly predict the good prognosis (LR) and poor prognosis (HR) in patients with EBC. In this analysis, as observed in other cohorts, women with a MP UL risk result had an excellent prognosis at 10 years while being treated mostly with endocrine therapy only. Taken together, with the low endocrine therapy adherence reported in the literature, these data suggest that patients with a MP UL result may be candidates for further treatment de-escalation to optimize the risk/benefit ratio of endocrine therapy in future studies.

Table. Clinical outcomes and treatment received in patients stratified by MammaPrint results

	MammaPrint			
	High Risk (n=100)	Low Risk (n=159)	Low Risk (n=159)	
			Low Non-UltraLow Risk (n=124)	UltraLow Risk (n=35)
Probability of (95%CI)				
10y-DMFI	0.90 (0.84 – 0.96) ^{a,b}	0.98 (0.96 – 1.00) ^a	0.97 (0.94 – 1.00) ^b	1.00 ^b
10y-BCSS	0.96 (0.91 – 1.00) ^{c,d}	0.99 (0.98 – 1.00) ^c	0.99 (0.97 – 1.00) ^d	1.00 ^d
Treatment received*, n (%)				
ET Only	39 (39.0)	123 (77.4)	97 (78.2)	26 (74.3)
CT +/- ET	57 (57.0)	24 (15.1)	21 (16.9)	3 (8.6)

* Patients were treated at the physician's discretion

a p = 0.011, MP LR vs MP HR.

b p = 0.032, MP UL vs LNUL vs HR.

c p = 0.061 MP LR vs MP HR.

d p = 0.170, MP UL vs LNUL vs HR.

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7:00 AM - 8:15 AM

P4-02-22

Breast microcalcification chemistry predicts DCIS prognosis

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Introduction: Microcalcifications are a common feature in mammographic detection of ductal carcinoma in situ (DCIS), and occur in >80% of cases. Known to be present as type I (calcium oxalate-CaO) and type II (carbonated calcium hydroxyapatite-CHAP) microcalcifications, their association with DCIS and their role in the progression of DCIS to invasive breast cancer (IBC) remains unexplored. In an effort to understand the factors involved in DCIS prognosis, it is hypothesized that changes in the chemical composition of calcifications, in tandem with molecular changes in the surrounding soft tissue, will define patients with DCIS who will progress to develop IBC from those who remain with a stable DCIS phenotype. To this end, a novel label-free approach of hyperspectral imaging using mid-infrared (mid-IR) and Raman spectroscopy was used to probe calcification chemistry and molecular composition of the surrounding ductal and stromal soft tissue. The main aim of the work is to identify biomarkers for DCIS prognosis, based on chemical and molecular compositional changes of calcifications and the surrounding soft tissue. It is anticipated that the spectral biomarkers will provide patients and clinicians an informed risk assessment whether to undertake treatment for DCIS or to be placed under active surveillance. **Methods:** Tissue samples from 422 patient have been obtained and include (i) 'pure DCIS' (DCIS without recurrence) (n=193), (ii) 'DCIS with invasive recurrence' (DCIS from patients who subsequently were known to develop invasive disease) (n=123), (iii) 'DCIS plus contemporaneous invasive cancer' (n=44) and 'benign' (n=62) samples. Serial tissue sections were measured using mid-IR and Raman hyperspectral imaging approaches targeting the same calcification and soft tissue regions from specific DCIS ducts. Hyperspectral imaging data was initially pre-processed to digitally remove paraffin and unintended spectral interferences. The pre-processed data was subjected to cluster analysis followed by unsupervised and supervised machine learning classification models to identify spectral features associated with DCIS and its progression to IBC. **Results:** Cluster analysis based segmentation of hyperspectral images revealed histopathological features including calcifications, epithelium, necrotic areas, connective tissue and stroma. Spectra were extracted from each of the histopathological features using image coordinates, and biomodelling analysis was performed. Initial analysis of 314 calcification images from 170 patients with (i) 'pure DCIS' (n=118) and (ii) 'DCIS with invasive recurrence' (n=52) showed an area under the receiver operating characteristic (AUROC) mean value of 85% in distinguishing pure DCIS from DCIS that later recurred as IBC. The calcification features appeared to indicate pathology specific changes in phosphate and carbonate content as well as changes in magnesium whitlockite content. Similar analysis of the surrounding soft tissue spectral features showed an AUROC mean value of 85% (necrotic regions surrounding calcifications) and 76% (epithelium) respectively. The epithelial features showed changes in protein secondary structure and content, which together with the calcification changes indicate structural remodelling in DCIS that progresses to IBC, from those that do not. **Perspectives:** In the ongoing analyses of imaging data from 422 patients, it is anticipated that molecular/structural features from calcification and soft tissue imaging data will provide important cues in understanding DCIS prognosis and could be a promising way forward in determining management of DCIS risk and treatment underpinned by the identification of specific discriminatory spectral markers. **Acknowledgments:** This work was supported by Cancer Research UK and by KWF Kankerbestrijding (ref. C38317/A24043).

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7:00 AM - 8:15 AM

P4-02-23

Integrating tumor-intrinsic and immunological factors to improve locoregional treatment individualization of high-risk breast tumors

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Background: The influence of the local immune infiltrate on tumor progression is dependent on tumor-intrinsic characteristics. Among highly aggressive subtypes, an immune infiltrate is associated with a favorable prognostic effect. The aim was to investigate whether the integration of histological grade and degree of tumor-infiltrating lymphocytes (TILs) permits improved treatment individualization for clinically high-risk tumors. Methods: The SweBCG91RT trial included 1178 patients with stage I-IIA breast cancer, randomized to breast-conserving surgery with or without adjuvant RT, and followed for a median time of 15.2 years. In total, 8% were treated with systemic therapy. Histological grade and TILs were evaluated on whole-tissue sections by board-certified pathologists. Grade III tumors were compared to grade I and II tumors. TILs were classified as high ($\geq 10\%$) or low ($< 10\%$). The primary endpoint was ipsilateral breast tumor recurrence (IBTR) within 10 years. Results: In total, 134 (57%) of the 235 grade III tumors had high TIL levels compared to grade I/II tumors where 142 (19.7%) out of 721 tumors exhibited high TIL levels. Grade III tumors with high TILs had a reduced risk of IBTR (HR 0.49, CI 95% 0.26-0.91, $p=0.025$) compared to grade III tumors with low TILs (HR 1.0). Among grade I/II tumors, high TILs was not prognostic (HR 1.02, CI 95% 0.62-1.68,

p=0.95) compared to grade I/II tumors with low TILs (HR 1.0). Grade III tumors with low TILs had a high risk of recurrence without RT (36.2%) and derived benefit from RT (HR 0.16, CI 95% 0.047-0.53, p=0.0029). In contrast, grade III tumors with high TILs had a lower risk of IBTR without RT (14.5%) and did not benefit significantly from RT (HR 0.71, CI 95% 0.26-1.90, p=0.50). Conclusion: Measurements of the local immune infiltrate may improve treatment individualization when integrated with tumor-intrinsic features of aggressivity, such as histological grade. High-risk tumors with an immune infiltrate may be candidates for RT de-escalation.

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Erik Holmberg, PhD: PFS Genomics (pre-commercial company acquired by Exact Sciences):

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Per Karlsson, MD, PhD: Exact Sciences: Patents pending (Ongoing), Royalty (Ongoing);

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P4-02-24

A 3D Visualization and Prediction Device for Breast Cancer Surgeons and their Patients

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Background: Despite chemotherapeutic advances, surgery remains a putative treatment modality for breast cancer. The type of surgery chosen, and its ultimate clinical and cosmetic consequences, depends on a surgeon's ability to accurately assess a tumor's size, distribution, and position in the breast relative to anatomical landmarks. Moreover, in cases in which the tumor-to-breast volume ratio is substantial, neoadjuvant chemotherapy (NAC) offers the potential to shrink a tumor such that enhanced cosmesis or breast-conserving surgery becomes possible. Therefore, doctors must not only build an accurate picture of the current tumor shape, size and location, but anticipate how they might change over time and during treatment. SimBioSys' TumorSight (TSi) offers doctors the ability to simulate the way a patient's tumor might respond to various drug therapies, volumetrically and morphologically. These predictions are critical for surgical planning, in which a patient's eligibility for breast-conserving surgery depends on the spatial distribution of the tumor. Primarily, this means consideration of (1) tumor multicentricity, (2) the extirpative tumor-to-breast volume ratio, and (3) the distance from the

tumor to nipple. TSi provides physicians with estimates of each of these three key metrics, in 3D, over time, and as a function of regimen, to facilitate accurate evaluation, visualization and forecasting of NAC response with respect to surgical planning. Methods: TSi was used to create 3D models across multiple patient cohorts using DCE-MRI. These included segmentations for skin, chest wall, nipple, adipose tissue, glandular tissue, vasculature, and tumor. Volumetric and morphological changes in the tumor and adjacent tissues were simulated throughout a chemotherapy treatment regimen, as described previously. The resulting tumor distributions were analyzed and compared to distributions in post-treatment MRI segmentations. Metrics of interest in this study were the distance of closest approach between the tumor and nipple, tumor volume-to-breast volume ratio, tumor convex hull-to-breast volume ratio, and whether the tumor was monocentric. Results: In a set of N=292 patients, both the predicted tumor volume and tumor volume from a post-treatment MRI segmentation were computed. We took the difference in these volumes, normalized by the total breast volume (also computed from an MRI segmentation), to assess how well TSi predicts the final tumor volume-to-breast volume ratio after treatment. We found that the median difference in this metric was $3.26e-07$, and 5th and 95th percentiles were 0.0035 and 0.0023, respectively. Similar performance was seen when using the volume of a convex boundary enclosing the tumor and a 1 cm margin (to simulate operative conditions). In a set of N=164 patients, the accuracy of our prediction of whether the tumor will be monocentric after treatment was assessed. We found that our simulations were 78.7% accurate in predicting monocentricity. Finally, in a set of N=134 patients, TSi predicted a distribution of changes in the closest distance between the nipple and tumor, with a median of 1.06 cm and standard deviation of 1.64 cm. In all studies, there was no difference in median values seen between cancer subtypes. Conclusion: The ability to accurately measure, visualize, and predict post-NAC metrics such as tumor-to-nipple distance, monocentricity, and tumor-to-breast volume ratio is critical to surgical planning in breast cancer. To assist in this planning, TSi provides a surgeon and their patient with a realistic three-dimensional representation of tumor volume, shape, and location in the breast, and reliably predicts how these metrics change during treatment.

Disclosure(s):

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7:00 AM - 8:15 AM

P4-02-25

Analysis of prognosis in different subtypes of invasive lobular carcinoma using a National Cancer Database Breast Cancer Registry of Japan

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[Introduction] Invasive lobular carcinoma (ILC) has different pathological and clinical features from invasive ductal carcinoma (IDC). ILC has more likely to be hormone receptor (HR) positive, and several studies reported that the prognosis of ILC was better than IDC. However, ILC also has different prognosis according to the subtypes as IDC does, and better prognosis of ILC might depend on their high HR positivity. Additionally, there are many reports that chemotherapy (CT) does not improve the prognosis of ILC due to the high positivity of HR. Therefore, we compared the prognosis of ILC and IDC in the same subtypes and considered necessity of CT for luminal ILC. ILC usually constitutes small population of invasive breast cancer. Thus, we have planed the analysis by using the Breast Cancer Registry (BCR) run on the National Cancer Database (NCD) in Japan. [Methods] 318,338 breast cancer patients were registered in BCR between 2004 and 2012. We selected 250,736 patients who were diagnosed as ILC or IDC. Patients with distant metastasis, those who did not receive surgery, and those who received preoperative therapy, and those who had bilateral breast cancer were excluded, and it resulted in 207,428 patients. Of these cases, the cases with 10-year follow-up data were 136,654, and we examined 5,705 ILC and 130,949, IDC. Because it was presumed that there are differences in pathological and clinical characteristics between ILC and IDC, we have planned to make the matched cohorts by using exact matching for comparing their prognosis. To evaluate the prognosis of each subtype, we compared DFS and OS for IDC and ILC in each subtype. To evaluate the effect of CT in luminal ILC, we corrected the data of luminal ILC with pT2N0M0 or pT1-2N1M0 patients and compared DFS and OS between endocrine therapy (ET) only group and ET+CT group. DFS was defined as the time from surgery to local or distant recurrence or death from any cause. OS was defined as the time between the surgery and the death from any cause. Peason's Chi squared test was used to identify the characteristics. Survival curves were constructed by Kaplan-Meier method and were compared by log-rank

test. [Results] We made the matched cohort by using exact matching and we identified 5,633 ILC and 5,633 IDC for prognosis analysis. In overall subtypes, the 10-year DFS of ILC was poor than those of IDC (76.56% vs 79.14%, $p=0.04$). In the analysis by each subtype, there was no statistical difference in DFS for luminal HER2, HER2, and TN cohorts, however luminal ILC had statistically significant poor DFS than luminal IDC (78.04% vs 81.17%, $p< 0.01$). The analysis of 10-year OS showed similar results, and there were no differences in the OS of luminal HER2, HER2 and TN cohorts between ILC and IDC. However, ILC had worse OS than IDC in luminal cohort (85.95% vs 89.13%, $p< 0.01$). To evaluate the effect of CT in luminal ILC, we made the matched cohort and we identified 95 luminal IDC and 95 luminal ILC in pT2N0 cohort, and 83 luminal IDC and 83 luminal ILC in pT1-2N1 cohort for the analysis. In pT2N0 cohort, the 10-year DFS was 82.12% in ET+CT group and 87.35% in ET only group ($p=0.99$). The OS of the ET+CT and the ET only group was 93.48% and 94.04% ($p=0.88$). In pT1-2N1 cohort, the ET only group had 54.17% and the ET+CT group had 77.03% of DFS ($p=0.34$). The OS in the ET only group and the ET+CT group was 61.96% and 94.81% ($p=0.01$). [Discussion] Although luminal HER2, HER2 and TN cohorts had no differences in prognosis between ILC and IDC, luminal ILC had a poor prognosis than luminal IDC. Therefore, luminal ILC needs stronger approach to improve their prognosis. And it was suggested that chemotherapy is effective for recurrent high-risk luminal ILC such as those with positive lymph node metastasis. [Conclusion] ILC had worse prognosis than IDC in luminal cohort, however it was comparable in luminal HER2, HER2, TN cohorts. A new strategy of treatments for luminal ILC might be needed to improve their prognosis.

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Quantitative estrogen receptor expression affects pathologic complete response to neoadjuvant chemotherapy in patients with early-stage breast cancer with low expression of HER2

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BACKGROUND Recent pooled analysis of four major clinical trials of neoadjuvant chemotherapy (NAC) indicated that tumors with low expression of HER2 (HER2-low) as defined by immunohistochemistry (IHC) could be a new subgroup of breast cancer, distinct from HER2-negative tumors. In estrogen receptor (ER)-positive/HER2-negative breast cancer, we previously reported that 9.5% ER expression by IHC was the most appropriate cutoff to predict survival outcomes. However, little is known about the effect of quantitative ER expression on NAC outcomes in patients with HER2-low breast cancer. The present study aimed to elucidate the role of quantitative ER expression as a predictive and prognostic biomarker in the newly established HER2-low subgroup. **MATERIALS AND METHODS** We retrospectively reviewed the charts of 2,016 patients with newly diagnosed ER- and/or progesterone receptor (PR)-positive breast cancer between January 1982 and January 2019 in an extensive clinical database at The University of Texas MD Anderson Cancer Center. Our analysis included

patients whose ER%, PR%, and HER2 IHC (0 to 2+) data were available. HER2-low was defined as IHC 1+ and 2+/situ hybridization (ISH)-negative. All patients had stage II or III disease at presentation and received NAC with anthracycline and a taxane-based combination regimen. Those with ER-positive tumors also received adjuvant endocrine therapy. The primary outcome measure was pathologic complete response (pCR) rate, compared between groups using logistic regression. Secondary outcomes were progression-free survival and overall survival after NAC completion, compared using Kaplan-Meier analysis and the log-rank test. The cutoff value for ER and PR positivity was 10% in the main analysis, identified by recursive partitioning and regression trees. RESULTS Among the 2,016 patients, 1134 (56%) had cStage II and 882 (44%) had cStage III disease. For IHC HER2 levels, 739 patients had 0 (37%), 926 had 1+ (46%), and 351 had 2+ (17%). For the primary outcome, 123 patients (6%) achieved pCR. The median follow-up period was 6.78 years. During the follow-up, 571 (28%) had distant metastasis. Mean ER expression (%) increased with HER2 IHC (HER2 IHC 0: 74.2%, 1+: 76.7%, 2+: 78.2%). In the multivariate logistic model, ER-negative ($p < 0.0001$), PR-negative ($p < 0.0001$), and high nuclear grade ($p < 0.05$) disease were associated with higher pCR rates. Although pCR rate did not differ among HER2 IHC groups (0 = 6.09%, 1+ = 6.26%, 2+ = 5.7%; $p = 0.93$), significantly higher pCR rates were observed in the HER2 IHC=0/1+ and 1% \leq ER< 10% group ($p = 0.0013$) than in the HER2 IHC=0/1+ and ER \geq 10%, and HER2 IHC=2+ and ER \geq 10% groups. Kaplan-Meier curves showed that patients in the ER \geq 10% group had marginally improved PFS ($p = 0.046$) and significantly longer OS ($p = 0.004$) regardless of HER2 IHC status. Multivariable analysis showed that HER IHC status did not affect survival outcomes. Exploratory analysis showed that the patients with 70% or less in ER expression and HER2 IHC 1+/2+ tumor had higher pCR rate (12.3%) compared to those with ER>70% (4.1%). CONCLUSIONS Patients with \geq 10% ER expression had better survival outcomes than those with ER< 10% regardless of HER2 expression level. The degree of HER2 expression in the HER2-low subgroup was not an independent predictive and prognostic factor for NAC response. The cutoff for ER expression for its predictive effect on pCR needs further validation in large external datasets.

Disclosure(s):

Toshiaki Iwase, MD PhD: No financial relationships to disclose

Takeo Fujii, n/a: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

P4-02-27

Preliminary Attainability Assessment of Real-World Data for Answering Clinical Questions about Breast Cancer Brain Metastases

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Background

Brain metastases is one of breast cancer's leading causes of death, and the incidence is increasing with advances in diagnosis and treatment techniques. Nevertheless, these patients have fewer opportunities to participate in prospective randomized clinical trials because of the design challenges of increasing target population heterogeneity or differentiating the definition of endpoints and how the endpoints are evaluated. Real-world data has the potential that reaches the information at a blinded area of RCT approaches. In recent years, observational studies using real-world data have gotten attention for their capability to enhance an understanding of hard-to-reach RCT approaches. However, the yet incomplete gold standard of the study protocol and the unpredictable 'hidden labor' of secondary use of clinical data become barriers to clinical researchers. In the study, we demonstrate data attainability assessment focused on clinicians' clinical unmet needs in breast cancer brain metastases (BCBM) as a preliminary step of the observational study for screening study feasibility on a certain data source.

Methods

A breast cancer registry based on the clinical data warehouse (CDW) of Samsung Medical Center has been used as the data source (N=45,219, up to 31 Dec 2021). A total of 5 clinical questions (CQ) were presented as the result of the interview of two breast cancer experts about

BCBM for the study (Table 1). Additionally, we conducted an attainability assessment for the population size and core variables constrained by a clinical question and a survey of 7 breast cancer clinicians for evaluation of the recognized clinical significance and research methods' suitability for each CQ.

A working group was formed for data attainability tests with a person with experience in clinical research for at least several years across interdisciplinary areas, including clinical expertise, medical informatics, and epidemiology. For the first step, we declare the operational definition for the study population and core variables in which the research question is inherent conceptually. And appropriate data fields and value sets are figured out from the data set. Data attainability is examined via RWD extraction on the population size and availability of core variables.

Result

The collected five CQs were mostly about the relationship between brain metastases, systemic metastases, and systemic treatments. Other CQs were related to the relationship between brain metastases incidence and the type of neoadjuvant treatment or patients' described symptoms. Assessment of the importance of clinical questions aligned well, especially for the questions with higher scores. ($r = -0.98$)

For CQ E, filtered out not to fit the SMC BCR dataset at the early stage of the data attainability screening process due to lack of explicit data field or semantically related value sets for one of the core variables, 'neurological symptom.' For CQ A, B, and D, we could confirm enough population size and dataset for conducting the study, but additional logical reconstruction of data elements had needed. For example, we used the 'clinical subtype' variable, which is provided from SMC BCR, as pre-processed feature variable using an expert-knowledge-based algorithm. For CQ C, we were able to obtain pertinent data for the study only with direct data field match and explicit code set definition.

Conclusion

To effectively use CDW, the variables have to be interpreted and defined in a clinically meaningful way with the cooperation of clinicians and data science experts. For observational studies based on RWD, understanding the data source contents and clarifying the research question enough to translate to the data level is essential. The step-by-step protocol presented in the study could be applied to the other clinical researcher using RWD at preliminary feasibility screening.

Table 1. List of clinical questions from expert interviews

A	A study on whether there is a difference in survival prognosis when brain metastases occurs as 1st metastases and when brain metastases is accompanied by systemic metastases
B	A study on whether or not systemic treatment for brain metastases patients makes a difference in survival prognosis according to subtype
C	A study on whether the timing of systematic treatment initiation differs on survival prognosis when brain metastases is accompanied by systemic metastases
D	A study on whether there is a difference in the prognosis for the occurrence of brain metastases compared to patients who previously received trastuzumab alone for neoadjuvant and patients who received pertuzumab and trastuzumab for neoadjuvant
E	A study on whether any record about neurological symptom in EMR which described by patients can be translated as surrogate factors of brain metastases

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-02-28

EMP1 low expressing tumor is associated with cell proliferation and poor overall survival of ER-positive breast cancer patients

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Background: Epithelial membrane protein 1 (EMP1) belongs to PMP22 gene family and is reported to be expressed low in numerous gastrointestinal cancers. However, little is known about its role in breast cancer. EMP1 functions to promote cell proliferation. In this study, we hypothesized that low EMP1 expressing breast cancer is associated with high proliferative characteristics and poor survival. Material and Methods: The clinicopathological data and transcriptome data of breast cancer patients from two independent large publicly available databases, The Cancer Genome Atlas (TCGA, n = 1090) and The Molecular Taxonomy of Breast Cancer International Consortium (METABRIC, n = 1904), were utilized in the current study. Survival analyses; Overall survival (OS), Disease-specific survival (DSS) and Disease-free survival (DFS) were performed by comparing the high and low expression groups. CYT score, xCell, and other immunological factors were used to evaluate intratumoral immune cell composition. Also, gene set enrichment analysis (GSEA) was performed between EMP1 high and low expression groups. Results: We divided each cohort into EMP1 expression high and low groups by utilizing median cutoff. The expression levels of EMP1 were not associated with clinical stage in any subtypes. However, interestingly lower expression of EMP1 was significantly associated with more advanced grades in ER positive/HER2 negative (ER+/HER2-) subtype in both TCGA and METABRIC cohorts ($p < 0.001$ and $p < 0.001$, respectively). Also, low EMP1 expressing tumors demonstrated higher MKI67 expression levels in ER+/HER2- subtype consistently in both TCGA ($p < 0.001$) and METABRIC cohorts ($p < 0.001$). Furthermore, GSEA demonstrated that low EMP1 expressing tumors enriched the gene sets associated with cell proliferation such as MYC Targets, E2F signaling, and G2M Checkpoint signaling, compared

with low EMP1 expressing tumors in ER+/HER2- of both TCGA and METABRIC cohorts. On the contrary, high EMP1 expressing tumors enriched the immune related gene sets such as Coagulation, Inflammatory_Response, Complement, and IL-6_JAK_STAT3 Signaling in ER+/HER2- of both TCGA and METABRIC cohorts. To this end, we further hypothesized that high EMP1 tumors were associated with favorable tumor immune microenvironment (TIME) and analyzed TIME utilizing xCell. However, to our surprise high EMP1 expressing tumors were not associated with favorable TIME. Low EMP1 expressing tumors demonstrated worse DFS, DSS, and OS compared with high EMP1 expressing tumors in ER+/HER2- breast cancer patients ($p=0.013$, $p=0.003$, and $p=0.006$) which was not the case in the other subtypes in METABRIC cohort. Conclusion: Low EMP1 expressing tumors were associated with improved OS, DSS, DFS in ER-positive breast cancer patients. Also, low EMP1 expressing tumors were found to associate with advanced grades and enriched gene sets related to cell proliferation and cell cycle, which may explain the poor survival of patients with low EMP1 expressing ER+/HER2- breast cancer.

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-02-29

A 3D Visualization Method for Breast Cancer Surgeons and Patients

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Background: Surgical oncologists currently rely on 2D image slices, such as those from mammograms, to assess the locations and extents of their patients' breast cancer tumors. In order to accurately evaluate the potential success of various surgical options, a surgeon must mentally translate these 2D images into more realistic, 3D image to visualize breast and tumor morphologies. For a patient without the same experience, it is even more difficult to imagine the true, 3D shape, size and location of their tumor and to participate fully in decision-making and surgical planning. Since the type of surgery chosen (nipple-sparing versus skin-sparing, mastectomy versus lumpectomy), and its ultimate clinical and cosmetic consequences,

depends on not only a surgeon's accurate pre-operative assessment, but also on the patient's understanding; a method of clear, precise, 3D visualization in the clinic would represent a significant advancement. Methods: Using DCE-MRI as input, we developed TumorSight (TSi) to provide surgical oncologists with an accurate, 3D representation of a patient's breast tissue and tumor, and to allow computation of useful metrics, such as the tumor-to-breast volume ratio and distance to surgically useful anatomical landmarks such as the nipple. TSi was used to create 3D models of breast cancer patient tumor using MRIs from the SimBioSys Virtual TumorBank which currently houses thousands of patients. Results: After creating the models, labels for tumor, as well as skin, chest wall, nipple, adipose tissue, glandular tissue, and vasculature were created. After tumor segmentation validation studies (of 49 patients) were completed, the median absolute volumetric error was 0.32 and the median maximum Hausdorff distance was 17.72mm. From these representations, we determine whether the tumor is monocentric, multifocal or diffuse, compute the tumor volume-to-breast volume ratio, and measure the distance of closest approach between the tumor and the nipple. In addition, by adding a margin to the tumor and computing the volume within a convex boundary containing the tumor+margin, TSi provides a pre-operative estimate of the extirpative volume and its fraction of the total breast volume. Conclusion: The ability to visualize, in 3D, a tumor's location and distribution in the breast, and to accurately measure important metrics such as tumor-to-nipple distance, multifocality, and tumor-to-breast volume, are critical to surgical planning in breast cancer. To assist in this planning, TSi provides a surgeon and their patient with a three-dimensional breast and tumor representation and reports measurements of key features of interest.

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-02-30

Association between tumor infiltrating lymphocytes (TILs) and the HER2DX assay in early-stage of HER2-positive (HER2+) breast cancer

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Background: The HER2DX assay is a genomic test in early-stage HER2-positive (HER2+) breast cancer that provides prognostic and predictive information. HER2DX is a supervised learning algorithm incorporating tumor size, nodal staging, and 4 gene expression signature scores (immune/IGG, tumor cell proliferation, luminal differentiation and the expression of the HER2 amplicon). Among them, the IGG signature is associated with both overall survival and probability of achieving a pathologic complete response (pCR). Here, we studied the association of percentage (%) of tumor infiltrating lymphocytes (TILs) with HER2DX scores, immune genes and other breast cancer-related genes. Methods: HER2DX and %TILs were evaluated in 670 formalin-fixed paraffin-embedded (FFPE) samples of HER2+ breast cancer, including in 3 clinical studies SHORTHOR (n=437), PAMELA (n=86), a cohort of patients treated with anti-HER2 therapy plus chemotherapy at Hospital Clínic of Barcelona (n=147). The %TILs were quantified by histological evaluation with hematoxylin eosin staining according to International TILs Working Group guidelines. The nCounter platform determined the expression of 192 genes and HER2DX scores. Pearson correlations (Cor) and Significance Analysis of Microarrays (SAM) with a false-discovery rate (FDR) < 5% assessed the association between %TILs and the expression of individual genes or HER2DX signature scores. Results: A moderate correlation was observed between %TILs and the immune IGG signature (Cor=0.56, p< 0.001). Of note, 171 (25.52%) cases had low %TILs (< 30%) and high IGG score, while 1 (0.15%) case had high %TILs (≥30%) and low IGG score. The %TILs were significantly associated with the expression of immune genes, ERBB2, IGG signature and HER2 amplicon score, and negatively associated with the expression of luminal genes (i.e., ESR1, PRG and BCL2). An unclear relationship between TILs and proliferation genes was observed. Finally, moderate correlations were observed between %TILs and HER2DX pCR score (Cor=0.48, p< 0.001) and between %TILs and HER2DX risk score (Cor=0.33, p< 0.001). Conclusions: Important differences exist between the %TILs and the HER2DX IGG signature in early-stage HER2+ breast cancer. The %TILs should not be used to predict the HER2DX scores. Biologically, a higher %TILs indirectly capture a higher ERBB2 expression and a lower expression of luminal genes, both associated with response to anti-HER2 treatment.

Disclosure(s):

Esther Sanfeliu, PhD: No financial relationships to disclose

Fara Brasó-Maristany, n/a: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

P4-03-01

Persistence with adjuvant endocrine therapy in patients with early breast cancer at high risk of recurrence: a US-based real-world study

Presenting Author(s) and Co-Author(s):

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Background: Previous studies have highlighted concerns regarding treatment persistence (TP) of patients with early breast cancer (EBC) taking adjuvant endocrine therapy (ET) but these data have not been analyzed based on patient's risk of recurrence. The aim of this study is to evaluate the TP of patients at high risk of recurrence based on clinicopathologic criteria used in the monarchE trial.

Methods: This observational retrospective cohort study used nationwide Flatiron Health electronic health record (EHR)-derived de-identified database of US patients diagnosed with EBC from Jan 2011 to Sept 2020. Overall, 4028 patients were selected based on the following criteria: adult female or male with diagnosis of HR+, HER2- EBC (stage IA-IIIC) with no evidence of distant metastasis who received surgical resection and adjuvant endocrine therapy. Patients were divided into 2 groups; GroupA: patients with clinicopathologic features suggestive of high risk of recurrence: ≥ 4 positive(+) axillary lymph nodes (ALN), OR 1-3+ ALN and either Grade3 disease, or tumor size ≥ 5 cm, or Ki-67 $\geq 20\%$. GroupB: patients with stage IA-IIIC disease who did not meet those high risk criteria. TP (time from start to discontinuation of adjuvant ET) was compared between the 2 groups. Patients who had a gap of >90 days after their last date of ET, as documented in the EHR, were considered to have discontinued ET. Patients whose last ET was ≤ 90 days from Sept 2020 were censored. Cumulative incidence functions of nonpersistence were estimated, treating recurrences or deaths occurring during ET as competing risks.

Results: While gender and race distributions were similar between groups, patients in GroupA (n=557) were younger and more likely to be premenopausal, have an ECOG PS score of 1 or 2+, and have received mastectomy, radiation and chemotherapy compared to GroupB (n=3471). Estimates of the cumulative incidence functions of nonpersistence were statistically different between the groups ($p < .001$). The Table shows the cumulative incidence (standard error) of nonpersistence at years 1-5 after initiating ET.

Conclusions: This study suggests that patients at high risk of recurrence have higher ET-TP than those at lower risk. The separation was most pronounced at 5 years. The steep increase

in 5-year nonpersistence in lower risk group could be due to a perception of less need to continue ET for longer periods of time in lower risk disease. The greater persistence in patients at high risk is noteworthy, but interventions to improve patient's TP are still warranted.

Cumulative incidence of nonpersistence after initiating ET

Risk Group	1 yr	2 yrs	3 yrs	4 yrs	5 yrs
GroupA	7.3% (1.1)	11.7% (1.4)	16.9% (1.8)	20.9% (2.0)	28.2% (2.5)
GroupB	9.6% (0.5)	14.6% (0.6)	19.3% (0.7)	24.6% (0.9)	43.6% (1.3)

Disclosure(s):

Kristin M. Sheffield, n/a: Eli Lilly and Company: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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12/8/2022

7:00 AM - 8:15 AM

P4-03-02

Low-dose aspirin prescriptions and breast cancer recurrence: a Danish nationwide cohort study with up to 23 years of follow-up

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Background Low-dose aspirin irreversibly inhibits the cyclooxygenase enzymes COX-1 and COX-2, which catalyze the formation of prostaglandins and thromboxanes, inhibiting platelet aggregation. Platelets are thought to play a role in tumorigenesis. As such, aspirin may have a beneficial effect on breast cancer prognosis, but results to date are conflicting. **Objectives** To evaluate the association between aspirin use and breast cancer recurrence up to 23 years after primary diagnosis. **Methods** We included all women diagnosed with non-metastatic breast cancer during 1996-2004 registered in the Danish Breast Cancer Group (DBCG) clinical database. We obtained information on aspirin prescriptions (≥ 2 prescriptions filled between

cancer diagnosis and the landmark) from the Danish National Prescription Registry. Information on early and late (>10 years after primary diagnosis) recurrence was obtained using the DBCG database (for recurrence within the first 10 years after diagnosis) and for late recurrence via a previously described and validated algorithm, drawing on data from the Danish National Patient Registry, the Danish Pathology Registry, the Danish Cancer Registry and a contralateral breast cancer database. We used Cox regression to compute crude and adjusted hazard ratios (HRs) with 95% confidence intervals (CI) employing landmark analyses starting follow-up at years 5, 10, 15, and 20 after primary diagnosis. We adjusted for potential confounders including calendar year of diagnosis, menopausal status, comorbidities, estrogen receptor status, clinical stage, grade, surgery type, chemo- and endocrine therapy, diagnostic codes for alcoholism and obesity, as well as co-medications (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, statins, bisphosphonates, metformin, digoxin, hormone replacement therapy, non-steroidal anti-inflammatory drugs, and vitamin K antagonists). We followed patients until recurrence, death, second cancer, loss to follow-up, or 31 December 2018. Results Among 21,684 women with non-metastatic breast cancer, 4,902 experienced recurrence during 242,427 person-years of follow-up. Our landmark analyses showed a reduced hazard of recurrence in the 5-, 10-, and 15-year landmark cohorts (5-year landmark adjusted HR = 0.80, 95% CI = 0.68, 0.94; 10-year landmark adjusted HR = 0.84, 95% CI = 0.71, 1.00, 15-year landmark adjusted HR = 0.83, 95% CI = 0.61, 1.14). The 20-year landmark analysis revealed an adjusted HR of 1.09 (95% CI = 0.49, 2.46). Conclusions The potential anti-cancer effect of aspirin appears most pronounced in the first 15 years after breast cancer diagnosis. Funding Elisabeth Solmunde is funded by the Danish Cancer Society (R320-A18464-B5768) and the Independent Research Fund Denmark (1149-00013B). This work was supported by grants to Deirdre Cronin-Fenton from the Danish Cancer Society ("Knæk Cancer" R147-A10100).

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12/8/2022

7:00 AM - 8:15 AM

P4-03-03

Elevated Risk of Breast Cancer Diagnosis in Women with Dense Breasts reflects a similarly Elevated Risk of Breast Cancer Onset that is Robust to the Effect of Density on Mammography Sensitivity

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Dense breasts are associated with a higher risk of breast cancer diagnosis, which has impacted risk prediction tools and patient notification policies. However, given that mammography is less sensitive for women with dense breasts and these women may be subject to different confirmation testing pathways, the true association between breast density and cancer risk is unknown. We investigated the relationship between breast density and onset using a natural history model that accounts for differential sensitivity and rates of exams by breast density. Data consisted of Breast Cancer Surveillance Consortium mammogram and cancer outcomes among women aged 40-54 with a first digital mammogram between 2000-2018 (N=33,542). Of these, 15,092 had non-dense (almost entirely fatty or scattered fibroglandular densities) and 18,450 had dense (heterogeneously dense or extremely dense) breasts. We estimated the empirical sensitivity of mammograms in dense and non-dense breasts (fraction of diagnosed cancers that were screen detected) and examined rates of mammograms by density. We estimated the relative risk of breast cancer diagnosis five years after the first exam using Kaplan Meier methods and the relative risk of breast cancer onset from a natural history model, assuming density-specific sensitivity was equal to the empirical sensitivity. Empirical sensitivity was .88 in women with non-dense and .78 in women with dense breasts. Mammogram utilization was somewhat higher in women with dense breasts (HR for subsequent mammograms 1.10 (95% CI [1.07, 1.12])). The relative risk of diagnosis for dense versus non-dense breasts was 1.80 (95% CI [1.46,2.57]); based on the natural history model the relative risk of onset was 1.73 [1.43,2.25]. The estimated relative risk of onset ranged from 1.67 to 2.03 under assumptions that the relative sensitivity of the screening episode for dense versus non-dense breasts was 1.0 to 0.4. In conclusion, the association of risk of breast cancer onset with breast density is robust to assumptions about the relative sensitivity in dense and non-dense breasts.

Disclosure(s):

JANE M. LANGE, PhD: No financial relationships to disclose

Charlotte Gard, PhD: No financial relationships to disclose

Ellen O'meara, PhD: No financial relationships to disclose

Ruth Etzioni, PhD: No financial relationships to disclose

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P4-03-04

The first population level description of all women diagnosed with breast cancer in Costa Rica from 2008 to 2012 using data from the National Tumor Registry.

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Background: Introduction: Cancer is the second leading cause of death worldwide. Every year 10 million cancer deaths are reported, 70% of which occur in low- and middle-income countries (LMICs). Breast cancer in the world is the second in incidence and the second in mortality. In Costa Rica cancer incidence occupies first place in incidence and fourth place in deaths. The Costa Rican health system is a public and universal system called the Costa Rican Social Security Fund (CCSS) and information on cancer is collected by the National Tumor Registry (RNT) which is governed by the Ministry of Health. Objectives: We sought to develop the first population-based description of the characteristics of women diagnosed with breast cancer in Costa Rica. This analysis allows us to measure the burden of breast cancer in Costa Rica and will enable assessments of quality of prevention, treatment, and care. These data will also inform how the burden of breast cancer in Costa Rica compares to other nations. Methods: Data from all patients registered in the CCSS with breast cancer was collected between January 2008 and December 2012. We evaluated sociodemographic, clinical, and treatment related characteristics. In this analysis we performed using SPSS, STATA version 17, and infostat. Results: In the CCSS, we identified 4,775 women of which 3,836 were diagnosed and 391 did not have clinical records. A total of 3,160 women were analyzed in the study. The mean age of diagnosis was 59.1 years old, 32.5% diagnosed were older than 65 years. 50.6% of the tumors originated in the left breast and 46.9% in the right breast. 50.7% of the tumors were in the superior outer quadrant. For diagnosis, core needle biopsies were used in 46.5% of the cases. About 60% of cases were diagnosed in early stages (IA, IIA, IIB), and 1.7% of cases in metastatic stages. Less than 40% of cases have positive lymph nodes and 76% of cases were infiltrating ductal carcinoma. Moderately differentiated tumors (40.7%) prevailed over poorly or well differentiated tumors. The most frequently affected site by metastasis was bone (3.0%). Most tumors did not have vascular (63.0%) or lymphatic invasion (52.5%) 80% are Ki-67 negative. We measured treatment-related characteristics and found that the average waiting time between diagnosis and surgery was 72 days, 77.9% waited less than 90 days for their treatment and the rest waited >90 days. 88.7% received surgery as the first treatment, 54.4% received some type of adjuvant and the combination of treatments was used in 58.3% of the patients. 85.6% of the patients successfully completed their treatment. Discussion: This study is the first to describe the population with breast cancer in Costa Rica using data from the National Tumor Registry. Currently, only 3 of Latin American (LATAM) countries have high

quality cancer registries and 20 of LATAM nations have a national registry. Some of the findings coincide with what is described in the world literature. We also identified novel information such as the impact of insurance type, occupation, and age on breast cancer that will inform the CCSS how the existing protocols for the care of breast cancer in Costa Rica can be improved.

Disclosure(s):

Percy G. Guzman, n/a: No financial relationships to disclose

Esmeralda Ramirez-Pena, n/a: No financial relationships to disclose

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P4-03-05

HER2 + Breast Cancer in Afro-Caribbean Women in New York City

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Background: Human Epidermal Growth Factor receptor 2 (HER2) protein overexpression and/or amplification positive breast cancer accounts for 14% of breast cancer cases in the United States. The use of anti-HER2 targeted therapy in combination with chemotherapy has resulted in better response rates leading to better outcomes in patients with this breast cancer subtype. Few studies directly investigate breast cancer outcomes in Afro-Caribbean women in the U.S, and fewer studies have investigated HER2 positive (HER2+) disease in this patient group. We describe the clinicopathologic characteristics and outcomes of HER2+ breast cancer in this minority patient group. Methods: This is a retrospective study conducted at Kings County Hospital (KCH), a public hospital in Brooklyn, a New York City borough with the highest population of Afro-Caribbeans in the United States, outside of Miami, Florida. Data of patients diagnosed with breast cancer from 2015-2018 was collected from the hospital's tumor registry. Clinical and pathologic data was collected and analyzed with descriptive statistics and Chi-

square testing. Results: A total of 299 women with breast cancer were screened and 18% (54) had HER2+ disease. 63% (34) of these patients were post-menopausal, with median age 56. 78% self-identified as Afro-Caribbean. 19% (11) of patients reported first- or second-degree relatives with a breast cancer diagnosis, 22% (13) reported first-degree relative with non-breast malignancy. Half of the patients younger < 45 years age reported a positive family history of any type of cancer. 74% of patients presented with Nottingham Grade 3 disease, 31% with localized disease, without lymph node involvement, 52% with regional lymph node involvement, and 17% with distant metastasis. 63% of patients were estrogen receptor (ER) positive and 37% were ER negative. Post-menopausal women presented with higher rates of lymph node involvement at 70.4% vs. 50% in pre-menopausal women (p=0.17). 41% (22) of patients received neoadjuvant chemotherapy while 31% received adjuvant therapy with standard chemotherapy and anti-HER2 targeted treatment. Of the 22 patients who received neoadjuvant treatment, 14% had complete pathologic response, 68% had partial response, and 18% had disease progression. Treatment response to neoadjuvant therapy was independent of lymph node status (90.9% in local disease vs. 85.7% in lymph node involvement, p=0.66). The median progression free survival was 48 months, overall survival at 7 years was not reached, and mortality rate was 16.7%. Conclusions: In our analysis, Afro-Caribbean patients with HER2+ breast cancer presented with high grade tumor, high incidence of regional lymph node involvement, and ER positive tumors. Noteworthy was the presence of strong family history of cancers, suggestive of familial or inherited cancers. Pathologic complete response to neoadjuvant chemotherapy was remarkably less than anticipated, and further research is warranted to study tumor biology and responses to standard HER2 systemic therapies in these patients. References: 1. <https://seer.cancer.gov/statfacts/html/breast-subtypes.html> 2. New York City Health and Hospitals <http://www.nychealthandhospitals.org/wp-content/uploads/2016/07/chna-kings-county.pdf> Kings County. 2016 Community Health Needs Assessment.

Disclosure(s):

Emanuela Cimpeanu, MD: No financial relationships to disclose

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P4-03-06

Clinical and socioeconomic disparities in treatment and survival between Hispanic and non-Hispanic Black women with non-metastatic Triple-Negative Breast Cancer

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Background: Breast cancer(BC) is a common female malignancy [1]. Triple-negative breast cancer (TNBC) is the least common (10-15% of cases)[2], but the most aggressive subtype. TNBC accounts for 5% of all-cancer-related deaths every year[3, 4].Hispanic women are 1.3 more likely to develop TNBC [3, 5]. Whether Hispanic and non-Hispanic patients suffering from TNBC show different survival. We aim: (1) to evaluate the differences in overall (OS) and breast cancer specific survival(BCSS) between Hispanic(H) and non-Hispanic black (NHB) women in non-metastatic TNBC, and (2) to assess the contribution of sociodemographic, clinical, and neighborhood factors to TNBC survival disparities. Methods: With the SEER database of the National Cancer Institute, we identified 4271 (39%) H and 6594 (61%) NHB patients who were diagnosed with non-metastatic TNBC between 2010 and 2016. Patients with tumor in situ were excluded from the analysis. Logistic regression was used to identify odd ratios for treatment modalities. Kaplan-Meier methods were used to estimate OS and BCSS. Competing risk analysis was used to asses the association between race/ethnicity and risk of breast cancer mortality adjusting for age, insurance, social, SDI, rurality, BC stage, tumor grade, surgery, chemotherapy, and radiation therapy. Results: The mean age at diagnosis for H vs. NHB was 53 and 56 years, respectively ($p < 0.001$). 54% of Hispanics were married vs. 35 % of NHB, $p < 0.001$. Tumor size > 5 cm was present in 14% NHB vs. 12% H patients, $p < 0.001$. Grade I tumors were only 1 % in both groups, grade II were 13% and grade III-IV were 82% also in both groups, $p > 0.99$. H (28% stage I, 50% stage II) had more advance disease as compared to NHB (30% stage I, 48% stage II) [$p < 0.001$]. Private insurance was more common in NHB than H (74% vs. 66%, $p < 0.001$). Rural residence was more common in NHB than H (8% vs. 3 %, $p < 0.001$). High level of SDI was more common in H as compared to NHB(43% vs. 36%, $p < 0.001$). Surgery was performed in 92% of NHB and 91% of H, $p = 0.03$. Radiation was given to 54% of NHB and 43% of H, $p < 0.001$, while chemotherapy was given to 79% of NHB and 79% of H patients, $p = 0.54$. After adjusting for clinicopathological features, the odds ratio (ORs) for receiving surgery, radiation, and chemotherapy for NHB as compared to H were 0.9 ($p = 0.32$), 1.57 ($p < 0.001$), and 0.89 ($p = 0.03$), respectively. The 5-year OS and BCSS rates were higher in H as compared to NHB(OS 76% vs. 72% , $p < 0.001$; BCSS 81% vs. 78%, $p < 0.001$). For stage I patients, neither 5-year OS (86% vs. 89%, $p = 0.054$) nor BCSS (91% vs. 93%, $p = 0.37$) was different between NHB and H patients. For stage II and III patients, the 5-year OS rates for Hispanics vs. NHB were (79% vs 74%, $p < 0.001$) and (51% vs 45%, $p < 0.004$), respectively. After adjusting for age, marital status, insurance, stage, grade, treatment, SDI, rurality; NHB have higher risk of BC death as compared to H patients (subdistribution Hazard Ratio (HR) = 1.39; 95% CI 1.2 – 1.56, $p < 0.001$). The association between race/ethnicity and risk of breast cancer death was not affected by age ($p = 0.44$) , insurance($p = 0.89$), SDI($p = 0.40$), or living in a

rural area($p=0.14$). The risk of BC death between NHB and H was even higher for patients who did not receive radiation (HR 1.5) than in those who received radiation (HR 1.2). The risk of BC death between NHB and H was also higher for patients who did not undergo surgery (HR 1.7) than in those who underwent surgery (HR 1.3). Conclusions: In patients with non-metastatic TNBC, H patients present with increased rates of high-grade and advanced stage tumors than NHB. NHB are 57% more likely to receive radiation and 11% less likely to receive chemotherapy than H women. NHB patients have a 39% higher risk of BC death as compared to H even after adjusting for clinicopathological, treatment and socioeconomic factors. Future studies need to assess potential etiologies for racial disparities in BC outcomes such as differences in tumor microenvironment, access to healthcare, tumor biology and treatment efficacy.

Disclosure(s):

Alvaro Alvarez Soto, fellow: No financial relationships to disclose

Ana Maria Bernal, clinical research associate: No financial relationships to disclose

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P4-03-08

Breast cancer incidence rates in Japan turned into bimodal age distribution in this decade.

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BACKGROUND: Japan is the globe's fastest ageing country: 32.0 % of the female population are 65 or older in 2021. The birth rate was 1.30 children per woman in 2021. Japan's population has been constantly shrinking since 2011 with aging. The number of breast cancer cases has increased rapidly in the course of low birth rate and aging population. Breast cancer has increased and accounted for the first place of all of cancers in Japanese women.

OBJECTIVES; Number of breast cancer has increased recently and accounted for the first place of all of female cancers in Japan. Detailed analytics of the increase and aging of breast cancer are not studied. We elucidate the transformation of Japanese breast cancer by ages at diagnosis over the past decade. **MATERIALS:** We used the registry data of Japanese Breast Cancer Society and Statistics Bureau of Japan in 2018. Female breast cancer new cases were 59,389 patients in 2008 and 93,858 patients in 2018, respectively. The total female population was 65.441 million in 2008 and 64.911 million in 2018, respectively. 65 years and older women accounted for 23.4% in 2008 and 31.0 % in 2018, respectively. **METHODS:** We compared incidences and incidence rates of breast cancer by ages in 2008 and 2018, respectively. We used the statistical method of Ameijeiras-Alonso et al for mode assessment. **RESULTS;** Total number of incidences and incidence rates of breast cancer in 2018 were higher than those in 2008 among all ages. Difference of number of incidences were maximum in age of 60-69 in both years. Difference of incidence rates in both years reached maximum in age of 75-79. Incidence rates in 2008 showed unimodal age distribution with the gentle peak. Incidence rates in 2018 showed bimodal age distribution with two peaks of 45-49 and 65-69. **CONCLUSIONS;** Incidences and incidence rates of breast cancer increased rapidly among all ages in this decade in Japan. The incidence rates increased most in ages of 75-79 and turned into bimodal age distribution in 2018.

Disclosure(s):

Ken Uchida, MD: No financial relationships to disclose

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P4-03-09

Risk of breast cancer after false-positive mammography recalls: a matched cohort study

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Background: False-positive mammography recalls are common and associated with an increased risk of subsequent breast cancer. But the long-term risk and whether the risk restricts to the breast cancer detected on the false-positive recalled side remain unclear. Objective: To examine long-term risk of breast cancer after false-positive recalls by side of breasts, mode of detection and tumor characteristics. Design: Matched cohort. Setting: The mammography screening program in Stockholm, Sweden. Participants: We included 45,588 women who received false-positive recalls (1991-2017) and 455,880 matched women who were not recalled, and then followed them until March 31st, 2020. Measurement: Breast cancer incidence; mode of breast cancer detection; tumor characteristics; re-attendance at mammography screening. Results: With Kaplan-Meier curves, we showed that women with false-positive recalls were more likely than those without to have breast cancers, on not only the previously recalled (false-positive) side but also the unrecalled side, up to at least 20 years since the next scheduled screen. We further found that risks were particular higher for breast cancer diagnosed on the false-positive side within first four years of follow-up (hazard ratio [HR]: 2.40; 95% confidence interval [CI]: 2.17-2.65), by the use of stratified Cox model while allowing for time-varying effects. In addition, when stratifying by age at matched mammograms, we found the association was stronger among old women (60-74) than young women (40-59). This was consistent with the result that the risk of breast cancer was higher among women with low density than those with high density. Of note, within the first four years, women with false-positive recalls were at an increased risk of clinical detected cancers (cancer detected among women who did not attend last scheduled screen or were at an age out of screening age ranges) on the false-positive side compared with those who were not recalled. In addition, we found that women with false-positive recalls had statistically significantly lower re-attendance rates at every of next five scheduled screenings. Conclusion: Women with false-positive recalls are at an increased risk of breast cancer for at least two decades, while these women are less likely to adhere to subsequent mammography screens comparing to women who were not recalled. Thus, women with false-positive recalls, especially older women, should be encouraged to re-attend the mammography screening program.

Disclosure(s):

Xinhe Mao, n/a: No financial relationships to disclose

Wei He, n/a: No financial relationships to disclose

Keith Humphreys, n/a: No financial relationships to disclose

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Kamila Czene, n/a: No financial relationships to disclose

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P4-03-10

BREAST DENSITY AND RISK OF BREAST CANCER

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Background: Early studies reported a 4-6-fold risk of breast cancer between women with extremely dense and fatty breasts. As most early studies were case-control studies, we took advantage of a population-based screening program to study density and breast cancer incidence in a cohort design. Methods: In the Capital Region, Denmark, woman aged 50-69 are invited to screening biennially. Women screened November 2012 - December 2017 were included, and classified by BI-RADS density code, version 4, at first screen after recruitment. Women were followed up for incident breast cancer, including ductal carcinoma in situ (DCIS), to 2020 in nationwide pathology data. Rate ratios (RR) and 95% confidence intervals (CI) were compared across density groups using Poisson-regression. Results: We included 189,609 women; 1,067,293 person-years; and 4110 incident breast cancers/DCIS. Thirty-three percent of women had BI-RADS density code 1; 38% code 2; 24% code 3; 4.7% code 4; and missing 0.3%. Using women with BI-RADS density code 1 as baseline; women with code 2 had RR 1.69 (95% CI 1.56-1.84); women with code 3, RR 2.06 (95% CI 1.89-2.25); and women with code 4, RR 2.37 (95% CI 1.05-2.74). Results differed between observations accumulated during screening and above screening age. Conclusions: This cohort study showed a 2.37-fold difference in breast cancer risk between women with highest and lowest breast density. Translated into absolute risk of breast cancer after age 50, this was a 6.2% risk for the one-third of women with lowest density, and 14.7% for the five percent of women highest density.

Disclosure(s):

Elsebeth Lynge, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-03-11

Population-based survival outcomes of pure vs mixed invasive lobular breast carcinoma in Ontario, Canada

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Purpose: We aim to determine incidence and survival rates of pure vs mixed invasive lobular breast carcinoma between 1990 and 2020 in the province of Ontario, Canada. We further evaluated patient and tumour factors that predict survival for invasive lobular carcinoma (ILC). **Methods:** Using population-based administrative healthcare datasets at Institute of Clinical Evaluative Sciences (ICES) Ontario, we calculated the crude 5-year incidence rates of pure ILC versus invasive ductal carcinoma (IDC) versus mixed ILC-IDC in the province of Ontario, Canada between 1990 and 2020. Kaplan-Meier survival curves were generated to determine the 5-, 10-, 15- and 20-year survival for ILC (and mixed ILC-IDC) as compared with IDC. Survival curves were compared using the log-rank test and stratified by stage. Using a multivariable Cox proportional hazards regression analysis, we identified patient (e.g. demographic, geographic, socioeconomic) and tumour (grade, stage, receptor subtype) factors that predicted survival for patients with ILC. Statistical analysis was performed using SAS® and P values < 0.05 were considered statistically significant. **Results:** We identified 18,551 (8%) pure ILC, 10,234 (4%) mixed ILC-IDC and 192,371 (81%) IDC cases. The crude incidence of pure ILC increased from 55.7 per 100,000 in 1990 to 80.2 per 100,000 in 2020. The crude incidence of mixed ILC-IDC peaked in the mid-2000s at 48.6 per 100,000 and subsequently declined to 32.1 per 100,000 in 2020. There was a significant difference in overall survival between the three breast cancer subtypes. Over a 30-year follow-up period (mean 9.3 +/- 7.3 years), overall survival of mixed ILC-IDC mirrors the survival of pure IDC, while women with pure ILC have inferior survival compared with IDC beginning after 10 years of follow-up (P < .001). The 20-year overall survival was 40% for ILC and 50% for IDC and mixed ILC-IDC. Older age > 55 years (vs. 50-54 years, P < .0001), lowest neighborhood income quintile (HR 1.1, P = .038), geographic location within Ontario (P < .01) and increasing Elixhauser Comorbidity Index score (P < .0001) predicted worse overall survival for ILC patients. Conversely, the increasing number of mammograms received in the five years prior to diagnosis predicted better overall survival (P < .0001). When stratified by cancer stage, the worse survival in ILC (compared with IDC and mixed ILC-IDC) was only observed for stage III patients (P = .01). Stage III and IV disease, grade 3 histology and ER/PR negativity predicted worse survival (P < .01). **Conclusion:** The crude incidence of ILC is increasing over time. Over a 30-year follow-up period (mean 9.3 +/- 7.3 years), ILC had worse overall survival compared with IDC and mixed ILC-IDC, particular

stage III patients. Patient demographic and tumour factors predict overall survival in ILC. While treatment paradigms for ILC mirror that for IDC, our data demonstrates worse overall survival for ILC and a need for more research and treatments focused on improving long-term survival for ILC patients.

Disclosure(s):

David Lim, MDCM MEd PhD FRCSC: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Merck & Co., Inc.: Consulting Fees (e.g., advisory boards) (Ongoing)

Vasily Giannakeas, MPH, PhD(c): No financial relationships to disclose

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P4-03-12

Cumulative Environmental Quality is Associated with Differential Breast Cancer Incidence by Summary Stage and Urbanicity

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Background: Individual environmental contaminants have been associated with breast cancer; however, evaluations of multiple exposures simultaneously are limited. The USPA has constructed an environmental quality index (EQI), which contains county-level environmental exposure data across five overarching environmental domains (air, water, land, sociodemographic, and built environment). Unfortunately, the links made between breast cancer and the EQI are lacking because these analyses used total breast cancer incidence quantities, masking potential associations between EQI domains and specific stages of disease. In this study, we investigated if multiple exposures in broad EQI domains was associated with incidence of breast cancer, stratified by stage.

Methods: The EQI data was linked to county-level age-standardized incidence rates (SIRs) obtained from the North Carolina Central Cancer Registry/NC CCR (2010-2014), a reporting system for all cancer cases diagnosed in residents of the state. Incidence rates and SIRs of total, in situ, localized, regional, and distant breast cancers were evaluated stratified by rural-urban status. Associations between county-level age-adjusted cancer incidence rates for each summary stage were assessed using general linear models (SAS 9.3), linear models with a continuous outcome with a p-value cutoff for statistical significance set at $p < 0.05$. We also evaluated incidence rates by summary stage comparing across rural versus urban counties using Mann-Whitney rank tests, since not all stages were normally distributed, confirmed by the

D'Agostino-Pearson normality test.

Results: In counties with poor environmental quality compared to those with good environmental quality, total breast cancer incidence was higher by 10.82 cases per 100,000 persons (95%CI: 2.04, 19.60, $p=0.016$). This association was most pronounced for localized breast cancer ($\beta=5.59$, 95%CI: 0.59, 10.58, $p=0.029$). Higher incidence of early-stage disease (carcinoma in situ $\beta=5.25$, 95%CI: 2.34, 8.16, $p=0.001$ and localized breast cancer $\beta=6.98$, 95%CI: 2.24, 11.73, $p=0.004$) and total breast cancer ($\beta=11.44$, 95%CI: 3.01, 19.87, $p=0.008$) occurred in counties with poor land quality, especially urban counties. Overall, NC counties averaged 21.6% percent African American (AA) which is higher than the US national average of 12.6% at the time of the U.S. 2010 Census. The percentage of AA in each county in bivariate analyses was associated with increased incidence of regional (incident cases 0.12 cases per % increase in AA population, 95% CI 0.01, 0.22, $p=0.022$) and distant breast cancers (incident cases 0.06 per % increase in AA population, 95% CI 0.02, 0.10, $p=0.003$) (Table 1). In addition, in stratified models, associations persisted and were strengthened in urban county models for regional breast cancer and in rural county models for distant breast cancer.

Conclusions: Environmental quality is variable across NC akin to variability across the US, as the interquartile range (25th-75th percentile) of total EQI in NC is -0.187 to 0.734 while the interquartile range is -0.606 to 0.706 for the US (USEPA), making NC EQI analyses generalizable to a number of states and counties across the U.S., although what drives poor environmental quality varied by region and by county. Our analyses indicate significant associations between EQI and breast cancer incidence, which differ by breast cancer stage and urbanicity, identifying a critical need to assess cumulative environmental exposures in the context of cancer stage. Funding: Duke Cancer Institute seed grant (GRD, KH) as part of the P30 Cancer Ctr grant; Duke Environmental Health Scholars Award and NIEHS T32-ESO21432-05 (LMG).

Table 1. Generalized linear model estimates and associated p-values for county characteristics, per 1% increase. Results are stratified by breast cancer stage and urbanicity. Bolded text indicates statistically significant estimates (p<0.05).

		Non-stratified		Urban		Rural	
		Estimate (95% CI)	p-value	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value
Total							
County Characteristics	Percent Smokers	-0.74 (-2.97, 1.48)	0.51	-2.16 (-4.76, 0.42)	0.10	0.57 (-4.08, 5.23)	0.80
	Percent African American	0.12 (-0.16, 0.40)	0.41	0.29 (-0.06, 0.65)	0.11	-0.04 (-0.54, 0.45)	0.85
	Mammography Screening Rate	0.26 (-0.42, 0.95)	0.45	-0.64 (-1.60, 0.30)	0.18	0.80 (-0.31, 1.91)	0.15
In situ							
County Characteristics	Percent Smokers	-0.23 (-1.05, 0.59)	0.58	-0.46 (-1.59, 0.67)	0.42	0.18 (-1.30, 1.67)	0.80
	Percent African American	-0.08 (-0.19, 0.02)	0.11	-0.12 (-0.27, 0.03)	0.13	-0.09 (-0.28, 0.06)	0.30
	Mammography Screening Rate	0.11 (-0.20, 0.44)	0.47	-0.05 (-0.47, 0.36)	0.79	0.34 (-0.25, 0.94)	0.25
Localized							
County Characteristics	Percent Smokers	-1.14 (-2.41, 0.12)	0.08	-1.33 (-2.79, 0.11)	0.07	-0.81 (-3.60, 1.97)	0.56
	Percent African American	0.11 (-0.05, 0.27)	0.19	0.13 (-0.07, 0.33)	0.20	0.07 (-0.22, 0.37)	0.59
	Mammography Screening Rate	0.04 (-0.35, 0.43)	0.83	-0.09 (-0.63, 0.43)	0.72	0.16 (-0.50, 0.83)	0.62
Regional							
County Characteristics	Percent Smokers	-0.27 (-1.09, 0.54)	0.50	-0.63 (-1.43, 0.15)	0.11	-0.10 (-1.94, 1.73)	0.91
	Percent African American	0.12 (0.01, 0.22)	0.02	0.26 (0.15, 0.37)	<.0001	0.03 (-0.16, 0.22)	0.76
	Mammography Screening Rate	-0.31 (-0.57, -0.06)	0.01	-0.47 (-0.76, -0.18)	0.002	-0.19 (-0.63, 0.24)	0.38
Distant							
County Characteristics	Percent Smokers	0.02 (-0.28, 0.33)	0.88	0.29 (-0.01, 0.61)	0.06	-0.47 (-1.26, 0.32)	0.23
	Percent African American	0.06 (0.02, 0.10)	0.003	0.01 (-0.03, 0.05)	0.55	0.14 (0.05, 0.22)	0.002
	Mammography Screening Rate	0.12 (0.00, 0.24)	0.05	0.06 (-0.06, 0.18)	0.33	0.20 (-0.06, 0.48)	0.12

Disclosure(s):

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7:00 AM - 8:15 AM

P4-03-13

AN EVALUATION OF BREAST CANCER RECURRENCE DATA REPORTED TO THE NCI SEER PROGRAM

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Background: There are currently 18.1 million cancer survivors in the U.S. and the number is expected to increase to 22.5 million in the next ten years. The increasing number of survivors also means that the population at risk for cancer recurrence will increase. Recurrence significantly impacts patients' health outcomes because there are limited treatment options. Currently, there are limited population level recurrence data in cancer registries world-wide. Most recurrence estimates have been derived from randomized clinical trials (RCTs) where the patient population only represents 4% of all cancer patients. Since 2018 the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program has been collecting abstract-based recurrence information. Our goal is to use the SEER recurrence data sources to develop a high-quality population-based recurrence database to disseminate to the public for future research. Measuring recurrence from population-based cohorts can enhance our understanding of what clinical, demographic, and geographic factors impact the risk of recurrence and can inform researchers on developing prevention strategies. Methods: In November 2021 we obtained a dataset that included recurrence information such as type of first recurrence (defined by the Standard for Oncology Registry Entry manual) and date of first recurrence. To evaluate the burden of breast cancer recurrence in the U.S. SEER population, we described the cohort of women diagnosed with breast cancer from 2010 to 2019. We then evaluated the patients with information on the status of recurrence including those that never experience recurrence and those that were never disease free (NDF). We measured frequencies of recurrence by multiple clinical variables such as age at diagnosis, race, stage at diagnosis, and tumor subtype. We followed patients from their date of diagnosis to the event defined by first recurrence, second primary, death, or last contact. We used the Kaplan-Meier method to estimate DFS. Results: The analytic dataset included 412,920 female breast cancer cases diagnosed between 2010 and 2019. Most women diagnosed with breast cancer were between 40 and 64 years old (53%, n=218,760), were White (78%, n= 320,555), were diagnosed with localized tumors (52%, n=213,824), were HER2 negative (HER2-) hormone receptor positive (HR+) (56%, n=230,874), and received treatment (95%, n=390,959). During the observation period, 67% (n = 278,098) of women did not have a recurrence, 3% (n=10,922) had a recurrence, and 16% (n=66,319) were NDF. After excluding patients with NDF status, we observed that the age group with the highest frequency of recurrence was 20-39 (9%). For reference, 4% of women in the 40 to 64 age group has a recurrence event during the observation period. Black women had higher recurrence (6%) compared to white women (3%). Triple negative breast cancers had the highest recurrence (9%) out of all subtypes. When we measured DFS, we observed significant differences by race, independent of tumor subtype. For

example, in patients with HER2+/HR+ tumors, the percentage of patients at 120 months who did not experience a DFS event were 73.6% (95% CI, 72.3% to 74.9%) in white women and 67.5% (95% CI, 63.9% to 70.8%) in black women. Discussion & Conclusion: We are reporting population-based recurrence estimates for breast cancer obtained through the SEER program. This is the largest breast recurrence database in North America. The size of the database allowed precise estimation of recurrence stratified by demographics, subtype, and extent of disease. We observe trends consistent with previous reports and have identified some novel findings that warrant further study. Our long-term goal is to assess how DFS estimates derived from a population-based cohort compares to previously published estimates which are largely derived from RCTs.

Disclosure(s):

Esmeralda Ramirez-Pena, n/a: No financial relationships to disclose

Serban Negoita, MD DrPH: No financial relationships to disclose

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P4-03-14

Proinflammatory Dietary Patterns and Risk of Total and Subtypes of Breast Cancer Among US Women

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Background: Dietary patterns promoting chronic inflammation, including the empirical dietary inflammatory pattern (EDIP), have been shown to strongly influence risk of weight gain, type 2 diabetes, cardiovascular disease, and colorectal cancer. However, it is unclear if this dietary pattern is associated with other tumors in which the mechanisms are not totally understood such as breast cancer. Methods: We prospectively followed 76,295 women from the Nurses' Health Study (NHS, 1984-2016) and 91,078 women from the Nurses' Health Study II (NHSII, 1991-2017). Diet was assessed by food frequency questionnaires (FFQs) every 4 years. The

inflammatory potential of diet was evaluated using the previously established EDIP based on plasma C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor alpha receptor 2 (TNF- α R2). Higher scores indicate higher inflammatory potential of the diet. Results: During 4,153,676 person-years of follow-up, we documented 10,632 invasive breast cancer cases (6,807 NHS; 3,825 NHSII). In the pooled multivariable-adjusted analyses, women in the highest, compared with the lowest, EDIP quintile were at higher breast cancer risk (HRQ5vsQ1=1.12; 95% CI 1.05, 1.20; P-trend< 0.001). This association was attenuated after adjusting for weight change since age 18 y, although it remained significant (HRQ5vsQ1=1.07; 95% CI 1.00, 1.14; P-trend=0.01). In subtype analyses, we found evidence that the inflammatory potential of diet influenced breast cancer risk differentially by ER status (P-heterogeneity=0.038) and by molecular phenotype (P-heterogeneity=0.007), with the association between EDIP and breast cancer limited to ER-negative tumors (HRQ5vsQ1=1.31; 95% CI: 1.11, 1.55; P-trend=0.002; for ER-positive tumors, HR Q5vsQ1=1.03; 95% CI, 0.96, 1.12;P-trend=0.10) and basal-like tumors (HRQ5vsQ1=1.78; 95% CI: 1.19, 2.65; P-trend=0.004). Further adjustment for weight change since age 18 y did not materially alter the association for these subtypes. Conclusions: Dietary patterns with high potential to contribute to chronic systemic inflammation, based on higher EDIP scores, were associated with a modestly increased risk of breast cancer, which was more pronounced for ER-negative and basal-like breast tumors.

Disclosure(s):

Andrea Romanos-Nanclares, PhD: No financial relationships to disclose

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Daniel G Stover, MD: No financial relationships to disclose

Sarah Asad, MPH: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-03-15

Does age affect outcome? Data from a large cohort from British Columbia, 2005-2014

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Background

Prior data has been conflicting about how age at diagnosis impacts patient outcomes and survival. Some studies suggest that younger age at diagnosis may negatively affect survival, independent of other disease characteristics. Accurate predictions of outcomes and patterns of relapse provide invaluable information to patients and help inform physician treatment recommendations, such as the role of extended adjuvant endocrine therapy.

Purpose

To determine the relapse free survival and overall survival data for all patients diagnosed with invasive breast cancer and treated at BC Cancer from 2005 to 2014.

Methods

Using the BC Cancer Breast Cancer Outcomes Unit (BCOU) database, we identified all patients referred with newly diagnosed invasive breast cancer at any stage between 2005 and 2014. For descriptive statistics, we analyzed clinical and pathological features at diagnosis and treatment specific variables compared across the following age cohorts: < 35, 35-39, 40-49, 50-59, 60-69, 70-79, and 80 years of age or more.

To model the non-linear relationship of age at diagnosis as a continuous variable with the risk of relapse and death, we used an additive Cox proportional hazards model adjusting for subtype, LVI status, use of RT, chemotherapy, hormone therapy, and nodal status. We employed the fitted model to extract estimates for specific values of age while fixing other covariates at different values to create high and low risk cohorts. For subtypes Luminal B, HER2 positive and triple negative breast cancer, high-risk subgroups were defined as node-positive plus treatment with chemotherapy. Low risk was defined as Luminal A and node-negative. The extracted estimates were used to investigate the patterns of relapse among different ages via the means of adjusted cumulative incidence curves and to report the 10 year adjusted relapse free survival and overall survival estimates.

Results

We identified 24,469 patients who met the inclusion criteria with a median follow-up of 11.5 years. Patients < 35 and between 35-39 years of age were more likely to be diagnosed with breast cancer that was ductal histology, grade 3, LVI positive, HER2 positive, triple negative, and more advanced TNM stage at diagnosis. These younger patients were also more likely to undergo mastectomy, neoadjuvant and adjuvant chemotherapy compared to older age cohorts. Additive Cox proportional hazards revealed a statistically significant and clinically meaningful reduction in 10-year relapse free survival amongst patients with early-stage disease aged 30 and 35 as well as those aged 80, compared to patients aged 50 when adjusted for stage and treatment exposure. This was consistent across all high- and low-risk subgroups (Table 1). 10-year overall survival was significantly and meaningfully reduced in patients aged 30 and 80 compared to age 50 only amongst the high-risk patient populations.

Conclusion

Both younger and elderly age at breast cancer diagnosis were independent risk factors for poorer prognosis. To our knowledge, this is the largest patient cohort detailing such outcomes differences. Furthermore, this represents a more contemporary clinical context, compared to earlier publications. This work will help clinicians more accurately estimate disease trajectory, and may influence treatments recommendations. Other parameters for the entire cohort will be presented, including a more detailed identification and assessment of patient risk categories and its impact on outcomes.

Table 1

Age	10 year estimate of relapse-free survival [95% CI]			
	30	35	50	80
High risk LumB	0.65 [0.58-0.72]	0.68 [0.63-0.73]	0.77 [0.74-0.80]	0.68 [0.63-0.73]
High risk HER2+	0.73 [0.67-0.78]	0.75 [0.71-0.79]	0.82 [0.80-0.85]	0.75 [0.71-0.79]
High risk TNBC	0.64 [0.58-0.71]	0.67 [0.63-0.72]	0.76 [0.74-0.79]	0.67 [0.63-0.72]
Low risk LumA	0.90 [0.88-0.92]	0.91 [0.89-0.92]	0.94 [0.93-0.95]	0.91 [0.89-0.93]
	10 year estimate of overall survival [95% CI]			
High risk LumB	0.74 [0.69-0.79]	0.77 [0.74-0.81]	0.82 [0.80-0.84]	0.35 [0.31-0.40]
High risk HER2+	0.79 [0.75-0.84]	0.82 [0.79-0.85]	0.86 [0.85-0.88]	0.45 [0.40-0.49]
High risk TNBC	0.76 [0.72-0.81]	0.79 [0.76-0.82]	0.84 [0.82-0.86]	0.39 [0.35-0.43]
Low risk LumA	0.89 [0.87-0.92]	0.91 [0.89-0.92]	0.93 [0.92-0.94]	0.67 [0.64-0.71]

Table 1: 10 year estimates of relapse-free survival and overall survival age estimates by additive Cox proportional hazards model adjusting for subtype, LVI status, use of RT, chemotherapy, hormone therapy, and nodal status.

10 year estimates of relapse-free survival and overall survival age estimates by additive Cox proportional hazards model adjusting for subtype, LVI status, use of RT, chemotherapy, hormone therapy, and nodal status.

Disclosure(s):

Emily B. Jackson, MD FRCPC: No financial relationships to disclose

Lovedeep Gondara, MSc: No financial relationships to disclose

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expert testimony (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly:

honoraria (Ongoing); Merck: honoraria (Ongoing); Novartis: honoraria (Ongoing); Pfizer:

Contracted Research (Ongoing), honoraria (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing); Seagan: Consulting Fees (e.g., advisory boards) (Ongoing)

12/8/2022

7:00 AM - 8:15 AM

P4-03-16

Association between tamoxifen and the incidence of cataract in ductal carcinoma in situ patients

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Background Tamoxifen is used to improve oncologic outcomes in a hormone receptor-positive breast cancer. High-dose tamoxifen induced ocular toxicities, and regular dose of tamoxifen is known to increase the risk of cataracts in landmark studies. The current study's objective is to review the incidence of cataracts in ductal carcinoma in situ (DCIS) patients who received adjuvant tamoxifen treatment, which can exclude the effect of other treatment modalities such as chemotherapy and target therapy. Method Data were obtained from the National Health Insurance claims database of the Health Insurance Review and Assessment Service in South Korea. Patients diagnosed with DCIS were sorted and retrospectively reviewed for the incidence of cataracts. The primary study outcome was the incidence of cataracts according to tamoxifen, and the incidence of cataracts was defined by concomitant diagnostic and behavioral code based on International Code of Disease, 10th revision. Results A total of 12,032 patients diagnosed with DCIS and received breast surgery from 2009 to 2015 were cut down to 4,759 patients, excluding those who already had cataracts, malignancies, or had developed cataracts within a year of breast cancer surgery. There were 3,037 patients who received tamoxifen and 1,722 patients who did not, median age of 49 years old. The incidence of cataracts was similar according to the use of tamoxifen, 7.6% and 7.7% respectively. The risk of developing cataracts did not increase with or without tamoxifen, even in the group who received adjuvant tamoxifen for more than two years (HR 0.978, 95% CI 0.782-1.222, p=0.843). The findings were consistent after propensity score matching (HR 1.072, 95% CI 0.829-1.388, p=0.595). Conclusions In a nationwide cohort study, the risk of cataracts in DCIS patients is similar whether the tamoxifen is used or not.

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Dooreh Kim, MD: No financial relationships to disclose

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Hye Sun Lee, PhD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-03-17

Parity, Use of Statins and Low-dose Aspirin, and Breast Cancer Risk – data from two large cohort studies

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Background: Statins and low-dose aspirin have been associated with a reduced breast cancer (BC) incidence, but results are inconsistent. Based on emerging evidence that parity, a protective factor for breast cancer, and these drugs modulate immunity, we hypothesized that the association between drug use and breast cancer risk may differ by parity. Objectives: To assess the associations of statin and low-dose aspirin use with BC incidence according to parity in French and Danish cohorts. Methods: We conducted two cohort studies, using data from the French E3N study and a Danish nationwide population-based cohort, respectively. From E3N, 51,482 women, mean age 65.5 years, were enrolled in 2005 and followed until 2014. Data on parity (here full-term pregnancies), drug use, and incident BC were acquired from questionnaires, a drug reimbursement database, pathology verified self-reports and the national cause-of-death registry, respectively. From nationwide health registries, we included all Danish women free of BC and aged 45 years in 2000-2005 (n=198,575), with follow-up to 2014. Use of the exposure drugs were defined as at least two reimbursements/filled prescriptions. In both cohorts, multivariable-adjusted Cox regression was used to compute hazard ratios (HR) for drug exposure, treated as time-varying lagged variables, and BC risk stratified by parity (0, 1, 2, 3+). Results: In E3N and Denmark, 1,878 and 5,436 incident BC cases occurred in a mean follow-up of 8.5 and 11.5 years, respectively. At the end of follow-up, 35% and 19% of E3N and 16% and 8% of the Danish cohort had been exposed to statins and low-dose aspirin, respectively. In E3N, effect modification was observed between parity and statins, but not low-dose aspirin. For statins, the HRs for use vs no use were 1.29 (0.97-1.72), 1.27 (0.99-1.65), 1.08 (0.91-1.27), and 0.76 (0.61-0.95) among women with 0, 1, 2, and 3+ full-term pregnancies, respectively (p-het=0.005). The corresponding estimates for low-dose aspirin were: 1.17 (0.80-1.71), 0.81 (0.54-1.20), 1.13 (0.90-1.43), and 1.22 (0.93-1.61; p-het=0.6). In contrast, the

Danish data did not suggest any effect modification. HRs for use vs no use of statins were 0.82 (0.60-1.13), 1.05 (0.80-1.37), 0.91 (0.75-1.10), and 1.09 (0.83-1.44) among women with parity of 0, 1, 2, and 3+, respectively (p -het=0.3). For low-dose aspirin HRs were: 1.09 (0.75-1.59), 0.79 (0.54-1.15), 1.04 (0.82-1.32), and 0.99 (0.71-1.40; p -het=0.8). Conclusions: We observed effect modification by parity for the association between statins and breast cancer risk in the French but not the Danish cohort. Whether the age difference between the cohorts explains the inconsistent results should be explored.

Disclosure(s):

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P4-03-18

Group-based trajectories of endocrine therapy adherence and risk of recurrence in a Danish premenopausal breast cancer cohort

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Background:

Adjuvant endocrine therapy (AET) approximately halves the risk of recurrence among the two-thirds of premenopausal breast cancer patients whose tumors overexpress the estrogen receptor (ER+). AET is recommended for a minimum five-year duration, but many premenopausal women discontinue AET prematurely. Adherence to AET is dynamic and influenced by many behavioral, societal, clinical, and genetic factors. Describing longitudinal patterns of AET adherence is an important first step towards identifying patients at highest risk of nonadherence—and therefore recurrence—who may benefit from adherence-enhancing interventions. We used group-based trajectory models to (1) describe AET adherence patterns, and (2) estimate associations between AET adherence and breast cancer recurrence in a Danish premenopausal, ER+ breast cancer cohort.

Methods:

Our cohort included 4,487 premenopausal women diagnosed with ER+, stage I–III primary breast cancer registered in the Danish Breast Cancer Group (DBCG) clinical database and treated with AET (2002–2011). We followed all patients from initiation of AET until recurrence,

mortality, 10 years of follow-up, another primary malignancy, or the end of available follow-up. We excluded individuals with less than 1.5 years of follow-up as breast cancer recurrences that occur in this time are unlikely to be related to AET. At semi-annual follow-up visits, women were registered as having received (or not) a six-month supply of AET. We created daily indicators to determine if a woman had at least 80% of days covered by an AET fill within each six-month period for the first 4.5 years following AET initiation, yielding 9 variables indicating time-varying adherence. We used these indicators to characterize adherence trajectory groups. We defined recurrence as local, regional or distant metastases or contralateral breast cancer registered in the DBCG using follow-up data through 2017. We fit Cox regression models, adjusted for age and clinical factors, to estimate the association between adherence trajectory groups and recurrence.

Results:

We identified distinct trajectory groups in the cohort (Table 1)—high adherence (69%), slow decline (23%), and quick decline (8%). Women with quick decline were more likely to have stage I disease, have no positive lymph nodes, to not be treated with chemotherapy, and to have lumpectomy instead of mastectomy when compared to women with high adherence. Compared with high adherence women, the estimated rate of breast cancer recurrence was higher among those with slow decline (HR=1.12, 95%CI=1.04–1.21) and those with quick decline (HR=1.38, 95%CI=1.22–1.56).

Conclusions:

Group-trajectory modeling facilitated empirical description of AET adherence patterns in a premenopausal breast cancer cohort. As expected, women who more rapidly became AET-nonadherent were at increased risk of breast cancer recurrence compared with those who remained adherent. Future analyses will explore the contribution of specific socioeconomic, genetic, and clinical factors to AET adherence patterns, which will inform the design of interventions to improve AET adherence and reduce recurrence risk in breast cancer patients.

Table 1. Trajectory group and the observed proportion of individuals adherent to their adjuvant endocrine therapy (AET) over 4.5 years of follow-up

Time since AET initiation	Proportion of individuals adherent to AET		
	High adherence (69%)	Slow decline (23%)	Quick decline (8%)
0.5 year	1	1	1
1 year	1	0.90	0.74
1.5 years	1	0.89	0.64
2 years	1	0.98	0.44
2.5 years	1	0.92	0.26
3 years	1	0.90	0.08
3.5 years	1	0.83	0.06
4 years	1	0.71	0.05
4.5 years	1	0.59	0.05

Disclosure(s):

Kirsten M. Woolpert, MPH: No financial relationships to disclose
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Thomas P. Ahern, PhD, MPH: No financial relationships to disclose
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Bent Ejertsen, MD: Astra Zeneca: Grant to my institution (Ongoing); Eli Lilly: Grant to my institution (Ongoing); MSD: Institutional (Ongoing); Novartis: Grant to my institution (Ongoing); Pfizer: Grant to my institution (Ongoing); Roche: Grant to my institution (Ongoing)
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12/8/2022

7:00 AM - 8:15 AM

P4-03-19

Expected real-world impact of escalation and de-escalation of Her2-directed therapy in breast cancer patients receiving neoadjuvant therapy.

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Background: For patients with palpable, early stage, Her2+ breast cancer, neoadjuvant therapy (NAT) is the preferred approach to curative treatment. While Trastuzumab (T) is standardly included in NAT protocols globally, there is variable ability to escalate or potentially de-escalate therapy due to perceived cost/benefit of additional Her2 targeting therapies, such as Pertuzumab (P) in the early stage setting. The impact of neoadjuvant Pertuzumab (NeoP) does have potentially significant impact on the need for therapeutic interventions in the setting of recurrence. It is challenging to estimate the real world impact financially on escalated therapy in the neoadjuvant setting and likewise the long-term effects of cost of recurrent therapy. We wanted to assess and estimate the impact of NeoP addition to T in British Columbian patients with Her2+ early breast cancer, and estimate incremental impact on short and long-term costs to our cancer system. Methods: Utilizing quality assurance database prospectively updated at BC Cancer Vancouver, we extracted cases of patients with Her2+ breast cancer who received NAT between 2012 – 2021 to provide real world estimations of prevalence of cases and estimated annual costs. Descriptive statistics were utilized to calculate rate of pCR in patients receiving neoadjuvant her2 directed therapy. Expected rates of improvement in pCR with the addition of NeoP were extracted from meta-analyses of Her2 directed therapy in the neoadjuvant setting. The publicly available national pCODR Economic Guidance Reports were utilized to identify cost per cycle per patient of Pertuzumab, Trastuzumab, TDM-1 and chemotherapy in the Canadian healthcare system. The additional cost of NeoP per centre, per year, was compared to the current cost of non-Pertuzumab containing neoadjuvant regimen. Based on recurrence data collected from the database, the expected impact of NeoP on rate of recurrence and subsequent need for Her2 directed therapy in the metastatic setting was calculated. Results: 347 patients with HER2+ breast cancer received neoadjuvant T + chemotherapy at the BC Cancer Vancouver Centre between May 2012 and May 2022. 137 patients (39.5%) achieved pCR and 210 (60.5%) did not achieve pCR. Of those who did not achieve pCR, 12% recurred and 6% died, compared to only 5% and 1% respectively in the group that did achieve pCR. Based on a risk ratio of 1.57, we calculated the expected rate of pCR in our real world cohort would have increased from 39.5% to 62.3% with the availability of NeoP routinely. For each year of data in our cohort, an average of 40 patients with Her2 positive disease were treated with neoadjuvant therapy. Using modeling based on our real world

cohort we predicted an added cost of \$669,920 to provide neoadjuvant pertuzumab at one Canadian Cancer centre per year. Based on extraction of data from current state, where adjuvant TDM-1 is provided for 13 cycles in the setting of no PCR, the adjuvant TDM-1 costs were estimated to be \$1,729,151 without NeoP and \$1,067,377 with NeoP. The cost difference for addition of NeoP in the treatment of early Her2+ breast cancer at one Canadian Centre per year was calculated as \$8,146 increase in cost. In patients who had recurrence in our cohort we observed a shorter median survival than expected with most patients succumbing to their recurrence within a 2-3 year period. We expanded our modeling to assess the incremental impact on estimated cost of treatment for those who may recur. We estimated a cost saving of \$85,054 per centre, per year, related to decrease in risk of recurrence of Her2+ breast cancer in those who receive NeoP. Conclusion: While the additional cost per centre of adding NeoP was \$8,146, the subsequent decrease in expected rate of recurrence resulted in a cost savings of \$85,054.

Disclosure(s):

Andrew Mollenthiel, BSc: No financial relationships to disclose

Aidan Morris, BSc: No financial relationships to disclose

Corke Lauren, BSc: No financial relationships to disclose

Christine Simmons, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Bayer: Consulting Fees (e.g., advisory boards) (Ongoing); Knight: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing)

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Association between reproductive factors (parity and age first full term birth) and the frequency of estrogen receptor negative breast cancer according to age at diagnosis

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Background: The frequency of early estrogen receptor (ER)-negative breast cancers (BC) decreases with increasing age at diagnosis (Partridge P, JCO 2016). Giving birth is generally considered a protective factor for the occurrence of BC in a woman's lifetime. However, for up to more than 20 years following childbirth, BC risk may be higher. This appears to be due to an increase in hormone receptor-positive BC, especially in women older at the time of 1st childbirth (Nichols HB, Ann Int Med 2019). This means that the ER-negative BC are relatively less frequent in these 2 decades after delivery. In this study, we aimed at retrospectively investigating the impact of parity and age at first full term pregnancy (FFTP) on the frequency of ER-negative BC according to the age at diagnosis in a large institutional cohort of patients diagnosed with BC.

Patients and Methods: We considered all patients diagnosed and/or treated with early BC in UZ Leuven between January 2000 and November 2020. ER-negativity was defined as < 1% positive cells. Age at diagnosis was subdivided in categories of 5 years. Parous women could be having a low (1 or 2 children) or high parity (> 2 children) and age of FFTP was arbitrarily divided into < or \geq 27 years of age. BMI was considered a possible confounder and was corrected for. A logistic regression model was used for data analysis with ER-negative status as binary outcome and FFTP class and multiparity as explanatory variables. To test whether the difference in ER-negative proportions between FFTP classes depends on multiparity, we modelled the interaction between multiparity and FFTP class.

Results: We included 9955 consecutive female patients after excluding missing values. 8358 out of 9955 women had at least 1 child (84%). In our study population, parity as such was not an independent variable for BC subtype. Women with a FFTP \geq 27y as compared to those with a FFTP < 27y were less likely to have an ER-negative BC. The p-value for the interaction term between high parity (>2 children) and FFTP class equals $p= 0.0044$. Hence, there is statistical evidence to suggest that the differences between FFTP categories with regards to ER-negative BC may depend on multiparity. Table 1 shows a lower incidence of ER-negative BC in the FFTP \geq 27y group compared to the FFTP < 27y group in case of high parity. Table 2 shows the absolute proportion. These results seem to be independent of BMI.

Conclusion: Women with a FFTP at 27 years of age or older and more than 2 children have proportionally less ER-negative type breast cancers as compared to women with a FFTP before 27 years of age. This difference between FFTP classes is not observed in absence of high parity.

Table 1: effect of FFTP class by multiparity

Comparison	Group	Odds Ratio (95% CI)	P-value
FFTP>=27y vs FFTP <27y	1-2 children	1.027 (0.892;1.182)	0.7089
FFTP>=27y vs FFTP <27y	>2 children	0.665 (0.510;0.866)	0.0025

OR: odds ratio, CI: confidence interval

OR>(<)1: higher (lower) probability of ER-negative BC for FFTP>27y compared to FFTP <27y

Table 2: proportion of ER-negative breast cancer subtype

Age at diagnose	All	Parous	Age FFTP	All	Para 1-2	Para > 2
Total number	% ER-neg	% ER-neg	% ER-neg	% ER-neg	% ER-neg	% ER-neg
<41 n=754	31,7	32,3 n=532	<27	32,7	32,1	34,5
			≥27	32,1	32,8	27,3
41-45 n=820	20,5	19,7 n=678	<27	22,1	22,9	20,2
			≥27	18,3	19,7	12,6
46-50 n=1323	15,1	14,8 n=1093	<27	17,9	16,8	20,9
			≥27	11,4	11,9	9,6
51-55 n=1396	17,4	17,8 n=1196	<27	17,6	17,9	16,8
			≥27	17,4	17,8	15,6
56-60 n=1272	14,1	14,6 n=1082	<27	15,5	15,0	16,8
			≥27	12,9	12,7	14,1
61-65 n=1265	12,6	12,7 n=1081	<27	13,9	11,5	19,1
			≥27	9,8	9,7	10,1
66-72 n=1429	13,7	13,8 n=1255	<27	15,3	14,0	17,5
			≥27	10,5	11,2	7,9
>72 n=1556	13,7	14,1 n=1322	<27	14,0	11,9	16,3
			≥27	13,9	14,1	12,9

Disclosure(s):

Maja Vangoitsenhoven, MD: No financial relationships to disclose

Evert Theys, n/a: No financial relationships to disclose

Karen Van Baelen, MD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-03-21

Racial disparities in survival trends in patients with metastatic Hormone receptor positive/Her 2 negative breast cancer: a SEER population-based study

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Hormone-receptor-positive (HR+) breast cancer (BC) accounts for around 70% of all BCs[1]. Targeting the estrogen-receptor (ER) pathway has been the therapeutic focus; however, a substantial subset of HR+ BCs are resistant to hormonal blockade. Addition of Cyclin-dependent kinases 4 and 6 inhibitors (CDKis) to endocrine therapy has demonstrated to improve progression-free and overall survival in patients with metastatic ER+ BC. However, these trials enrolled mostly non-Hispanic White patients, with minimal inclusion of non-Hispanic Black and Hispanic patients. The goal of this study is to assess survival trends for different racial/ethnic groups in patients with HR+ HER2- BC before and after introduction of the CDKis as standard of care (year 2015). Methods: Using the SEER database of the National Cancer Institute, we identified patients with metastatic HR+ HER2- breast cancer. We obtained patients with ICD-0-3 codes 8500/3, 8501/3, 8502/3, 8503/3, 8507/3, 8520/3, 8521/3, 8522/3, 8523/3 and 8524/3. We divided them in two time-based cohorts: patients diagnosed in 2010-2013 and patient diagnosed in 2015-2018. SEER*STAT and Kaplan-Meir methods were used to estimate breast cancer specific survival at 6, 12, 24, 36 and 48 months for each group. Trends in survival were compared among Hispanic (H), Non-Hispanic White (NHW), and Non-Hispanic Black (NHB) patients. Results: We identified 10,019 patients that met our inclusion criteria, 4,667 (47%) diagnosed during 2010-2013 and 5,352 (53%) diagnosed during 2015-2018. For the patients diagnosed during 2010-2013, there were 4610 (99%) female and 57 (1%) were male. In the 2010-2013 group non-Hispanic white patients were 3,124 (67%) vs. 3,443 (64%) in 2015-2018, Non-Hispanic black patients were 639 (14%) vs. 736 (14%) and 521 (11%) vs. 645 (12%) were Hispanic of any race. For the 2010-2013 group, 3,463 (74%) had bone, 884 (19%) liver, 239 (5%) brain and 1,222 (26%) lung metastasis. There were 3,830 (83%) ER+/PR+ tumors, 777 (17%) ER+/PR- and 60 (1%) ER-/PR+. For the 2015-2018 group, there were 5266 (98%) female and 86 (2%) were male. 4011 (75%) had bone, 961 (18%) liver, 257 (4%) brain metastasis and 1469 (27%) lung metastasis. There were 4,424 (82%) ER+/PR+ tumors, 876(16%) ER+/PR- and 52 (1%) ER-/PR+. The 48-month BCSS rate for all patients improved from 2010-2013 to 2015-2018 (46.3% vs. 40.2 %), with an absolute improvement in 7.4%, 1.4%, 3.6% for NHW, NHB, and H patients, respectively. The 36-month BCSS rate for all patients improved from 2010-2013 to 2015-2018 (55.6% vs. 51.3%), with an absolute improvement in 4.9%, 2.6% for NHW, H patients, respectively, whereas NHB showed an absolute decrease of 4.5%. The 12-month BCSS rate for all patients improved from 2010-2013 to 2015-2018 (81.5% vs. 80.2%), with an absolute improvement in 2.4% and 0.8% for NHW, and H patients respectively. For NHB there was an absolute decrease in survival of 2.4%. Conclusions: Using population data, we report that the 48-month BCSS has improved from 2010-2013 to 2015-2018 by about 5.9%. However, the magnitude of the improvement was

different by racial/ethnic groups. The magnitude of improvement in BCSS is higher in NHW as compared to NHB and H patients. Our results suggest that despite recent advancements in the management of ER+/HER2- metastatic BC, racial disparities in outcomes still persist which could be explained by either intrinsic genetic differences in response to novel agents or lack of access to them in some ethnical/racial groups.

Disclosure(s):

Alvaro Alvarez Soto, fellow: No financial relationships to disclose

Ana Maria Bernal, clinical research associate: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-03-22

Linking Internal Medicine Care to Metastatic Breast Cancer Patients for Success: LIMBS

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Background: The Advanced Breast Cancer (ABC) program at The University of Texas MD Anderson Cancer Center was created by metastatic breast cancer (MBC) patients for MBC patients. The ABC Program seeks to improve quantity and quality of life for patients living with MBC. MD Anderson actively treats 2,076 patients living with MBC. ABC program patient advocates voiced the need to increase MBC patients' access to internal medicine services coordinated with oncology care.

Significance: Previous literature suggests patients living with MBC have difficulty receiving oncology coordinated internal medicine services due to their terminal diagnosis and indefinite prescription of anti-cancer treatment. Comorbidities in this setting are known to be associated with inferior outcomes. ABC Program patient advocates reported various challenges seeking care from community based medical professionals including, timely awareness of their local provider on the status of their cancer. Other challenges included the lack of familiarity of some providers with novel MBC cancer treatment, side effects, and interactions of their cancer

treatment with non-cancer conditions and treatment. Therefore, with the increasing life expectancy of MBC patients, there is a growing realization of the importance of managing the medical comorbidities in coordination with the MBC patient's cancer treatment.

Purpose: To increase access and coordinate internal medicine services for MBC patients with medical comorbidities.

Interventions: In partnership with ABC Program patient advocates, the Linking Internal Medicine and Metastatic Breast cancer for Success (LIMBS) clinic was created in February 2021. The LIMBS clinic aimed to bridge the gap in lack of oncology coordinated internal medicine service for MBC patients.

Evaluation: Breast Medical Oncology providers requested LIMBS clinic consults for 108 patients for comorbidity management since the clinic inception. This is a 44% increase in internal medicine consultations prior to LIMBS clinic creation (60 vs 108). The LIMBS clinic consults resulted in 474 follow up visits. Compared to MBC patients at MD Anderson, LIMBS patients were more likely to be African American (20% vs 13%) and were more likely to be older (59 years vs 57 years). Gender, marital status, and clinical trial enrollment did not differ between LIMBS patients and MBC patients. LIMBS patients had significantly higher rates of hypertension (46% vs 19%), Type II DM (19% vs 6%), hyperlipidemia (13% vs 10%), and hypothyroidism (13% vs 6%) compared to MBC patients in general. LIMBS patients had lower rates of anxiety (8% vs 11%) and depression (2% vs 7%) when compared to the MBC patients in general. The top 10 comorbidities for all MBC patients versus LIMBS patients are listed in Table 1.

Discussion: It is feasible to build and integrate internal medicine with breast medical oncology services for patients with metastatic breast cancer. Future research should focus on exploring, describing, and meeting the internal medicine needs of MBC patients. Future initiatives are needed to bridge the gap in care for oncology coordinated internal medicine services between community and tertiary care centers.

Table 1. Top 10 Comorbidities of all MBC patients versus LIMBS clinic patients

Table 1.

Top 10 Comorbidities of all MBC patients versus LIMBS clinic patients

Diagnosis	% MBC Patients (n=2,076)	% LIMBS patients (n=108)
Hypertension	19.4	46.3
Menopausal climacteric status	13.9	6.5
Allergic rhinitis	13.6	0.1
Gastroesophageal reflux	11.8	12.0
Anxiety	10.9	8.3
Hyperlipidemia	10.4	13.9
Osteoarthritis	7.6	4.6
Major depression	7.3	1.9
Diabetes Mellitus, Type II	6.3	19.4
Hypothyroidism	6.0	13.0

Note. This table demonstrates the top 10 comorbidities for MBC population and the LIMBS population.

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Disclosure(s):

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Debu Tripathy, MD: AstraZeneca: Fees for lectures (educational) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); GlaxoSmithKline: Consulting (Ongoing); Novartis: Clinical research support (paid to institution) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing); OncoPep: Steering committee (Ongoing); Pfizer: Consulting (Ongoing)

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7:00 AM - 8:15 AM

P4-03-23

Comparison of Breast Cancer vs Cardiovascular Disease Risk and Uptake of Chemoprevention vs Statins in a Cohort of Predominantly Hispanic Women Undergoing Screening Mammography

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Background: Atherosclerotic cardiovascular disease (ASCVD) and breast cancer are two of the most diagnosed chronic diseases among women in the U.S. Although prevention of ASCVD with statins is widely practiced, breast cancer chemoprevention with selective estrogen receptor modulators (SERMs) or aromatase inhibitors (AIs) is underutilized in the primary care setting, despite significant evidence in randomized controlled trials demonstrating its clinical benefits. We compared the risk of ASCVD and breast cancer among predominantly Hispanic women undergoing screening mammography, as well as uptake of statins and SERMs/AIs for ASCVD and breast cancer risk reduction, respectively, among high-risk women.

Methods: We conducted a retrospective cohort study among 1,655 English or Spanish-speaking women, age 40-79 years, with no prior history of breast cancer, who underwent screening mammography from 2014 to 2016 at Columbia University Irving Medical Center in New York City. Participants completed a survey collecting data on sociodemographic and

breast cancer risk factors and had available data in the electronic health record (EHR) for calculating ASCVD risk, including systolic blood pressure, total and HDL cholesterol, history of diabetes, treatment for hypertension, and current smoking status. The main outcomes included 5-year and lifetime invasive breast cancer risk according to the Gail model, and 10-year and lifetime ASCVD risk score according to the 2013 American College of Cardiology (ACC)/American Heart Association (AHA) ASCVD risk calculator. High-risk was defined as a 5-year invasive breast cancer risk \geq 1.67% and 10-year ASCVD risk \geq 7.5%. Secondary outcomes included uptake of chemoprevention with SERMs or AIs and statins among women at high-risk for breast cancer and ASCVD, respectively, based upon medication lists in the EHR. We compared mean lifetime risk of breast cancer vs ASCVD for the entire cohort using a paired t-test, and the proportion of high-risk women taking statins vs chemoprevention using McNemar's test.

Results: Among 1,655 evaluable women, mean age was 58 years (SD=10.1 years), with 76% Hispanic, 6% non-Hispanic White, 3% non-Hispanic Black, 2% Asian, and 13% other. About half (48%) of women met high-risk criteria for ASCVD compared to 15% who met high-risk criteria for breast cancer. Among all women, mean lifetime ASCVD risk was higher than mean lifetime breast cancer risk (10.71% vs. 5.46%, $p < 0.001$). Among women at high risk for ASCVD or breast cancer, respectively, statin uptake was higher compared to SERM/AI uptake for breast cancer chemoprevention (84% vs. 7%, $p < 0.001$). Overall, fewer Hispanic compared to non-Hispanic women met high-risk criteria for ASCVD (47% vs. 51%, respectively) and breast cancer (9% vs. 34%, respectively).

Conclusions: In a population of predominantly Hispanic women undergoing screening mammography, we found that more women met high-risk criteria for ASCVD compared to breast cancer. Among women at high risk for ASCVD, statin uptake was about 12-fold higher compared to uptake of breast cancer chemoprevention among women at high risk for breast cancer. Given significant underutilization of breast cancer chemoprevention, placing this in the context of prevention of other chronic diseases, such as statins for ASCVD, may enhance uptake of SERMs or AIs in the primary care setting.

Characteristic	Hispanics (N=1263, 74%)	Non-Hispanics (N=392, 26%)	Total (N=1655)	P-value
High-risk for ASCVD, N (%)				0.0165
Yes	597 (47.3)	201 (51.3)	798 (48.2)	
No	666 (52.7)	191 (48.7)	857 (51.8)	
High-risk for Breast Cancer, N (%)				<.0001
Yes	118 (9.3)	132 (33.7)	250 (15.1)	
No	1145 (90.7)	260 (66.3)	1405 (84.9)	
Mean lifetime ASCVD risk, % (SD)	10.72 (18.95)	11.86 (17.53)	10.71 (18.95)	0.2910
Mean lifetime breast cancer risk, % (SD)	5.47 (3.25)	8.57 (4.65)	5.46 (3.25)	<.0001

Disclosure(s):

Luisa Nilan, BA: No financial relationships to disclose

Mary M. McDermid, MPH: No financial relationships to disclose

Jacquelyn N. Amenta, BS, MPH: No financial relationships to disclose

Julia E. McGuinness, MD: Seagen: Consulting Fees (e.g., advisory boards) (Ongoing)

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7:00 AM - 8:15 AM

P4-03-24

State variation in racial and ethnic disparities in triple-negative breast cancer rates: NPCR-SEER incidence data, 2015-2019

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Background: Triple-negative breast cancer (TNBC) (i.e., estrogen receptor-negative, progesterone receptor-negative, and human epidermal growth factor receptor type 2-negative) is an aggressive subtype of breast cancer, more frequently diagnosed among non-Hispanic Black women than other racial/ethnic groups in the United States. TNBC risk also varies by location, but limited data exist for state-level variation in the racial/ethnic disparities in TNBC risk. Methods: Data for TNBC diagnosed at all ages during 2015-2019 were obtained from the National Program of Cancer Registries and Surveillance, Epidemiology & End Results for racial/ethnic groups classified as non-Hispanic American Indian/Alaska Native (AIAN), non-Hispanic Asian or Pacific Islander (API), non-Hispanic Black (Black), Hispanic, or non-Hispanic White (White). State-specific incidence rates were available for 8, 23, and 36 states for AIAN, API, and Hispanic women, respectively, and 38 states and Washington, D.C. for Black women and 50 states and Washington, D.C. (hereafter referred to collectively as “states”) for White women. State-specific rates were compared within and between racial/ethnic groups using incidence rate ratios (IRR). Results: Nationally, the age-standardized incidence rate of TNBC was the highest among Black women (25.1 per 100,000), followed by White (12.9 per 100,000), AIAN (11.1 per 100,000), Hispanic (11.1 per 100,000), and API (9.0 per 100,000) women. The highest state-specific rates were found among Black women in Delaware, Missouri, and Louisiana (>30 per 100,000) and the lowest rates were among API women in Oregon and Pennsylvania (< 7 per 100,000). State variations within a population were relatively larger among AIAN (2.8-fold) and Hispanic (2.3-fold) women, and smaller among White women (1.65-fold). Compared with White women, Black women had a higher rate of TNBC in all 39/39 states with the greatest IRRs in Delaware (2.31, 95%CI=1.90-2.81), Missouri (2.28, 95%CI=2.08-2.50), and Louisiana (2.20, 95%CI=2.02-2.38) and the lowest IRRs in Minnesota (1.38, 95%CI=1.12-1.68) and Colorado (1.38, 95%CI=1.12-1.68). In contrast, API women had a lower rate than White women in 22/23 states, except for Nevada, with the lowest IRR in Oregon (0.50, 95%CI=0.34-0.70) and the highest IRR in New York (0.82, 95%CI=0.75-0.90). The rate among Hispanic compared with White women did not differ statistically significantly in 23/36 states but was lower in 12/36 states, with the lowest IRR in Ohio (0.57, 95%CI=0.43-0.74), and higher in Massachusetts (1.21, 95%CI=1.04-1.39). The rate among AIAN compared with White women did not differ in 5/8 states but was lower in Arizona (0.53, 95%CI=0.38-0.73) and North Carolina (0.68, 95%CI=0.46-0.96), and higher in Oklahoma (1.30, 95%CI=1.09-1.54). Conclusions: State variations in TNBC incidence rates both within and between populations are

substantial, signifying the important role of potentially modifiable risk factors in determining the risk of TNBC by state and race/ethnicity. This finding highlights the need for more research to identify factors contributing to these variations to develop more effective preventive measures. Meanwhile, to mitigate the impact of the disproportionate burden of TNBC across states and racial/ethnic groups, universal access to screening modalities and timely, guideline-concordant treatments is essential.

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Hyuna Sung, Ph.D.: No financial relationships to disclose

Daniel Wiese, Ph.D.: No financial relationships to disclose

Ismail Jatoi, M.D., Ph.D.: No financial relationships to disclose

Ahmedin Jemal, D.V.M., Ph.D.: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-03-25

Patient-level predictors of skipping screening mammograms during the COVID-19 pandemic at a large tertiary care center in Texas

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Background:

Following the declaration of the COVID-19 national emergency, screening mammograms (SM) abruptly dropped across the United States. Stay-at-home orders discourage cancer patients from seeking care, and cancer screenings and surgeries were postponed. Upon resumption of screening services, rates of screening were slow to recover. At Baylor St. Luke's CHI (BSL), one of the largest tertiary care centers providing comprehensive cancer screening in Houston, we investigated patient level predictors, including comorbidities and area deprivation index (ADI), and the risk of skipping SM in the first year of the COVID-19 Pandemic.

Methods:

We used the local PENRAD database to retrieve the monthly gross number of SM performed at all BSL sites from 02/2018 to 01/2021. We obtained patient level data through EPIC, including address and demographics, comorbid conditions e.g., diabetes, hypertension, obesity (BMI \geq 30), chronic kidney disease and cardiovascular diseases (CVD). We identified ADI associated with patient addresses. We included patient who received at least one SM between 02/2018 to 01/2020. We compared patients did not get a mammogram in the first year of the pandemic; 02/2020 to 01/2021, to those who maintained screening during the pandemic. We performed a logistic regression analysis to assess the influence of age, 0 to +3 comorbid conditions, and ADI in quartiles on the odds ratio of skipping SM in the first year of the pandemic. Statistical significance was set at $p < 0.05$. The study was IRB approved.

Results:

Out of the 4591 women that screened in 2018 and/or 2019, only 1628 came back for SM in 2020 (35.5%). Women who obtained SM during the pandemic vs those who did not were slightly older, mean age 58 vs 56 (P< 0.001), were less likely to be living in the most deprived neighborhood, Q4 of ADI, 23.8% vs. 25.6%, more likely to be obese 39% vs. 35% (P< 0.001), more likely to have diabetes 48% vs. 41% (P< 0.001), more likely to have CVD, 16% vs. 13% (P< 0.001), and more likely to have hypertension 80% vs. 71% (P< 0.001). On multivariate logistic regression, living in Q4 ADI was associated with 22% higher risk of skipping SM in 2020 (95% CI 1.02-1.42), having one vs. two vs. three comorbid conditions increased the likelihood of obtaining SM in 2020 by 25% (95% CI 0.62-0.91) vs. 30% vs (95% CI 0.58-0.85), 42% (95% CI 0.48-0.7) compared to no comorbid conditions.

Conclusion:

Women living in Q4 of the ADI (most deprived neighborhood) were more likely to miss 2020 screening when compared with the Q1 women (least deprived neighborhood). The more chronic diseases women had, the less likely they were to skip 2020 screening when compared with those that had no chronic disease. This could be because women with many health issues have to frequent health facilities at higher rates and thus less likely to miss mammograms.

Descriptive Table

		MMG before COVID only		MMG before and during COVID		p value	Added to multivariable regression models
Mean (SD)							
Age in Years		56	11	58	10	<0.001	Yes
Body Mass Index		26.03	6.58	25.79	6.51		
N (%)							
ADI Quartile	Quartile 1	716	24.2%	442	27.1%	0.132	Yes
	Quartile 2	747	25.2%	390	24.0%		
	Quartile 3	739	25.0%	408	25.1%		
	Quartile 4	757	25.6%	388	23.8%		
Obesity (Y vs. N)	No	1934	65.3%	998	61.3%	0.007	Yes
	Yes	1029	34.7%	630	38.7%		
Diabetes (Y vs. N)	No	1745	58.9%	853	52.4%	<0.001	Yes
	Yes	1218	41.1%	775	47.6%		
Chronic Kidney Disease	No	2569	86.7%	1389	85.3%		
	Yes	394	13.3%	239	14.7%		
Coronary heart disease / IHD	No	2588	87.3%	1361	83.6%	<0.001	Yes
	Yes	375	12.7%	267	16.4%		
Hypertension	No	849	28.7%	326	20.0%	<0.001	Yes
	Yes	2114	71.3%	1302	80.0%		
Sum of Diseases (4 category)	No Disease	642	21.7%	244	15.0%	<0.001	Yes**
	Only 1 Disease	726	24.5%	376	23.1%		
	2 Diseases	747	25.2%	418	25.7%		
	3+ Diseases	848	28.6%	590	36.2%		

** sum the count of chronic diseases that any single individual has (from zero chronic disease to 3 or more).

Regression: Outcome is "missing 2020 screening" = odds of screening in 2018 or 2019 (pre-covid) but not screening in 2020 (durin

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Up
Age in Years	-0.010	0.003	12.344	1	0.000	0.990	0.984	0.9
ADI Quartile								
ADI Quartile(1)	0.168	0.088	3.700	1	0.054	1.183	0.997	1.
ADI Quartile(2)	0.123	0.087	2.002	1	0.157	1.131	0.954	1.
ADI Quartile(3)	0.194	0.088	4.925	1	0.026	1.215	1.023	1.
No Disease								
Only 1 Disease	-0.286	0.099	8.366	1	0.004	0.751	0.619	0.
2 Diseases	-0.351	0.098	12.875	1	0.000	0.704	0.581	0.
3+ Diseases	-0.544	0.095	33.101	1	0.000	0.581	0.482	0.

Disclosure(s):

Maryam Nemati Shafaei, MD MPH: No financial relationships to disclose

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Randall Parker Kirby, n/a: No financial relationships to disclose

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P4-03-26

Blood DNA Methylation and Breast Cancer: a Prospective Case-Control Analysis in the Breast Cancer Prospective Family Study Cohort

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Breast cancer has increased dramatically in young women < 50 years in the US over the past decade. DNA methylation is a type of epigenetic change that plays an important role in cancer etiology by silencing tumor suppressor genes or DNA repair-related genes through hypermethylation or activating oncogenes through hypomethylation. Previous genome-wide association studies have suggested DNA methylation in blood is a potential epigenetic markers of breast cancer risk. In this study, we applied targeted methyl-seq to examine the DNA methylation profile in regulatory sequences of 57 known DNA repair pathway genes, together with 123 other genes, located in immune-related loci and genome-wide association peaks for breast cancer. We used a nested case-control design within the Breast Cancer Prospective Family Study Cohort (FroF-SC) and examined DNA methylation profile in DNA from the blood of breast cancer cases (N=293) and age-matched controls (N=327). In the preliminary data analysis, we observed that the methylation levels in 5 genes were statistically significantly different between cases and controls using Wilcoxon Rank Sum Test (Table 1). Some candidate loci show methylation values spanning a wide range (Std Dev) in both cases and controls, suggesting the presence of genotype-dependent allele-specific methylation (ASM). We then conducted generalized estimating equations (GEE model) adjusting for age at blood draw and calculated the odds ratios (ORs) and 95%CI for the association between methylation levels in the 90th and 10th percentiles of differentially methylated genes (90% vs 10% methylation) and breast cancer risk. The ORs (95% CI) from the GEE models were 1.26 (0.97, 1.63, p=0.08) for CD6, 1.27 (0.85, 1.91, p=0.24) for SDCCAG3, 1.12 (0.85, 1.48, p=0.40) for DCLRE1B, 1.29 (0.88, 1.90, p=0.20) for IP09, and 1.63 (1.08, 2.45, p=0.02) for GNPDA1 (Table 2). The associations were not different by age group. Our preliminary results suggest that DNA methylation measured in blood may be a biomarker of breast cancer susceptibility.

Disclosure(s):

HuiChen Wu, n/a: No financial relationships to disclose
Angelica Castano, n/a: No financial relationships to disclose
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P4-03-27

The impact of Sociodemographic Disparities on Overall Survival of Adolescent and Young Adults (AYA) with Invasive Breast Cancer

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Background: Women of racial/ethnic minorities more often receive a diagnosis of advanced breast cancer (BC) at a younger age, and have higher morbidity, risk of recurrence and mortality. In addition to clinicopathologic and biological differences, sociodemographic factors may influence overall survival (OS) in these patients. BC care in AYA is particularly challenging and requires a multidisciplinary approach. In this National Cancer Database (NCDB) analysis, we aim to investigate various socioeconomic variables and their impact on survival in AYA patients with invasive BC. Methods: Using de-identified data accessed from the NCDB, we conducted a retrospective cohort analysis. Patients diagnosed with invasive BC between 2004-2019 and belonging to the age group of 15-39 years, defined as AYA, were included in the study. We performed an exploratory analysis and divided patients based on race/ethnicity, primary payer (government, private or uninsured), community median income (\leq \$40K, \$40-50K, \$50-63K, \geq \$63K), residence area (metropolitan, rural or suburban) and high school degree achievement. Step-wise univariate regression models were used to analyse the impact of the relevant factors on overall survival. Survival estimates were calculated using the Kaplan Meier method. Results: We identified 18,018 AYA patients with invasive BC. Median age was 36 years, the median time from diagnosis to treatment was 25 days and the median follow-up was 82.9 months (range 0.1 - 207.1 months). The majority of patients were Caucasian (66%), followed by Black (14%), Hispanic (10%) and Asian (6%). 61% of Asian and 47% of Caucasians had an income of \geq \$63,000, whereas only 31% of Hispanic patients and 26% of Black patients were in this income bracket. While Black patients constituted the majority of the lower income community (median income \leq \$40K), Hispanics had the largest amount of patients without a high school degree (44%). Considering all patients, the 5-year OS was 92% (95% CI 0.91-0.92) for this study period. However, improved survival was observed in patients with

private insurance versus government insurance (93% vs 84%, $p < 0.0001$); patients with median income $\geq \$63,000$ compared to $< \$40,000$ (94% vs 88%, $p < 0.0001$); a lower percentage of no high school degree quartile $< 6.3\%$ in contrast to $\geq 17.6\%$ (95% vs 88%, $p < 0.0001$); and lastly, patients living in a metropolitan area as opposed to suburban area (92% vs 89%, $p < 0.0001$). Additional details are noted in Table 1. Conclusions: In our analysis we have found that AYA patients with invasive BC included in the NCDB have a variable OS that is impacted by demographic factors and socioeconomic status. Patients with private insurance, higher income, higher level of education and living in a metropolitan area had improved OS at 2 and 5 years. Understanding and narrowing the disparities in the care provided to AYA patients with invasive BC, particularly to those with sociodemographic disadvantages, could lead to improve outcomes.

Disclosure(s):

Nerea Lopetegui-Lia, M.D.: No financial relationships to disclose

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Megan L. Kruse, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Biotheranostics Inc: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Lilly Oncology: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Novartis Oncology: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); PUMA biotechnology: Consulting Fees (e.g., advisory boards) (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing)

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7:00 AM - 8:15 AM

P4-03-28

Patient Reported Symptom Burden Amongst Immigrant and Canadian Long-Term Resident Women Undergoing Breast Cancer Surgery.

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Background: Disparities in breast cancer outcomes are well documented, with a burgeoning body of literature shedding light on the influence of multiple factors. Much of the literature comes from the US, with the current situation in Canada less well understood. Canada's universal health care system may mitigate some, but unlikely all differences. First generation immigrants comprise 21.9% of the Canadian population. Differences in breast cancer screening rates and stage at diagnosis have been demonstrated between immigrant and non-immigrant Canadian women. However, breast cancer outcomes in the Canadian immigrant population have not been well studied. Patient reported outcomes are one such set of outcomes and crucial in understanding the patient experience. The purpose of this study is to compare symptom burden and trajectories between immigrant and Canadian long-term resident women with breast cancer undergoing breast cancer surgery in Ontario. Methods: A population-level retrospective cohort-study using linked Ontario administrative databases was constructed. Women >18 years of age with newly diagnosed breast cancer between 2010-2016 undergoing surgery at a regional cancer center were included. Baseline variables including immigration status, age, stage, comorbidity and income quintile were collected. The proportion of patients reporting moderate/severe Edmonton Symptom Assessment System Scale (ESAS) scores for each of 9 individual symptom categories over time was collected. Multivariable logistic regression models using generalized estimating equations with exchangeable correlation structure to account for repeated measures were constructed to assess the probability of a moderate/severe score for each of the individual ESAS symptom categories. Results: The cohort included 14,056 women, of which 12,250 (87.2%) were categorized as long-term Canadian residents and 1,806 (12.8%) as immigrants. Immigrant women had a younger mean age of diagnosis (53 vs. 61 years), were more likely to reside in a lowest income quintile neighbourhood (22.2% vs 15.4%), were less likely to be on a primary care physician roster within the last 2 years (83.7% vs. 90.4%) and were less often diagnosed with Stage I/II disease (80.9% vs. 84.6%) (all $p < 0.0001$). The proportion of women reporting moderate/severe scores

was significantly higher amongst immigrant women for 7/9 symptom categories (anxiety, depression, drowsiness, nausea, pain, shortness of breath and well-being) with the largest difference observed for depression (13.1% vs 10.8%, $p < 0.0001$) and pain (14.8% vs. 12.0%, $p < 0.0001$). Comparing symptom trajectories, differences between groups were most pronounced within the first 12 months, though for depression and pain, statistically significant differences also existed at 36 months. On multivariable regression analysis, immigration status was persistently associated with higher proportion of moderate/severe score for pain only (OR 1.12, 95% CI 1.02-1.23). Immigration status was associated with a protective effect for anxiety (OR 0.86, 95% CI 0.78-0.94), drowsiness (OR 0.81, 95% CI 0.73-0.89) and tiredness (OR 0.86, 95% CI 0.79-0.94). Conclusions: To our knowledge, this is the first study comparing symptom burden amongst immigrant and non-immigrant Canadian women with breast cancer at a population-level. Immigrant women undergoing breast cancer surgery were found to have a higher burden of symptoms across most categories, and for depression and pain this difference was found to persist even at 3-years. However, the higher burden of symptoms in many categories seemed to be explained by factors such as younger age and more advanced disease. Adjusting for other factors, immigrant women with breast cancer reported more pain, indicating a need for better symptom management in this population.

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7:00 AM - 8:15 AM

P4-03-29

Impact of the COVID-19 pandemic on breast cancer incidence and tumor stage in the Netherlands and Norway

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Introduction. The SARS-CoV-2 infection rate and the COVID-19 death rate were relatively high in the Netherlands during the first wave of the COVID-19 pandemic (2.7 and 7.2 times higher than in Norway, respectively). Moreover, social measures differed between the two countries. This study aimed to compare the effect of the pandemic on breast cancer incidence and stage between the Netherlands and Norway.

Methods. Women diagnosed with DCIS or invasive breast cancer between January 2017 and December 2021 were selected from the Netherlands Cancer Registry and from the Cancer Registry of Norway. The COVID-19 period was divided in three approximately equal periods: March-September 2020 (first wave), October 2020-April 2021 (second wave), May-December 2021 (post-second wave). Breast cancer incidence during the COVID-19 periods was compared with averaged data of the corresponding reference period: March-September 2017, 2018, 2019 (first wave_ref), October-April 2017, 2018, 2019 (second wave_ref), May-December 2017, 2018, 2019 (post-second wave_ref). Incidences were compared by age group, clinical tumor stage, and method of detection.

Results. The number of breast cancer diagnosis and the breast cancer incidence are shown in Table 1. Compared to the reference period, breast cancer incidence was lower during the first wave in the Netherlands and Norway (IRR: 0.72; 95%CI: 0.70-0.75; IRR: 0.83, 95%CI 0.78-0.88, respectively), and was higher post-second wave in Norway (IRR: 1.10, 95%CI: 1.04-1.16) (Table 1). During the first wave, breast cancer incidence was lower in all age groups in the Netherlands (age < 50 IRR: 0.85, 95%CI: 0.79-0.91; 50-69 IRR: 0.64, 95%CI: 0.61-0.67; 70-74 IRR: 0.61, 95%CI: 0.56-0.67; >74 IRR: 0.86, 95%CI: 0.80-0.93, respectively). During the first wave, incidence was lower in women aged 50-69 in Norway (i.e., women eligible for screening; IRR: 0.68, 95%CI: 0.62-0.74). Post-second wave incidence was higher in women aged 50-69 and >74 in Norway (IRR: 1.09, 95%CI: 1.01-1.17; IRR: 1.13, 95%CI: 1.00-1.28, respectively). In

the first wave the incidence of DCIS, stage I tumors, and screen-detected tumors was lower in the Netherlands (IRR: 0.55, 95%CI: 0.50-0.61; IRR: 0.62, 95%CI: 0.59-0.65, IRR: 0.36, 95%CI: 0.33-0.38, respectively) as well as Norway (IRR: 0.66, 95%CI: 0.54-0.79; IRR: 0.73, 95%CI: 0.66-0.81, IRR: 0.46; 95%CI: 0.40-0.52, respectively).

Conclusion. The current study showed that the incidence of early-stage tumors mainly decreased. Moreover, during the first wave of the pandemic breast cancer incidence decreased in all age groups in the Netherlands but only in women aged 50-69 in Norway. The relatively high infection and death rate in the Netherlands might have increased the fear of patients to visit the general practitioner (GP) and/or to overburden the healthcare system at the start-up of the pandemic. In addition, it might have reduced the capacity at the GP. As a result, appointments with the GP might have been postponed, resulting in a decrease in the number of breast cancer diagnoses in all age groups. A catch-up in breast cancer diagnoses was seen post-second wave in Norway, but not in the Netherlands. Incidence rates should therefore be monitored in the coming period.

Table 1 Number of breast cancer diagnoses (breast cancer incidence) during the COVID-19 pandemic and during the corresponding reference period (incidence is expressed per 100.000 women living in the Netherlands or Norway during the period of interest)

	Period A_ref March- Sept 2017/2019	Period A March- Sept 2020	Period B_ref October- April 2017/2019	Period B October 2020- April 2021	Period C_ref May-December 2017/2019	Period C May-December 2021
Netherlands	9,300 (132.8)	6,849 (96.0)	9,220 (131.7)	9,559 (133.6)	10,621 (151.7)	11,048 (154.0)
Norway	2,242 (107.9)	1,892 (89.4)	2,415 (116.2)	2,607 (122.7)	2,628 (126.5)	2,964 (139.1)

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7:00 AM - 8:15 AM

P4-03-30

Patient characteristics, treatment patterns, and clinical outcomes associated with tucatinib therapy in HER2-positive metastatic breast cancer

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Background: Tucatinib is an oral HER2-targeted therapy that was approved by the FDA in April 2020 for use in combination with trastuzumab and capecitabine for treatment of patients with previously treated HER2+ metastatic breast cancer (MBC). In the randomized HER2CLIMB trial median (95% CI) overall survival (mOS) and progression-free survival (PFS) for patients receiving tucatinib with trastuzumab and capecitabine were 21.9 (18.3, 31.0) and 7.8 (7.5, 9.6) months, respectively. HER2CLIMB utilized a placebo + trastuzumab + capecitabine comparator arm and included patients with active and stable brain metastasis (BM).

Objectives: Describe patient characteristics, treatment patterns, and clinical outcomes for tucatinib-based treatment in the real-world setting.

Methods: This retrospective cohort study included patients treated for HER2+ MBC between

January 2017 and March 2022 in the nationwide de-identified electronic health record-derived Flatiron Health Metastatic Breast Cancer database who received tucatinib-based treatment outside of a clinical trial setting. Demographic and clinical characteristics of patients were described at baseline (MBC diagnosis) as well as at initiation of each oncologist-defined, rule-based line of therapy (LOT). Key outcomes included time to next treatment (TTNT), persistence, and mOS.

Results: Of 2,057 patients treated for HER2+ MBC in the study period who met the inclusion criteria, 154 received tucatinib-based treatment. Of these patients, 18 (12%), 44 (29%), 33 (21%) and 59 (38%) received tucatinib-based treatment in the first-line (1L), second-line (2L), third-line (3L), and fourth-line or further (4L+) respectively. Median age at MBC diagnosis was 54 years. Median follow-up from tucatinib-based treatment initiation was 8.6 months. Overall, 106 (69%) had BM prior to initiating tucatinib therapy (14 [78%], 37 [84%], 20 [61%], and 35 [59%] in 1L, 2L, 3L, and 4L+ respectively). Those with BM initiated tucatinib-based treatment after a median of 2 prior therapies, compared with 2.5 in the non-BM group. The most common metastatic treatment regimens prior to 2L tucatinib-based treatment were trastuzumab + pertuzumab-based, and the most common regimens immediately following 2L tucatinib-based treatment were trastuzumab-based and trastuzumab deruxtecan. The most common regimens immediately prior to and following 3L tucatinib-based treatment were T-DM1 and trastuzumab deruxtecan, respectively. The median (95% CI) TTNT was 8.4 (6.3, 11.3) months overall, and 12.8 (5.5, not reached [NR]) months, 9.8 (4.8, NR) months, and 9.5 (6.1, 15.3) months in 1L, 2L, and 3L, respectively, the median OS was not reached overall (Table 1). Of patients with sufficient follow-up since treatment initiation, 65% (62/96) remained on tucatinib-based treatment after 6 months and 40% (20/50) after 12 months.

Conclusion: The majority of patients receiving tucatinib-based treatment in clinical practice have BM at treatment initiation, constituting a larger proportion of the population than in HER2CLIMB (47.5% of patients). Tucatinib-based treatment use in the real-world setting is associated with a similar mOS and TTNT as in HER2CLIMB.

Median overall survival and time to next treatment in HER2CLIMB and this study

	HER2CLIMB (N=410)	Flatiron Health overall (N=154)
mOS, months (95% CI)	21.9 (18.3, 3.10)	NR (18.8, NR)
Survival probability		
6-month, % (95% CI)	-	84.0 (78.0, 90.4)
9-month, % (95% CI)	-	75.9 (68.8, 83.8)
12-month, % (95% CI)	75.5 (70.4, 79.9)	71.1 (63.1, 80.0)
TTNT, months (95% CI)*	7.8 (7.5, 9.6)	8.4 (6.3, 11.3)
Proportion not on new therapy		
6-month, % (95% CI)	62.9 (56.9, 68.4)	60.2 (52.4, 69.0)
9-month, % (95% CI)	-	47.6 (39.5, 57.2)
12-month, % (95% CI)	33.1 (26.6, 39.7)	38.0 (29.8, 48.5)

*Time to next treatment was used as a proxy for progression-free survival in the HER2CLIMB clinical trial population.

CI, confidence interval; mOS, median overall survival; NR, not reached; TTNT, time to next treatment.

Disclosure(s):

Peter A. Kaufman, MD: Amgen: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), received research support and/or served as a consultant/advisor (Ongoing); Eisai, Inc: Consulting Fees (e.g., advisory boards) (Ongoing), Received research support and/or served as a consultant/advisor (Ongoing); H3 BioMedicine: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), travel support (Ongoing); Macrogenics: Contracted Research (Ongoing), Received research support and/or served as a consultant/advisor (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Polyphor: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), travel support (Ongoing); Roche/Genentech: Consulting Fees (e.g., advisory boards) (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), received research support and/or served as a consultant/advisor (Ongoing)

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7:00 AM - 8:15 AM

P4-03-31

Lifestyle factors are associated with breast cancer risk in women biopsied for benign breast diseases in China: 10-year results of a multi-center, hospital-based, case-control study

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Objective: Benign breast disease (BBD), especially benign proliferative breast disease (BPBD), is related to increased breast cancer risk. However, few studies have examined whether conventional breast cancer risk factors influence risk of breast cancer among women with BBD. The aim of this study was to evaluate the associations of lifestyle factors with risk of breast cancer among women biopsied for BBD within a multi-center, hospital-based, case-control study in China, in order to provide scientific basis of health guidance for BBD patients and lay the foundation for primary prevention of breast cancer.

Methods: A multi-center, hospital-based, case-control study was conducted. Patients with BPBD (n=608) and patients with non-proliferative breast disease (NPBD) (n=366) were collected from 23 hospitals in 11 provinces during April 2012 to April 2013. A face-to-face survey, baseline data and fasting blood was collected with all study subjects. Serum adiponectin levels were assayed using ELISA. After 10 years, the cumulative incidence rate of breast cancer in the two groups was counted through follow-up. Logistic regression analysis was used to obtain the association between specific factors and risk of breast cancer.

Results: After 10 years' follow-up, 388 BPBD and 240 NPBD cases were included in the final analysis (Table 1), of which 16 (4.12%) and 3 (1.25%) developed breast cancer, respectively. The cumulative incidence of breast cancer between the two groups was significant difference (P=0.041). Compared with women in the NPBD group, BPBD group were more likely to be central obesity (with higher waist-to-hip ratio (WHR)) (OR 24.98, 95% CI 1.845-336.203, P=0.015) and less likely to have physical activity (OR 0.626, 95% CI 0.416-0.943, P=0.025) and less often to eat carrots (OR 0.616, 95% CI 0.398-0.953, P=0.030) (Table 2). Subgroup analyze indicated that, physical activity, eat carrots and ham sausage, body weight, BMI, waist circumference and WHR were statistical differences in premenopausal BPBD patients, while only physical activity (OR 0.423, 95% CI 0.269-0.665 P < 0.001) was the independent risk factors. Meanwhile, among the factors of Tea consumption, Glycemia, Body weight, BMI, Waist

circumference, WHR and HMW/total adiponectin ratio in postmenopausal group, only HMW/total adiponectin ratio (OR 0.041, 95% CI 0.002-0.820 P=0.037) was statistically significant factor. These stratified multivariate logistic regression analysis results are shown in Table 3.

Conclusion: In patients with BBD, physical activity may be the protect factor for breast cancer carcinogenesis in premenopausal women while lower HMW/total adiponectin ratio is a risk factor for postmenopausal women, which can provide direction for primary prevention of breast cancer.

Table 1. Pathological types of all subjects.

Pathology	N(%)	Pathology	N(%)
Benign non-proliferative breast disease	240	Benign proliferative breast disease	388
Simple fibroadinoma	167(69.58)	Complex fibroadenoma	109(28.09)
Inflammation	18(7.50)	Hyperplasia	177(45.62)
Duct ectasia	13(5.42)	Multiple papilloma	79(20.36)
Cysts	9(3.75)	Apocrine metaplasia	7(1.80)
Plasma cell mastitis	9(3.75)	Sclerosing adenosis	4(1.03)
Lipomyoma	10(4.17)	Radial scar	2(0.52)
Fat necrosis	6(2.50)	Atypical hyperplasia	10(2.58)
Accessoria	6(2.50)		
Cystic fibrosis	0(0.00)		
Apocrine secretion	0(0.00)		
Epithelial metaplasia	0(0.00)		
Others	2(0.83)		

Table 2. The results of multivariate Logistic regression analysis.

Variables	P	OR	95%CI
Age	0.064	1.023	0.999 1.049
Times of pregnancy and delivery	0.196	1.179	0.918 1.515
Body weight (Kg)	0.450	1.023	0.965 1.084
BMI (Kg/m ²)	0.662	0.996	0.827 1.128
Waist circumference (cm)	0.138	1.025	0.992 1.058
Waist-hip ratio	0.015	24.908	1.845 336.203
History of nipple discharge	0.999	0.000	0.000
Physical activity	0.025	0.626	0.416 0.943
Carrots	0.030	0.616	0.398 0.953
Fried foods	0.293	0.796	0.521 1.217
Ham sausage	0.287	0.803	0.535 1.203

Table 3. Stratified multivariate Logistic regression analysis by menopause status.

Variables	P	OR	95%CI
Group1 Pre-menopause			
Physical activity	<0.001	0.423	0.269 0.665
Carrots	0.112	0.678	0.419 1.096
Ham sausage	0.073	0.669	0.432 1.038
Body weight (Kg)	0.853	1.006	0.942 1.075
BMI (Kg/m ²)	0.877	1.014	0.850 1.210
Waist circumference (cm)	0.308	1.018	0.984 1.054
Waist-hip ratio	0.122	9.837	0.541 178.757
Group2 Post-menopause			
Tea consumption	0.065	0.420	0.167 1.057
Body weight (Kg)	0.677	0.972	0.849 1.112
BMI (Kg/m ²)	0.647	1.081	0.774 1.511
Waist circumference (cm)	0.125	1.071	0.981 1.170
Waist-hip ratio	0.094	162.522	0.420 62944.162
Glycemia (mmol/L)	0.183	1.216	0.912 1.620
HMW/total adiponectin ratio	0.037	0.041	0.002 0.820

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7:00 AM - 8:15 AM

P4-03-32

Association between androgen receptor expression and recurrence free survival among locally advanced triple negative breast. Real world data from a single Institution in Mexico City

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Background The androgen receptor (AR) is expressed in 12-41% of the TNBC, contributes with differentiation, proliferation, apoptosis, and angiogenesis; its expression is associated with better recurrence free survival (RFS) and overall survival (OS). **Objective** The aim is to determine the association between AR and pathologic complete response (PCR), recurrence free survival (RFS) in TNBC patients treated with neoadjuvant chemotherapy (neoCT). **Patients and methods** Cross-sectional, retrospective cohort trial. Adult women with stage II-III TNBC, treated with neoCT from 2014 to 2021 were included. Incomplete medical record, AR not-determined, secondary malignant neoplasm were excluded. AR was determined with the VENTANA assay system, > 1% were considered as positive. Statistical analyses included frequencies and range, comparison was done with X2, cox regression model was made for the prognostic association with a two-sided significance level of 0.05 95% CI. RFS were evaluated with Kaplan Meier method and log-rank test. **Results** 309 patients were analyzed; AR prevalence was 14.6%. Median age was 49 years (21-87), tumor size was 6.3 cm (0.1-22), ductal histology (95.1%) and nuclear-grade 3 (79%), these findings were not different between the AR+ vs AR-. Median Ki67 was 52% within AR+ vs 65% AR- (p=0.05). All patients were treated with neoCT, 14.9% had disease progression, PCR rates were similar among two groups (48.5% vs 42.2%) p=0.78. At a mean follow up of 19 months, 7 recurrences presented in AR+ (15.5%) vs 67 in the AR- (25.4%) p=NS. Median RFS was 54.9 (IC 95% 45.2-64.6) and 65.5 months (IC 95% 60.4-70.7), p=0.3. We analyze the prognostic factors, for RFS we found statistically significant the locally advanced stage OR 5.6 (1.4-22.9), residual cancer burden (RCB) OR 2.8 (2.1-3.9), N stage OR 1.4 (1.1-1.8) and progression during neoCT OR 2.8 (1.5-5.1); and for OS the RCB OR 2.8 (1.9-4.1) and progression during neoCT OR 3.1 (1.5-6.9). **Conclusions** In this trial the AR expression did not show significant association neither with PCR and RFS; main reasons are the low prevalence of AR expression, high rate of disease progression and high residual cancer burden after neoCT. We found association with other known factors (RCB, N stage, progression during neoCT and locally advanced stage), which are more important factors that determine the bad prognosis of TNBC.

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A Population-based Analysis of Prophylactic G-CSF Biosimilar and Originator Administration over time among Patients Diagnosed with Breast Cancer

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A Population-based Analysis of Prophylactic G-CSF Biosimilar and Originator Administration over time among Patients Diagnosed with Breast Cancer Pawloski PA1, McDermott CL2, Vazquez Benitez G1, DeFor T1, Mendelsohn A3, Marshall J3, Moyneur E4, Lockhart CM2; on behalf of the G-CSF Comparative Effectiveness Research Team. 1HealthPartners Institute, Bloomington MN USA 2Biologics and Biosimilars Collective Intelligence Consortium, Alexandria VA USA 3Harvard Pilgrim Healthcare Institute, Boston MA USA 4StatLog, Montreal QC Canada Objectives: To characterize G-CSF product use, including product switching, among patients diagnosed with breast cancer in the Biologics and Biosimilars Collective Intelligence Consortium's (BBCIC) Distributed Research Network (DRN). Methods: A retrospective analysis of electronically extracted insurance claims from 2015-2019 at 4 Research Partner Sites was conducted. Patients aged ≥ 20 years with a diagnosis of breast cancer who received chemotherapy associated with a risk of febrile neutropenia (FN) risk per National Comprehensive Cancer Network guidelines and any prophylactic granulocyte-colony stimulating factor (G-CSF), defined as before day 2 of the first cycle of chemotherapy were included. Results: A total of 11,788 patients were included; 89 (0.8%) were male sex per insurance records. The age distribution was 5,743 (49%) 50-64 years; 4,296 (36%) 20-49 years, and 1749 (15%) 65+ years. Chemotherapy regimens included cyclophosphamide/doxorubicin (n=7,377), carboplatin/docetaxel/trastuzumab/pertuzumab (n=1,862), cyclophosphamide/docetaxel (n=1,383), carboplatin/docetaxel/trastuzumab (n=430),

cyclophosphamide/docetaxel/doxorubicin (n=147), and docetaxel/trastuzumab/pertuzumab (n=128). Overall, 218 patients (1.8%) developed FN during the first chemotherapy cycle. G-CSF utilization was pegfilgrastim 10,895 (92%), pegfilgrastim-cbqv 315 (3%), pegfilgrastim-jmdb 225 (2%), filgrastim 156 (1%), filgrastim-sndz 118 (1%), tbo-filgrastim 46 (< 1%), a combination of pegfilgrastim+filgrastim 26 (< 1%), and a combination of filgrastim+biosimilar 7 (< 1%) received. A total of 10,953 (93%) patients received high-risk chemotherapy and G-CSF utilization was 10,162 (93%) pegfilgrastim, 288 (3%) pegfilgrastim-cbqv, 200 (2%) pegfilgrastim-jmdb, 132 (1%) filgrastim, 101 (< 1%) filgrastim-sndz, 40 (< 1%) tbo-filgrastim, and 30 (< 1%) combination of products. Eight hundred fifteen (7%) patients received intermediate-risk chemotherapy and G-CSF utilization was, 716 (88%) pegfilgrastim, 27 (3%) pegfilgrastim-cbqv, 25 (3%) pegfilgrastim-jmdb, 23 (3%) filgrastim, 16 (2%) filgrastim-sndz, 5 (< 1%) tbo-filgrastim, and 3 (< 1%) combination. Twenty patients received low risk chemotherapy and of those 17 (85%) received pegfilgrastim. In 2019, the first full year of pegfilgrastim biosimilar availability, pegfilgrastim use was 76% pegfilgrastim, 13% pegfilgrastim-cbqv, and 9% pegfilgrastim-jmdb. Most patients who received a second cycle of chemotherapy received the same G-CSF product in the second cycle, specifically 67% received filgrastim, 71% tbo-filgrastim, 73% filgrastim-sndz, 96% pegfilgrastim, 84% pegfilgrastim-cbqv, and 81% pegfilgrastim-jmdb. Conclusions: The most common chemotherapy agents included cyclophosphamide, carboplatin, doxorubicin, docetaxel, or pertuzumab. Pegfilgrastim biosimilar uptake occurred following market availability. Within each G-CSF product, most patients received the same product during the second cycle of chemotherapy rather than switching products.

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P4-03-34

Treatment Patterns and Associated Outcomes Among Patients with HER2+ Metastatic Breast Cancer in the United States

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Background Historically, standard-of-care treatments for human epidermal growth factor receptor 2-positive (HER2+) metastatic breast cancer (mBC) have been pertuzumab and trastuzumab combined with a chemotherapeutic agent in first line (1L), and trastuzumab emtansine (T-DM1) in the second line (2L). However, two new treatments have recently been approved for patients who previously received HER2-targeted therapy; fam-trastuzumab deruxtecan-nxki [Enhertu®] and tucatinib [Tukysa] (in triplet combination) in 2019 and 2020, respectively. The goal of this study was to characterize treatment patterns of patients with HER2+ mBC from receipt of first line therapy and subsequent treatments received in real world community oncology practices. Methods Adults diagnosed with HER2+ mBC from January 2013 – January 2021 were selected from the Flatiron Health electronic health record–derived database; a US-wide database curated from community clinics that comprises de-identified patient-level structured and unstructured data. Patients were followed from index date (start of 1L therapy) to death or last activity date. Descriptive statistics reported baseline patient characteristics and treatment patterns. Time to treatment discontinuation (TTD), real-world progression-free survival (rwPFS), and real-world overall survival (rwOS) were estimated using the Kaplan-Meier method. Results A total of 2,074 mBC HER2+ patients with at least 1 line of therapy were included during the study time period. Median follow-up time was 26.0 months (Interquartile range [IQR]: 12.6-44.7). Patients were mostly white (62.7%), median age 61 years (IQR:24-84), 43.0% were stage IV at initial breast cancer diagnosis, and 62.8% had positive hormone receptor (HR) status. Of the 2,074 patients in our study population, 1,159 (55.8%) received 2L therapy, and 584 (28.2%) received a 3L therapy. In terms of 1L therapy, 1,607 (77.5%) received a trastuzumab-based (T-based) regimen, 205 (9.9%) received chemotherapy only, and 153 (7.4%) received a T-DM1 based therapy. The most common regimens across 1L included pertuzumab+trastuzumab+taxane (THP) (38.9%), THP + a platinum agent (7.5%), and T-DM1 (6.1%). From start of 1L, overall median TTD was 10.8 months (95% confidence interval [CI]: 10.1-11.5), median rwPFS was 11.5 months (95% CI: 10.8-12.3), and median rwOS was

40.3 months (95% CI: 37.8-43.4). Among the 1,607 patients who received any T-based regimen in 1L, 496 (30.9%) received T-DM1, 175 (10.9%) received a T-based regimen again, 78 (4.9%) received any other HER2-based regimen, 59 (3.7%) received hormonal therapy alone and 33 (2.1%) received chemotherapy. The most common regimens across 2L (n=1,159) were T-DM1 monotherapy (35.7%), THP (11.2%), and T-DM1+hormone therapy (8.0%). From start of 2L, overall median TTD was 8.3 months (95% CI: 7.6-9.0), median rwPFS was 7.4 months (95% CI: 6.8-8.1), and median rwOS was 27 months (95% CI: 25.9-30.0). Conclusions Variability, which may impact outcomes, is observed in treatment approaches for HER2+ mBC. Additionally, more than half the patients on 1L treatment progressed within a year of initiating treatment, highlighting a remaining need for effective therapies that limit progression and maintain clinical benefit in 1L.

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Determinants of severe COVID-19 infection in Patients with Breast Cancer from a Community Oncology Practice in Brazil

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Purpose: The SARS-CoV-2 pandemic was declared a global public health emergency. Determinants of mortality in the general population are now clear, but specific data on patients with breast cancer (BC) remain limited, particularly in developing nations. Materials and methods: We conducted a longitudinal, multicenter cohort study in patients with BC and confirmed SARS-CoV-2 infection. The primary end point was the proportion of patients on treatment for severe SARS-CoV-2 infection (defined as need for hospitalization) or early death (within 30 days of diagnosis). Data were evaluated sequentially in the following way: i) univariate Fisher's exact test; ii) multivariable logistic regression analysis; and iii) multivariable logistic regression. In items i and ii only those with $P < 0.1$ are considered significant and in stage iii only those with $p < 0.05$ were the final significant variables. We divided patients' data into three major variable domains: a) signs and symptoms; b) comorbidities; and c) tumor and treatment characteristics; in item ii each variable domain was tested separately, finally, in item iii the significant variables of all domains were tested together and we called it the integrative step. Results: From April 2020 to June 2021, 413 patients with BC and COVID-19 were retrospectively registered, of which 288 (70%) had an identified molecular subtype and 273 (66%) had stage information. Most patients were on active systemic therapy or radiotherapy (73.2%), most of them in the curative setting (69.5%). The overall rate of severe SARS-CoV-2 was 19.7% (95% CI, 15.3-25.1). In the integrative multivariate analysis, factors associated with severe infection were metastatic setting, chronic pain, acute dyspnea, and cardiovascular comorbidities. Recursive partitioning modeling used acute dyspnea, metastatic setting, and

cardiovascular comorbidities to predict non-progression to severe infection, yielding a negative predictive value of 84.9% (95% CI, 78.9%-88.3%). Conclusion: The rate of severe COVID-19 in patients with BC is influenced by prognostic factors that partially overlap with those reported in the general population. High-risk patients should be considered candidates to active preventive measures to reduce the risk of infection, close monitoring in the case of exposure or SARS-CoV-2 -related symptoms and prophylactic treatment once infected.

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7:00 AM - 8:15 AM

P4-03-37

The characteristics of male breast cancer by molecular subtypes: a population-based study

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Background: To explore the characteristics of molecular subtype in male breast cancer.

Methods: A retrospective study was conducted to investigate the characteristics and prognosis of patients with male breast cancer using the data recorded in the Surveillance, Epidemiology, and End Results (SEER) database from 2010-2014. Results: A total of 1597 cases were enrolled, including 1373 cases with HR+/HER2- (86%), 182 cases with HR+/HER+ (11.4%), 13 cases with HR-/HER2+ (0.8%) and 29 cases with Triple Negative (1.8%), respectively. There were significant differences in distributions in age, race, grade, tumor size and AJCC stage between the molecular subtypes. The molecular subtypes differed significantly in 5 years overall survival and 5 years cause specific survival, establishing the following sequence with HER2-/HR+ > HER2+/HR+ > HER2+/HR- > Triple negative. According to Cox regression, age>65y, ER negative, PR negative, TN subtype, advanced AJCC stage, larger tumor size, stage T3 and M1 were independent prognostic factors for poorer survival. Conclusion: The prognosis of male breast cancer varied by molecular subtypes. Age, ER and PR, status, stage as well as tumor size were independent prognostic factors.

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Rare Breast Cancer Histologic Subtypes: 30-year experience in a Mexican Cancer Center

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Introduction

Breast cancer (BC) is a heterogeneous disease composed of multiple histologic subtypes. Invasive ductal carcinoma is the most common subtype, accounting for 75% of all BC cases and is followed by lobular carcinoma which represents another 15%. Other rare histologic subtypes make up the remaining 10%. To date, limited evidence exists regarding about the frequency, clinicopathologic characteristics, and prognoses of these uncommon variants in Mexico.

Methods

A single center retrospective cohort including women diagnosed with invasive BC between January 1990 and December 2019 was conducted. Only patients with rare histologic subtypes, excluding not otherwise specified ductal and lobular carcinoma, were included. The main objective of this study was to describe the frequency, clinicopathological characteristics, and outcomes of these histologic subtypes. Descriptive statistics including means, medians, and standard deviations, were used to analyze clinicopathological characteristics. Recurrence-free

survival (RFS) and overall survival (OS) were calculated using the Kaplan-Meier method and compared by the log-rank test. A p value of < 0.05 was considered statistically significant.

Results

Out of 1744 women diagnosed with invasive BC, 106 patients (6.1%) had a rare histologic subtype. Among the most frequent subtypes, 39 (36.8%) were mucinous, 12 (11.3%) metaplastic, 11 (10.4%) tubulolobular, 11 (10.4%) papillary, 10 (9.4%) tubular, and 8 (7.5%) medullary carcinomas. In the less common histologic subtypes (referred as “others”), 7 (6.6%) were apocrine, 4 (3.8%) neuroendocrine, 1 (0.9%) micropapillary, 1 (0.9%) signet cell, 1 (0.9%) acinic cell, and 1 (0.9%) histiocytoid carcinoma.

In the overall population, the median age at diagnosis was 58 years, 76.4% were postmenopausal at diagnosis, 29.2% had a family history of BC, and 7.5% had personal history of BC. Seventy percent of the patients were overweight or obese at time of diagnosis and 82.1% had diabetes mellitus type 2 diagnosis. An important proportion of women were diagnosed by self-detected tumors (61.3%), as opposed to less than a quarter (24.5%) detected by screening mammography. The median time of diagnosis interval was 3 months, 71.7% were diagnosed with early (I – IIA), 22.6% with locally advanced (IIB – IIIC) and 5.7% with metastatic (IV) disease. Most tumors (58.3%) expressed hormone receptors (HR), 7.2% were HER2 enriched, 8.3% expressed both HR and HER2, whereas 26% were triple negative. Clinicopathological characteristics according to the most frequent histologic subtypes are listed in Table 1.

With a median follow-up of 108 months, 12 recurrences were identified (5 mucinous, 3 metaplastic, 2 tubulolobular and 2 apocrine), 41% were local and 59% were distant recurrences. Globally, 15-year RFS and OS were 83% and 61%, respectively. Differences in RFS and OS were not statistically different according to histologic subtypes. The 15-year RFS and OS was 83% and 80% for mucinous, 100% and 78% for tubular, 100% and 58% for medullary, 65% and 52% for metaplastic, 77% and 86% for tubulolobular, and 100% and 49% for papillary carcinoma, respectively.

Conclusions

To our knowledge, this is the first study describing the frequency, clinicopathological characteristics, and outcomes of rare histologic BC subtypes in a large Mexican cohort. Our results show that these subtypes represent 6% of all invasive BC cases, that they are commonly diagnosed at an early stage, and present long RFS and OS.

Table 1

	Mucinous n = 39	Metaplastic n = 12	Papillary n = 11	Tubulolobular n = 11	Tubular n = 10	Medullary n = 8	Others n = 15
Median age at diagnosis (y)	57	67	66	57	61	59	55
Menopausal status							
- Premenopausal (%)	10 (25.6)	3 (25)	1 (9.1)	5 (45.5)	2 (20)	0	4 (26.7)
- Postmenopausal (%)	29 (74.4)	9 (75)	10 (90.9)	6 (54.5)	8 (80)	8 (100)	11 (73.3)
Clinical stage							
- Early (I – IIA) (%)	28 (71.8)	6 (50)	11 (100)	10 (90.1)	9 (90)	5 (62.5)	7 (46.7)
- Locally advanced (IIB – IIIC) (%)	9 (23.1)	6 (50)	0	1 (9.1)	0	3 (37.5)	5 (33.3)
- Metastatic (IV) (%)	2 (5.1)	0	0	0	1 (10)	0	3 (20)
Immunohistochemical subtypes							
- Hormone receptor positive (%)	25 (71.4)	1 (8.3)	10 (90.9)	9 (81.8)	6 (75)	3 (50)	2 (15.3)
- Triple positive (%)	4 (11.4)	0	0	2 (18.2)	1 (12.5)	0	1 (7.6)
- HER-2 enriched (%)	3 (8.5)	1 (8.3)	0	0	0	0	3 (23)
- Triple negative (%)	3 (8.5)	10 (83.3)	1 (9.1)	0	1 (12.5)	3 (50)	7 (53.8)

Clinicopathological characteristics according to the most frequent histologic subtypes

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7:00 AM - 8:15 AM

P4-03-39

Breast density and Body Mass Index association with breast cancer molecular subtypes in early breast cancer Spanish population.

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Obesity is a major health problem and is closely related to the incidence and progression of breast cancer (BC). Likewise, mammogram breast density (MBD) is a risk factor for breast cancer. This study aims to analyze the potential association between BMI (Body Mass Index) and MBD with different molecular subtypes of BC. The interaction with cholesterol, vitamin D, insulin levels, and lifestyle, will also be evaluated. Materials and methods: This is a transversal, descriptive, multicenter study involving women with a recent diagnosis of early BC for one-year duration (November 2019 to October 2020). BMI was classified as obesity (BMI ≥ 30 kg/m²), overweight (≥ 25 kg/m²), and normal weight (18-25 Kg/m²). American college of radiology was

used to classify MBD into 4 categories: A, B, C, and D. Data of weight, height, MBD, molecular subtype (according to 13th St Gallen International Breast Cancer Panel), cholesterol, insulin, vitamin-D, hypertension, diabetes, exercise, and lifestyle were collected at the moment of diagnosis. Results: 162 women with a recent diagnosis of early BC have been successively evaluated in 3 Spanish hospitals. The median age was 52 years, and 49.1% were postmenopausal. Molecular subtypes were: 43% luminal-A, 25% luminal-B, 17% HER2+, and 15% triple-negative. 7% of patients were MBD type A, 17% type B, 55% type C, and 21% type D. 52% were normal weight, 32% overweight, and 16% obese. 48% of women had normal cholesterol levels and 60% normal vitamin D. There was not association between BMI and molecular subtype, however considering menopausal status, BMI was significantly higher in postmenopausal patients with Luminal A subtype ($p= 0.011$) and HER2+ subtype ($p= 0.027$). There was no association between MBD and molecular subtype. However, there were significant differences between BMI and MBD ($p< 0.001$) with lower BMI in patients who had MBD type C or D. Patients with higher BMI had lower HDL-Cholesterol ($p< 0.001$) and higher levels of insulin ($p< 0.001$). Conclusion: This study showed a higher BMI in Luminal A and HER2 positive postmenopausal BC patients. Higher BMI was shown in patients with low MBD independently of menopausal status. More studies are needed to understand the role of obesity and molecular subtype of breast cancer.

Disclosure(s):

Isabel Calvo, MD, PhD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-03-40

Patient and treatment characteristics in HR+/*HER2*- metastatic breast cancer in a real-life setting

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Background and aim: HR+/HER2- is the most common molecular subtype of breast cancer (BC), also associated with improved survival compared with other subtypes in the metastatic setting. This study evaluated the patient and treatment characteristics of women with luminal subtype (HR+/HER2-) advanced (locally or metastatic) BC to identify patients' general characteristics and outcomes in a real-world setting in Turkey.

Methods: This study was designed as a retrospective, multicentered, non-interventional, and observational study to describe the patient demographics, clinical and disease characteristics, and treatment patterns of locally advanced and metastatic HR+/HER2- BC patients in routine practice between January 1, 2019, and December 31, 2020, in Turkey.

Results: After screening 823 patients, 758 women (median age 56 years) were included in the analyses. The median (Q1-Q3) follow-up duration was 12.0 (6.0-17.7), 12.2 (6.1-17.4), 19.3 (14.0-25.3) months for the 1st, 2nd, 3rd lines of treatment; 22% of the women were premenopausal. Metastatic disease was present in 57% at diagnosis, most commonly in bones (71%), distant lymph nodes (24%), and lungs (19%). The most common pathology was invasive ductal carcinoma (67%), followed by lobular carcinoma (6.5%). The CDK4/6 inhibitors (CDK4/6i) plus endocrine therapy (ET) administration rates before and after May 2020, the date of reimbursement in Turkey, were 14% vs. 71% in the 1st line, 14% vs. 61% in the 2nd line, and 15% vs. 56% in the 3rd line. Meanwhile, ET as monotherapy rates decreased from 37% to 8%, 43% to 11%, and 29% to 5%, whereas chemotherapy rates decreased from 49% to 21%, 44% to 28%, and 57% to 39% in 1st to 3rd lines of treatment, respectively. The median progression-free survival (PFS) increased from 10 months before May 2020 to 17.5+ months after May 2020 for 1st line treatment. Dose reduction during CDK4/6i+ET was 5.3%, 9.4%, and 6.6% in the treatment lines, and the most frequent toxicity leading to dose reduction was neutropenia. The best response rate assessments for CDK4/6i+ET showed an objective response rate (ORR) of 62.7%, 57.5%, and 63.9% and a disease control rate (DCR) of 71.3%; 63.2%, and 65.6% in the 1st, 2nd and 3rd lines of treatment (Table 1). Moreover, overall ORR independent of treatment lines for CDK4/6i+ET was found as 61.1%.

Conclusion: This study provided the most recent data from a large sample of HR+/HER2- metastatic breast cancer patients in Turkey. The results presented showed the current treatment preferences and the treatment efficiencies in a real-world scenario. In addition, the epidemiological characteristics identified will serve as a basis for detecting the changes in the patient characteristics over time and determining the best candidates for specific treatments. Missing data in patient files due to retrospective design of the study and limited experience with CDK4/6i and poly adenosine diphosphate ribose polymerase (PARP) inhibitors in Turkey (due to registration and reimbursement status) could be considered limitations of the current study.

Table 1.

Table 1. Treatment characteristics

Treatment Groups, n (%)	Treatment lines for metastatic disease		
	1 st line	2 nd line	3 rd line
CDK4/6 i + ET			
<i>Before May 2020</i>	40 (13.7)	26 (13.5)	16 (14.8)
<i>After May 2020</i>	112 (70.9)	82 (61.2)	46 (56.1)
ET Mono			
<i>Before May 2020</i>	108 (37.1)	82 (42.5)	31 (28.7)
<i>After May 2020</i>	13 (8.2)	15 (11.2)	4 (4.9)
Chemotherapy			
<i>Before May 2020</i>	143 (49.1)	85 (44)	61 (56.5)
<i>After May 2020</i>	33 (20.9)	37 (27.6)	32 (39)
Drug combinations, n (%)			
<i>Palbociclib-Fulvestrant</i>	26 (17.1)	30 (27.8)	24 (38.7)
<i>Palbociclib-Letrozole</i>	60 (39.5)	27 (25)	13 (21)
<i>Ribociclib-Anastrozole</i>	1 (0.7)	2 (1.9)	1 (1.6)
<i>Ribociclib-Fulvestrant</i>	17 (11.2)	24 (22.2)	14 (22.6)
<i>Ribociclib-Letrozole</i>	46 (30.3)	23 (21.3)	10 (16.1)
<i>Abemaciclib-Letrozole</i>	1 (0.7)		
<i>Abemaciclib-Anastrozole</i>	1 (0.7)		
<i>Palbociclib-Anastrozole</i>		2 (1.9)	
Best Response			
CDK4/6 i + ET			
<i>CR</i>	12 (8)	5 (4.7)	5 (8.2)
<i>PR</i>	82 (54.7)	56 (52.8)	34 (55.7)
<i>SD, n (%)</i>	13 (8.7)	6 (5.7)	1 (1.6)
<i>Median Duration of SD, months; median (Q1-Q3)</i>	8.05 (5.22-13.04)	8.38 (4.37-12.22)	10.22 (5.31-15.08)
<i>PD, n (%)</i>	29 (19.3)	25 (23.6)	11 (18)

ET: Endocrine Therapy, CR: Complete Response, PR: Partial Response; SD: Stable Disease, PD: Progressive Disease.

Treatment characteristics

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12/8/2022

7:00 AM - 8:15 AM

P4-03-41

Prospective observational study of breast cancer patients during the cycle of chemotherapy with taxanes: evaluation of the incidence and prevalence of peripheral neuropathy

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OBJECTIVE: To evaluate the prevalence of sensitivity changes in patients during the cycle of chemotherapy with taxanes and the impacts on quality of life. **DESIGN:** A prospective, observational, Approved study was conducted at the Oncomastology outpatient clinic of Hospital São Paulo- Unifesp, in the period from November 2018 to February 2022, where 102 women with breast cancer were selected and 79 patients who underwent chemotherapy with paclitaxel were included. **METHODS:** Collection of demographic and clinical information. Used stesiometer that assessed sensitivity in dermatos and myotomes in the following body regions: arms, hands, legs and feet. **FACT/GOG-Ntx Questionnaire** analyzed the quality of life and chemotherapy-induced peripheral neuropathy of the patients before starting chemotherapy. All participants were informed and signed an informed consent form. **RESULTS:** The mean age was 49 years, mean BMI was 27.95Kg/m², NICC (Invasive Carcinoma not special) represented 89.9% of the sample, 88.6% had Neoadjuvant Chemotherapy, regarding the size of the tumor 45.6% presented from 2 to 5 cm, of the pre existing diseases Diabetes mellitus 15.2% and Systemic Arterial Hypertension 30.4%. The initial moment in relation to sensitivity alterations, of the arm regions presented (right C6 (HC 1.05-1.23) left C6 (HC 1.05- 1.23), and legs (right L5 (HC 1.14 -1.55) left L5 (HC1.22 - 1.52) and right S1 (HC 1.21-1.47) left S1 (HC 1.21-1.48). The conversion of the Estesiometer colors into numbers followed as follows, Green (1.0): normal sensitivity, Blue (2.0): decreased sensitivity. The **FACT/Taxane (TOI)** quality of life Questionnaire (30 items) its scores 0-120,(average 91.44 points) demonstrates in its response impairment in more than 80 % in the quality of life in the domains. **Physical Well-Being-PWB** (0-28 points) (mean 20.28/HC 18.88-21.66), **Functional Well-Being-FWB** (0-28 points) (mean16.00/HC14.22-17.22) and in the specific questions about chemotherapy-induced peripheral neuropathy (CPIN), **TaxS** (0-64 points) (mean 55.16/HC 52.74-57.26) reduced

scores. CONCLUSION: It is concluded that mean age, overweight, tumors between 02 and 05 cm were the most prevalent among patients diagnosed with breast cancer. At the beginning of chemotherapy containing paclitaxel, sensitivity changes were not present characterizing arthralgia, myalgia and the hand-foot syndrome (CPIN). The quality of life evaluated by FACIT/Taxane, showed a reduction of 80% in the scores of the domains Physical Well-Being-PWB, Functional Well-Being-FWB and general quality of life, that is, the quality of life of patients from the time of diagnosis is already very compromised.

Key words: Breast neoplasm, adjuvant drug treatment, chemotherapy, quality of life.

Number of Opinion: 2.351.174 DATA OF THE OPINION, CEP Number: 0934/2017 of the ethics in research committee. Registered in Clinical Trials on 12/12/2017, protocol number -NCT 03373032.

Table 1 Results of the sensitivity of dermatos and myths (monofilaments) undergoing chemotherapy cycles with paclitaxel (eyes closed)

Results of the sensitivity of dermatos and myths (monofilaments) undergoing chemotherapy cycles with paclitaxel (eyes closed)				
N= 79	Mean	Std.Deviation	HC (95%)	
Sensitivity C6 Right	1,14	0,38	1,05	1,23
Sensitivity C7 Right	1,15	0,43	1,06	1,27
Sensitivity C8 Right	1,19	0,43	1,08	1,28
Sensitivity T1 Right	1,16	0,44	1,06	1,24
Sensitivity L5 Right	1,38	0,85	1,14	1,55
Sensitivity S1 Right	1,38	0,58	1,21	1,47
Sensitivity Foot Right	1,65	0,68	1,49	1,8
Sensitivity C6 Left	1	0,38	1,05	1,23
Sensitivity C7 Left	1,25	0,55	1,12	1,37
Sensitivity C8 Left	1,22	0,51	1,1	1,34
Sensitivity T1 Left	1,14	0,45	1,03	1,24
Sensitivity L5 Left	1,37	0,66	1,22	1,52
Sensitivity S1 Left	1,34	0,58	1,21	1,48
Sensitivity Foot Left	1,66	0,73	1,49	1,83

Legend: Analysis of quantitative frequencies, Mean, Standard Deviation and Confidence Interval, Percentage (%) and Absolute number.

Legend: Analysis of quantitative frequencies, Mean, Standard Deviation and Confidence Interval, Percentage (%) and Absolute number.

Disclosure(s):

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7:00 AM - 8:15 AM

P4-03-42

Evaluating the Impact of Race and Body Mass Index on the Diagnosis and Prognosis of Early Onset Breast Cancer

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Background: Early-onset breast cancer is typically defined as a diagnosis of disease before age 40-45. Prior studies have shown interesting associations between race and obesity on the incidence and prognosis of breast cancer. Data from the SEER program at the National Cancer Institute has shown increased mortality amongst African American women (0.2%) compared to Non-Hispanic White (NHW) women (0.1%) who were diagnosed with breast cancer at age 45 years or younger. This is despite a similar risk of diagnosis between racial groups of this age range (1.27%, 1.27%). Other large studies have shown that African American patients tended to present with more advanced disease had worse clinical outcomes. Our study sought to determine the impact of race and obesity on the diagnosis and prognosis of early onset breast cancer amongst the patient population at Georgetown University Hospital (GUH). Methods: We compiled a database of all new patients, 652 in total, seen at Lombardi Cancer Center at Medstar GUH from 10/2020- 6/2022. We reviewed patient charts in the EMR and documented age at diagnosis, race, ethnicity, stage at diagnosis, and BMI. The BMI was categorized by underweight (BMI < 18.5), healthy weight (BMI 18.5-24.9), overweight (BMI 25-25.9), obese (BMI 30-34.9), and morbidly obese (BMI ≥ 35). Stage at diagnosis was determined by comparing the pathology report with the NCCN guidelines version 4.2022. We identified 136 patients who were diagnosed at GUH at age 45 years old or younger and compared our findings to SEER data from 2017-2019. Results: Out of 136 patients who met our age criteria, 131 had racial data available: 29 AA (0.22), 68 NHW (0.52), 4 Hispanic (0.03), 30 Other (0.23). Out of the 34 patients with advanced disease (stage 3 and 4) 16 were NHW (0.47), 4 were AA (0.12), 2 were Hispanic (0.06) and 12 were Other (0.35). 131 patients had BMI data available: 5 underweight (0.04), 56 healthy weight (0.43), 41 overweight (0.31), 21 obese (0.16), and 8 morbidly obese (0.06). 18 patients with advanced disease were overweight or obese, out of which 11 were NHW (0.61), 3 were AA (0.16), 3 were Other (0.16), and 1 was Hispanic (0.06). Conclusion: In contrast with the SEER data, our study found that the patient population at GUH had a much higher proportion of Non-Hispanic White (NHW) patients who were diagnosed with advanced disease compared to African American (AA) patients. It also found a higher proportion of NHW patients amongst those who were diagnosed with advanced stage disease and were overweight or obese compared to AA patients. This data suggests that in our patient population, Non-Hispanic White women who were overweight or obese at the time of diagnosis of early onset breast cancer (≤ 45 years old) were more likely to be diagnosed with advanced stage disease than women in other demographic groups. It is possible that this discrepancy is related to racial variations in receptor status. Further investigation is required to correlate these associations in clinical practice with other known demographic variables and disease-specific

risk factors in order to better understand how they impact the diagnosis and prognosis of early-onset breast cancer.

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-03-43

Disease characteristics and outcomes of people with metastatic breast cancer in a single center cohort study: The Dallas Metastatic Breast Cancer Study.

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Background: Breast cancer is the most common cancer in women, and metastatic disease accounts for most breast cancer related deaths. Identifying risk factors for the onset and progression of metastatic breast cancer (MBC) can help us understand how to address and improve morbidity and mortality due to MBC. Large national databases, such the Surveillance, Epidemiology, and End Results (SEER) Program are limited in their ability to capture granular details from patients' cancer histories. The Dallas Metastatic Breast Cancer Study (DMBCS) is a clinical database established at a single academic medical system to track patient demographics, associated pathology, treatments, and other variables to improve outcomes for patients with MBC. Methods: The DMBCS database was generated from a registry of breast cancer patients submitted to the National Cancer Institute from 2010 to 2021. Patients were initially excluded if they were identified as non-metastatic from this list. Chart review was then done to identify MBC patients from this subsequent group. Demographics, clinical history, pathologic features, lines of treatment, and subsequent recurrences were collected for all patients. Clinical data was stored in REDCap, a secure data collection platform for entering and managing data. Results: 230 cases were included in this preliminary data set. Of the 230 cases, 185 cases were metastatic at time of diagnosis while 45 cases were metastatic recurrences of breast cancer. At diagnosis, 14.8% were less than 40 years of age, 17.3% were

40-49, 35.7% were 50-59, 18.7% were 60-69, and 13.5% were greater than 70 years of age. In terms of ethnicity, 63.5% were White, 27.4% were Black, and 21.7% identified as Hispanic. At time of diagnosis, 30.9% of patients had a BMI classified as overweight and 40.4% were considered obese. Medical comorbidities included hypertension in 43% of cases, diabetes (18.3%), hyperlipidemia (27.4%), and autoimmune disease (13.0%). Clinical subtype analysis revealed 57.8% of patients were hormone receptor positive, 24.8% HER2 positive, and 17.4% triple negative, at diagnosis. 14.8% of cases were diagnosed as inflammatory breast cancer. The most common site of metastasis at presentation was bone with 69.1% of cases, followed by lung (33.9%), liver (30.0%), and brain (15.2%). Over 90% of patients were treated with at least one antineoplastic regimen and 39.6% underwent at least 4 therapies. Calculated 1-year survival after diagnosis was 85.7%. Conclusions: The introduction of the DMBCS will allow continued investigation into clinical drivers of MBC. In this first cohort of patients, we characterized key, yet often underreported, variables and outcomes. Potential applications of this database include investigating the association between obesity and overall survival in patients with MBC, understanding how socioeconomic disparities affects outcomes of patients with MBC, and exploring correlations between autoimmune disease and the progression of MBC.

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Meng Cao, MD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-03-44

A Case Series of Male Breast Cancer Patients at Methodist Dallas Medical Center

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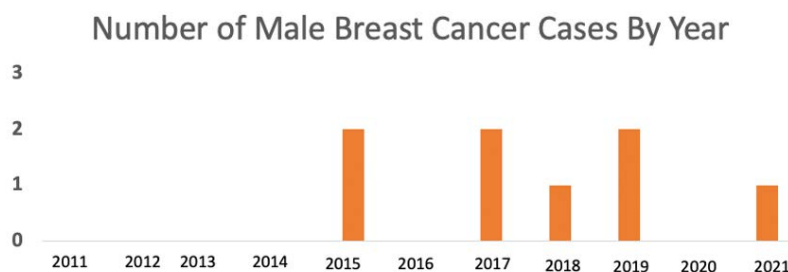
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Male breast cancer is a rare disease accounting for less than 1% of all breast cancer diagnosis. Male breast cancers occur later in life and are more estrogen receptor-positive compared to female breast cancers. Breast cancer in men is often diagnosed later and survival rates are lower than in female cases. The aim of this retrospective study is to analyze the epidemiological, clinical and therapeutic data of all male breast cancer cases over the span of 11 years to at Methodist Dallas Medical Center between 2010 – 2021. During this time period, there was a total of 1,784 cases of breast cancer diagnosed. There were 8 cases male breast cancers, accounting for 0.45% of all breast cancer cases. The average age of diagnosis was 69.5 years old. The most common type of male breast cancer was invasive ductal carcinoma with 7 cases (87.7%). The remaining 1 case (12.5%) were ductal carcinoma in situ (DCIS). 100% of our male breast cancer cases were estrogen receptor and progesterone receptor positive. No male breast cancer case had Her2/Neu receptor over-expression. Of all male breast cancer cases, 75% had a family history of cancer suggesting that genetic factors play a significant role in the development of breast cancer in men. At time of diagnosis, 4 cases (50 %) were staged at cT4 and the remainder of cases were between cT0 - cT2. 37.5% of all cases had sentinel lymph node involvement at time of diagnosis. From the time period of 2010 – 2014 there were no incidences of male breast cancer; however, from 2015 – 2021 there were 8 total cases. There were 2 cases (25%) of death.

Number of Male Breast Cancer Cases by Year



Number of male breast cancer cases diagnosed by year at Methodist Dallas Medical Center

Epidemiological and Clinical Data of Male Breast Cancer Cases

	Total Number of Cases	Percentage
Male Breast Cancer	8	0.45%
Female Breast Cancer	1,776	99.55%

+

Histology	Number of Male Cases	Percentage
Invasive Ductal Carcinoma	7	87.50%
DCIS	1	12.50%

Tumor Receptors	Number of Male Cases	Percentage
ER+	7	87.50%
PR+	7	87.50%
Her2/Neu	0	0.00%

History	Number of Male Cases	Percentage
PMHx of Cancer	2	25.00%
<u>FHx</u> of cancer	6	75.00%

Ethnicity	Number of Male Cases	Percentage
White	4	50.00%
Black	4	50.00%
Spanish Origin	1	12.50%

Disclosure(s):

Huy Nong, MD: No financial relationships to disclose

Vasu Moparty, MD: No financial relationships to disclose

Atisha Manhas, MD: No financial relationships to disclose

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P4-04-01

Safety and efficacy of cryotherapy in the prevention and treatment of chemotherapy-induced peripheral neuropathy in breast cancer patients

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Introduction Chemotherapy-induced peripheral neuropathy (CIPN) is a serious clinical problem that can be caused by some cytotoxic agents used in breast cancer (BC) treatment, most commonly seen following taxane-based therapy[1,2]. Several strategies have been studied for CIPN prevention and treatment, but, still, there is no standard recommendation, options are limited and results unsatisfactory [1]. Cryotherapy is a technique that consists of reducing the blood flow in a certain area of the body by cold temperatures, in order to limit the cytotoxic reach. A few studies have been conducted to analyze the safety and efficacy of this strategy in CIPN prevention and treatment, and results are controversial [3,4,5]. More data is needed to clarify cryotherapy role in this clinical context. Methods This is a retrospective analysis of 40 BC patients treated at a single Brazilian institution between December 2019 and June 2022, aiming at efficacy and safety of cryotherapy in the prevention and treatment of CIPN. Cryotherapy was administered by the Hilotherm Clinic Chemo HT02 device (Hilotherm GmbH - Oberwil bei Zug, Switzerland [6]). The procedure consisted of patients using glove and sock-like devices on hands and feet throughout the chemotherapy infusion. The devices were pre-cooled to 10oC and then put on patients 30 minutes before starting, till one hour after the end of chemotherapy infusion. A questionnaire, as proposed by Leonard et al [7], was administered to patients every cycle to assess the development and severity of CIPN symptoms. Statistical analyses were performed by using a Cox regression model. Results Of the 40 patients analysed, 33 (83.5%) underwent a taxane-based regimen. The median number of cryotherapy sessions was three (ranging from 1 to 12), and, when excluded patients who underwent only one session of

cryotherapy, the median was 4 (range 2 to 12). 75% of the 40 patients underwent cryotherapy in all chemotherapy sessions, or were still receiving chemo with cryotherapy by the time of our analysis. 80% of those who left treatment did so after the first session (HR 40.44 (CI95: 8.34 – 196.1; p< 0.0001). CIPN was stable or better than the baseline status for 26 (87%) of the 30 patients that underwent more than 1 session of cryotherapy; only 1 (25%) of the four patients who developed CIPN worse than the baseline status had grade 2 symptoms. Conclusion Cryotherapy is a safe and tolerable strategy that can be used during chemotherapy for breast cancer. Our data suggests that this is an efficient approach to prevent and treat CIPN, but the retrospective nature of the study and the small sample size must be considered when interpreting the results. Finally, strategies must be developed to further improve adherence and tolerability, and prospective randomized trials are needed to confirm the efficacy of cryotherapy in this context. 1. Loprinzi et al. Prevention and Management of Chemotherapy-Induced Peripheral Neuropathy in Survivors of Adult Cancers: ASCO Guideline Update. J Clin Oncol 38:3325-3348. 2020 2. Rivera et al. Chemotherapy-Associated Peripheral Neuropathy in Patients With Early-Stage Breast Cancer: A Systematic Review. JNCI J Natl Cancer Inst, 2018, Vol. 110, No. 2 3. Rosenbaek et al. Effect of cryotherapy on dose of adjuvant paclitaxel in early-stage breast cancer. Supportive Care in Cancer (2020) 28:3763–3769 4. Ruddy et al. Randomized controlled trial of cryotherapy to prevent paclitaxel-induced peripheral neuropathy (RU221511); an ACCRU trial. The Breast Volume 48, December 2019 5. Shigematsu et al. Cryotherapy for the prevention of weekly paclitaxel-induced peripheral adverse events in breast cancer patients. Support Care Cancer. 2020 6. <https://www.hilotherm.com/en/about-hilotherm/> accessed on July 15 2022 at 23:03 7. Leonard et al. Survey of oxaliplatin-associated neurotoxicity using an interview-based questionnaire in patients with metastatic colorectal cancer. BMC Cancer 2005, 5:116

Disclosure(s):

Rafael B. Costa, MD: AstraZeneca: Speaker (Ongoing); Daiichi Sankyo: Speaker (Ongoing); Lilly: Speaker (Ongoing); Merck Sharp & Dohme: Speaker (Ongoing)

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7:00 AM - 8:15 AM

P4-04-02

Evaluation of Dronabinol to Decrease Opioid Use for Cancer- Induced Bone Pain

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Purpose Bone metastases (BM) from breast cancer cause significant complications including pain, hypercalcemia, spinal cord compression, and pathologic fractures, collectively referred to as skeletal related events (SREs). Of all SREs, bone pain impacts the quality of life (QOL) most significantly. Cancer- induced bone pain (CIBP) is difficult to treat with limited treatment options and requires a multimodal approach. Management of CIBP is primarily by opioids which have notable side effects like sedation, constipation, and concern for addiction. In addition, pre-clinical evidence suggests that opioids accelerate bone loss and increase risk of fractures. There is an unmet need for novel analgesic therapy interventions to optimize QOL for patients with BM from metastatic breast cancer. Preclinical studies have shown that the endogenous cannabinoid (CB) system is involved in pain modulation, bone regulation, immunity, and restraint of cancer pathogenesis. CB2 receptor activation has been shown to inhibit proinflammatory cytokines/chemokines in pre-clinical models. Treatment with selective CB2 agonist in mice with BM led to significant antinociception, decreased cancer-induced bone degradation, and reduced side effects of morphine. In addition to alleviating pain, CB2 agonists were shown to enhance bone growth/strength in these mice. Based on this pre-clinical data, we hypothesized that the addition of a CB2 agonist will improve pain symptoms and decrease opioid requirement in patients with bone metastases from breast cancer. We proceeded to conduct a pilot study by repurposing a clinically approved CB2/CB1 agonist, dronabinol. Methods We conducted a prospective, single site study among patients with BM from breast cancer at our center (NCT03661892). Patients had to have been on opioids for CIBP for at

least 4 weeks and not using marijuana or CBD products. Patients were treated with 10mg dronabinol BID for 8 weeks. Our primary objective was to determine the proportion who decrease their opioid use by $\geq 20\%$. The null hypothesis value was 5% of women would have a 20% decrease. With 14 participants, we could detect an increase from 5% to 29% ($n=4$) with 80% statistical power using a one-sided alpha level of 0.05. Participants completed Brief Pain Inventory and the European Organization for Research and Treatment of Cancer quality of life questionnaires pre and post treatment. Results Twenty participants consented with 14 patients completing the study and evaluable for primary analysis. No patients received any palliative radiation therapy or other therapies for bone pain within 3 months prior to enrollment to this study. Four patients decreased their opioid use by $\geq 20\%$ meeting the primary objective. Patients reported significant improvement in pain severity, interference scores, quality of life and insomnia based on the questionnaires. There were no grade 4 side effects and only 1 patient had grade 3 adverse event (dizziness) related to study drug. Of the 14 patients who completed the study, 9 desired to continue dronabinol therapy after completion. Conclusion Our pilot study shows that the addition of dronabinol resulted in decreased opioid requirements for CIBP in patients with metastatic breast cancer. Patient-reported outcomes also demonstrated improved pain and QOL with the addition of dronabinol. While we did not see any significant AEs tolerability may be of concern due to CB1 psychoactive effects. Our results are promising and warrant further investigation into evaluating CB2 agonists for improved pain control from CIBP and to decrease opioid use.

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Jennifer Segar, MD: No financial relationships to disclose

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Mary Junak, MD: No financial relationships to disclose

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Pavani Chalasani, MD, MPH: Gilead: Advisory board (Terminated, June 12, 2022); Pfizer: Contracted Research (Ongoing)

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7:00 AM - 8:15 AM

P4-05-01

Cancer-Related Distress and Unmet Needs Among Triple Negative Breast Cancer Patients: Findings from the Cancer Experience Registry

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Background: Cancer patients and survivors experience distress related to physical, psychological, social and financial concerns. Individuals diagnosed with triple negative breast cancer (TNBC) may be at increased risk of distress due to the aggressive nature of the illness and high rates of recurrence. The aim of the present study was to describe how TNBC patients characterize cancer-related distress and concerns and identify factors associated with distress. Methods: Cancer Support Community's Cancer Experience Registry® (CER) is an online research initiative examining the physical, emotional, practical, and financial impact of cancer. The CER measures cancer-related distress using CancerSupportSource™ (CSS), a 25-item validated distress screening tool in which participants rate their level of concern (0=Not at all; 4=Very seriously) across five key domains: (1) emotional well-being (EWB; 8 items, $\alpha=.91$); (2) symptom burden and impact (SYM; 8 items, $\alpha=.90$); (3) body image and healthy lifestyle (BHL; 4 items, $\alpha=.80$); (4) healthcare team communication (HCC; 2 items, $\alpha=.74$); (5) relationships and intimacy (REL; 2 items, $\alpha=.71$). CSS subscale scores were calculated as the average item rating. For item analysis, the proportion indicating moderate to very serious concern was reported. From January 2015 to August 2021, a total of 195 US residents with a history of TNBC took part in the CER and completed CSS. Multiple linear regression analysis was used to estimate the relationships between CSS subscales and socio-demographic variables (age,

low-income status, employment status) and clinical history (time since diagnosis, advanced or metastatic disease, and currently receiving treatment). Results: The sample was 82% Non-Hispanic White, 7% Non-Hispanic Black, 5% Hispanic, and 7% Non-Hispanic other/multiracial. 17% reported annual household income <\$40K. 44% was employed full-time, 12% part-time, 18% retired, and 24% unemployed due to disability or other reason. Mean age was 53 (SD=10) years; 11% were < 40 years. 14% of participants were < 1 year of cancer diagnosis, 27% 1 to < 2 years, 34% 2 to < 5 years, and 25% ≥5 years. 41% were currently receiving treatment, and 27% were diagnosed with advanced or metastatic disease. The mean distress subscale score was highest for concerns about BHL (1.61), followed by EWB (1.29), SYM (1.27), REL (1.04), and HCC (0.83). With regard to concerns about BHL, over half were moderately to very seriously concerned with eating and nutrition (55%) and exercise (55%). Regarding EWB, the items of greatest distress were worrying about the future (53%) and worrying about family (39%). For SYM, over half (53%) were concerned about thinking clearly, and 49% were concerned about fatigue. Participants reported moderate to very serious concern about intimacy, sexual function, and/or fertility (36%) and relationships (22%). Regarding HCC, 24% reported concern related to treatment decisions, while 22% reported concern about communicating with their doctor. In multivariate analysis, time since diagnosis was inversely associated with concerns about EWB ($B=-0.03$, $p=.030$), such that distress was higher closer to diagnosis. TNBC patients with advanced or metastatic disease status had significantly higher distress related to SYM ($B=0.40$, $p=.009$) and HCC ($B=0.61$, $p=.001$). Younger age was associated with concerns about BHL ($B=-0.02$, $p=.011$) and REL ($B=-0.02$, $p=.006$). Finally, unemployment was associated with higher distress related to EWB ($B=0.57$, $p=.001$), SYM ($B=0.63$, $p<.001$), BHL ($B=0.42$, $p=0.03$), and REL ($B=0.70$, $p<.001$). Conclusions: In this sample, average levels indicated slight distress across multiple domains. Many TNBC patients reported concerns that were physical and future-oriented, highlighting critical areas of unmet need. Factors of less time since cancer diagnosis, advanced/metastatic disease, younger age, and unemployment were predictors of higher levels of distress.

Disclosure(s):

Caroline Lawrence, n/a: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

P4-05-02

oncoplastic breast surgery and involvement of plastic surgery improve quality of life by Breast-Q score in breast conserving surgery

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Introduction: Breast cancer surgery is a life altering event which can have profound consequences on a woman's physical, mental and emotional health. Breast Surgery creates cosmetic changes which can harm a woman's emotional well-being and quality of life. Breast reconstruction following mastectomy has been found to improve many quality of life measures and has been well studied. This has been less well studied in breast conserving surgery. The addition of oncoplastic breast surgical techniques and involvement of a plastic surgeon for immediate reconstruction following partial mastectomy can improve the cosmetic outcome for patients, reduce symptoms of breast hypertrophy and improve quality of life. To assess this, we applied the Breast Q scale before and after surgery and found a significant improvement in multiple quality of life indices. Methods: Between January 2020 through May 2022, 136 women undergoing breast conservation were given the Breast Q Version 2.0 Breast conserving therapy module (pre-and postoperative scales) written questionnaire before and again between 3 and 6 months after surgery. The Breast Q survey is a standard tool used by surgeons to assess a variety of quality of life factors following breast surgery. The patients were prospectively studied but not randomized in any specific way. The surgical technique used for the procedure was determined by a discussion between the patient and her breast surgeon. Results were divided into groups based on type of surgery and differences between groups with respect to the Breast-Q questions were analyzed with the student T test for p values. Results: Patients were divided into three categories; simple closure, the control group (20% n=26), oncoplastic closure with internal tissue rearrangement greater than 10 cm² (60% n=79) and patients who had involvement of a plastic surgeon for therapeutic mammoplasty and contralateral symmetry procedure (25% n=31). Significant improvement (p<.05) over the control arm and patients undergoing standard oncoplastic closures without a plastic surgeon was noted in several areas. These include an increase in confidence in a social setting, acceptance of her body, overall attractiveness, overall emotional health, sexual confidence and comfort wearing clothing and/or bra. Relative to the control group, the addition of oncoplastic closure also showed significant improvement in scores over patients without these techniques although the magnitude was smaller than with the use of a plastic surgeon. Conclusion: In breast conserving surgery, the addition of oncoplastic closure and especially the involvement of a plastic surgeon for therapeutic mammoplasty is highly effective at limiting some aspects of the deficits in quality of life and, surprisingly, significantly improved this from baseline in many patients. Where appropriate, these techniques should be employed to enhance individual patients quality of life..

Disclosure(s):

Michael E. Stuntz, MD: No financial relationships to disclose

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Jenna Garcia, n/a: No financial relationships to disclose

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P4-05-03

Investigating Financial Toxicity among Breast Cancer Patients Diagnosed during the Pandemic: The Role of Cancer Care Disruptions and Social Isolation

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Background: Financial toxicity (FT) is a multi-faceted construct, encompassing material hardship, psychological responses, and coping behaviors. FT adversely impacts patient-reported outcomes by decreasing mental health, affecting health-related quality of life (HRQOL), and deteriorating healthcare adherence. Few studies have assessed the relationship between financial toxicity, distress, coping, self-efficacy, and HRQOL within the context of cancer care disruptions resulting from the pandemic. Methods: In the COVID-19 Breast Cancer Care Survey, 46 women with primary breast cancer were cross-sectionally evaluated for financial hardship (FACIT-COST), distress (Perceived Stress Scale), coping behaviors (Brief COPE), self-efficacy (Cancer Behavior Inventory–Brief) and HRQOL using the Functional

Assessment of Cancer Therapy General (FACT-G) measure. Cancer care disruptions were measured with a series of questions investigating the impact of COVID-19 guidelines on access to healthcare services, treatment, and transition to telemedicine. Given the role of informal caregivers for patients' outcomes, social isolation was additionally included (PROMIS Social Isolation Scale). Descriptive statistics were computed, and bivariate correlations examined. Then, a subsequent regression model investigated predictors of FT in the present sample. Statistical analyses were performed using SAS 9.4 and significance level was set at $p < 0.05$. Results: Overall, participants were adult (Mean = 46.3 ± 10.9) women diagnosed with early-stage breast cancer (75.61% Stage I/II). Approximately half of the participants were in active treatment (51.2%) and received multiple types of treatment (85.4% surgery; 61% chemotherapy, and 36.5% radiation). Although all participants were insured at time of the study, the mean score of FT was 22.75 (SD=4.10, range: 0-44). Correlation analyses indicated that cancer care disruptions ($r = -0.57, p < .001$), health-related quality of life ($r = -0.51, p = 0.0007$), coping behaviors ($r = -0.33, p = 0.037$), well-being ($r = 0.56, p = 0.0001$), social isolation ($r = -0.40, p = 0.0096$), and psychological distress ($r = -0.42, p = 0.0064$) were significantly correlated with FT. That is, women who reported greater disrupted cancer care delivery, greater difficulties managing the illness, reduced physical and mental health, and those experiencing more social isolation reported worse financial toxicity. Results of the final regression model showed that women who experienced greater COVID-19-related cancer care disruptions ($\beta = -2.82, p = 0.0013$) and isolation ($\beta = -0.44, p = 0.0196$) from supportive networks were more likely to indicate elevated FT scores. Conclusions: A multidisciplinary and patient-centered FT management approach can be implemented to extend current financial navigation models to address psychosocial and behavioral factors exacerbated by altered care delivery protocols.

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7:00 AM - 8:15 AM

P4-05-04

Health-Related Quality of Life and Work Impairment Among Individuals Living with HER2+ Breast Cancer with Brain Metastases

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Background: Roughly 20% of people diagnosed with breast cancer (BC) will be considered HER2+. HER2+ BC patients are among those at highest risk for developing brain metastases, with up to 50% developing brain metastases. Brain metastases are associated with faster disease progression, shorter survival, and myriad increased impairments. Despite the significant burden faced by HER2+ BC patients living with brain metastases (BMBC), there is little empirical research available regarding the unique experiences of this population. The goals of this exploratory study were to examine the feasibility of recruiting HER2+ BMBC patients to complete an online survey, and to describe their health-related quality of life (HRQOL) and experiences with work impairment. Methods: 62 women with HER2+ metastatic BC were recruited via advocacy partners, Living Beyond Breast Cancer and Metastatic Breast Cancer Alliance, and completed an online survey in January 2022. Participants reported sociodemographics, clinical history, current caregiving support received, physical health (Patient-Reported Outcomes Measurement Information System (PROMIS) Global Physical Health 2av1.2), HRQOL (PROMIS-29v2.0 and PROMIS Cognitive Function Short Form 8a) and work impairment (Work Productivity and Activity Impairment Questionnaire–Specific Health Problem (WPAI-SHPv2.0)). Descriptive statistics were calculated for study variables; PROMIS measures were converted to T scores (M=50, SD=10), enabling comparisons to established population benchmarks. Results presented in this study are restricted to the 30 HER2+ participants living with BMBC. Results: Participants were 47% White, 23% Hispanic, 23% Asian, 3% Black/African American, 3% American Indian/Alaska Native; mean age=43y (range: 33-72); 83% held a Bachelor degree or higher; 70% were married or partnered; mean years since BMBC diagnosis=2.7 (range: < 1-20); mean years between diagnosis and onset of metastatic disease=1.8 (range: 0-11). 67% of participants reported receiving constant care from a caregiver; the remaining participants reported receiving an average of 10.2 hours/week of care. 50% of participants reported physical health corresponding to poor levels (>2 SD on

PROMIS). The majority of participants reported HRQOL impairments corresponding to moderate to severe levels (>1SD on PROMIS): Anxiety (84%); Physical Function (80%); Pain Interference (77%); Depression (70%); Fatigue (70%); Sleep Disturbance (67%); Cognitive Function (63%); and Ability to Participate in Social Roles and Activities (53%). Mean symptom burden T-scores (range: 60.4-67.7) and mean functional impairment T-scores (range: 36.0-39.9) were poorer relative to several reference groups (i.e., other women with HER2+ MBC, overall BC population benchmarks, general US population benchmarks). At the time of the survey, 73% of participants were not employed due to disability. Among those employed (n=7); 100% reported that BMBC negatively affected their employment in the past week: mean percent of scheduled work hours missed=37% (range: 14-74%); mean percent of reduced productivity while working=39% (range: 0-80%); and mean overall work impairment=60% (range: 39-95%). Conclusions: HER2+ BMBC patients experience substantial emotional, physical, social, and cognitive quality of life impairments, high work absenteeism, reduced productivity, and overall work impairment, suggesting significant unmet needs for this population. Efforts to recruit HER2+ BMBC patients were successful, suggesting high feasibility of future work with a more robust sample. Despite the small sample size, our descriptive results provide a key foundation for future research with HER2+ BMBC patients to formally test hypotheses and evaluate predictor variables impacting patient HRQOL and work impairment.

Disclosure(s):

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P4-05-05

The Psycho-Social Factors Impacting Black Women Breast Cancer Survivors

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Background: Breast Cancer (BC) mortality rates disproportionately affect African American (AA) women over any other racial or ethnic group in the United States. However, questions about how AA women who survive the disease navigate psychosocial factors such as body image, self-esteem, stigma and shame, thoughts and fears surrounding fertility, and romantic relationships remain unanswered. This study's primary research question is, "How do AA women BC survivors create a new normal post-breast cancer while figuring out their own identity?" Methods: This qualitative study aims to address the psychosocial factors experienced by 20 AA women BC survivors in the U.S. The 20 women were recruited to participate in the IRB-approved study (University of Illinois at Urbana-Champaign) through the Tigerlily Foundation, a non-profit breast cancer advocacy organization. The total duration of the study lasted a maximum of 1 hour and 45 minutes with participants answering one pre-interview questionnaire for demographic purposes and one interview with a member of the research team. Results: Preliminary results from the data conclude that AA women BC survivors, and potentially all cancer survivors, mirror individuals in the postpartum phase. Being postpartum is not inherently harmful; however, if one begins to experience symptoms of depression, loss of appetite, irritability, and insomnia for an extended period, there is a high possibility they are experiencing Postpartum Depression (PPD). BC survivors experience numerous changes that can drastically impact their quality of life. AA women BC survivors struggle immensely with body image and self-confidence issues after experiencing breast cancer, various surgeries, and treatments. Conclusion: If BC survivors, particularly AA women BC survivors experiencing systemic and institutional racism, are treated with the same care postpartum individuals are given, there can be a shift in how oncologists work with BC survivors. Creating more personalized survivorship care plans between patients, oncologists, and hospital-based social workers can improve psychosocial factors experienced by AA women BC survivors.

Disclosure(s):

Virginia Leach, B.A.: Tigerlily Foundation: Contracted Research (Ongoing)

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P4-05-06

SURGICAL OUTCOMES FOR RECONSTRUCTION AFTER DELAYED CONTRALATERAL PROPHYLACTIC MASTECTOMY.

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Background: Challenges for breast reconstruction (BR) after delayed CPM relate to previous ipsilateral reconstructive procedures, adjuvant therapies and co-morbidities. The same type of BR for both sides may be impossible and use of an abdominal flap-based reconstruction for the therapeutic side precludes a similar technique for the contralateral side; an implant-based reconstruction may be difficult to size match with autologous tissue reconstruction. Alternative sites for tissue harvest are the latissimus dorsi and gluteal artery perforator flaps but these can be associated with significant donor site morbidity and poorer breast symmetry. Types of reconstruction and complications were evaluated in the context of BR and delayed CPM. Methods: A retrospective analysis examined breast cancer patients undergoing CPM either as an immediate or delayed procedure with or without breast reconstruction (BR) between January 2009 and December 2019. Clinical information was extracted from a prospectively maintained database with collection of data on demographics, timing and type of surgery, previous adjuvant treatments and complications. Patients undergoing delayed CPM were categorized into 4 groups based on BR or no BR and its timing in relation to both CPM and therapeutic mastectomy. Complications were listed according to the Clavien-Dindo system (scale of 1 – 5) with major adverse events being wound infection requiring intravenous antibiotics or drainage and explantation. Despite small numbers, complications were compared for therapeutic and prophylactic mastectomy together with the type and timing of reconstruction. Results: A total of 39 CPM patients were analyzed with 12 (31%) undergoing immediate BR at the time of cognate mastectomy, 22 (56%) choosing bilateral BR simultaneously with delayed CPM, 3(8%) opted for bilateral delayed BR following delayed CPM whilst 2 (5%) had no reconstruction. The mean patient age was 52 years (24–73) and the average interval between initial and delayed mastectomy was 2.67 years (0–22). The majority of reconstructions (28/39) were implant-based (72%) rather than exclusively autologous reconstruction and most patients had a similar type of BR for contralateral and ipsilateral sides. More than half of patients received neoadjuvant therapy and 85% had post-mastectomy radiotherapy prior to CPM. Major complications occurred in 8 patients (67%) with unilateral BR compared with 5 patients (23%) with bilateral immediate BR and 3 patients (100%) undergoing bilateral delayed BR. Small numbers and confounding factors preclude any robust statistical analysis but no statistically significant differences between the immediate and delayed BR groups were found on Fisher's exact test. Complication rates appeared higher when immediate BR was performed after delayed CPM

compared with therapeutic mastectomy. Conclusion: Potential complications and limitations of BR in the context of delayed CPM should be discussed with patients and used to inform decision-making processes for timing of CPM and associated reconstruction. There are no clear differences in rates of complications depending on laterality, type or timing of reconstruction. This study provides reassurance that reconstruction can be successfully performed either at the same time as delayed CPM (with or without BR on therapeutic side) or as a delayed procedure.

Disclosure(s):

Chien Lin Soh, BA: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-05-07

Making Choices with Scarce Resources While Battling Breast Cancer In Nigeria

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Background Breast cancer diagnosis in Nigeria is perceived by most as a death sentence and women who have been diagnosed have to battle with different choices at any given time, whether to fight so as to survive, what if they fight and lose, or maybe it is better not to fight at all judging from different cases discussed during our monthly cancer patient support group meetings. Making informed choices with limited resources is the bane of many breast cancer patients who feel guilty spending so much on their medical care while their family suffers financial neglect. This is because health insurance covers barely 10% of the country's population and most families pay out of pocket. Some women on the other hand completely ignore their treatment and channel these resources towards education and general welfare of other members of their families. Aim To determine the extent to which financial choices made by women who are diagnosed and are undergoing treatment of breast cancer in Nigeria affects their treatment journey. Method A qualitative research approach was used and structural interview was used to collect data. Female breast cancer patient who are undergoing treatment and those who are through with their treatment {chemotherapy , surgery, and radiotherapy} and are currently on periodic check up with their oncologists participated in the study. Grounded theory was used in data analyses. Results Most of the patients interviewed had at one time or the other suspended their treatments in order to take care of pressing family issues and these had caused delays in proceeding with their treatment with its attendant consequences. Presentation Oral Presentation

12/8/2022

7:00 AM - 8:15 AM

P4-06-01

Platinum-based chemotherapy for early triple-negative breast cancer: A Cochrane systematic review and meta-analysis

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In early triple-negative breast cancer (eTNBC), platinum-based chemotherapy has been shown to improve pathological complete response, but recommendations to include platinum chemotherapy are not consistent in international guidelines. We performed a systematic review of published randomized control trials to assess to assess survival outcomes and quality of life for people with early TNBC. The results presented in this abstract have not yet been peer-reviewed by Cochrane. If the final version of the review meets the necessary standards, the review is expected to be published in the Cochrane Database of Systematic Reviews. Methods: Randomized controlled trials examining neoadjuvant or adjuvant platinum chemotherapy for eTNBC were included. We searched for published and unpublished data using standard Cochrane search strategies. The primary outcomes assessed were disease free survival (DFS) and overall survival (OS). Secondary outcomes included rate of pathological complete response (pCR), dose intensity and completion of regimens, grade III or IV toxicity related to chemotherapy, and quality of life. Prespecified subgroups included BRCA mutation status, HRD status, lymph node status, frequency of chemotherapy, type of platinum agent used, and the presence or absence of anthracycline chemotherapy. Results: From 3972 records, 19 published studies were eligible. Twenty six ongoing studies were identified. Risk of bias was judged low for most trials. There were 14 neoadjuvant chemotherapy trials, 4 adjuvant

chemotherapy trials, and one trial of neoadjuvant and adjuvant therapy. Most trials used carboplatin (16 trials) followed by cisplatin (2), and lobaplatin (1). Eight trials had an anthracycline free intervention arm, 5 of which had a carboplatin-taxane intervention compared to an anthracycline-taxane control. All studies reporting DFS and OS used carboplatin. Twelve of 19 studies with a total of 3347 participants reported DFS data. Inclusion of platinum chemotherapy improved DFS in neoadjuvant and adjuvant setting (HR 0.63, 95% confidence interval (CI) 0.53-0.75; HR 0.69, 95% CI 0.54-0.88 respectively). Eleven studies collected OS data, with a total of 3229 participants and 460 deaths reported. Inclusion of platinum chemotherapy in the regimen improved OS (neoadjuvant: HR 0.69, 95% CI 0.69, 0.55-0.86; adjuvant: 0.70, 95% CI 0.50 to 0.96). Median follow up for survival outcomes ranged from 36 – 97.6 months. Our analysis confirmed platinum chemotherapy increased pCR rates (RR 1.46 [1.33-1.61], $p < 0.00001$). Subgroup analysis revealed that survival outcome benefits were seen regardless of BRCA mutation status, HRD status, lymph node status, or whether the intervention arm contained anthracycline chemotherapy or not. Platinum chemotherapy was associated with reduced dose intensity, with participants more likely to require chemotherapy delays (RR 2.23 [1.70-2.94], 4 studies), dose reductions (RR 1.77 [1.56-2.02], 6 studies) and early cessation of treatment (RR 1.20 [1.04-1.38], 16 studies). Increased hematological toxicity occurred in the platinum group who were more likely to experience grade III/IV neutropenia (RR 1.55 [1.45-1.66]), anemia (RR 10.12 [6.61-15.50]) and thrombocytopenia (RR 7.59 [5.10-11.29]). There was no increase in febrile neutropenia (RR 1.16 [0.89-1.49]). Treatment-related death was very rare (7 events in 3094 patients) and similar across treatment groups (RR 0.58 [0.14-2.33]). Five studies collected quality of life data but did not report it. Conclusion: Platinum-based chemotherapy using carboplatin in the adjuvant or neoadjuvant setting improves long-term outcomes in eTNBC, regardless of the examined subgroups. This was at the cost of more frequent chemotherapy delays and dose reductions, and greater haematological toxicity. Benefit from platinum was seen both when platinum agents were added to anthracycline containing regimens, as well as in anthracycline-free regimens.

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7:00 AM - 8:15 AM

P4-06-02

Complete response of ductal carcinoma in situ to neoadjuvant systemic therapy in HER2-positive invasive breast cancer patients: a nationwide analysis

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Introduction Neoadjuvant systemic therapy (NST) is increasingly applied in breast cancer to increase breast-conserving surgery (BCS) rates and to improve oncological outcomes. Ductal carcinoma in situ (DCIS) can be present adjacent to invasive breast cancer (IBC), especially in HER2-positive IBC. DCIS was previously considered to be insensitive to NST. Consequently, mastectomy rates are higher in IBC with adjacent DCIS. Recent studies have shown that DCIS can be sensitive to NST, however, only small populations were investigated. Therefore, the aim of this study was to determine the rate of complete response of adjacent DCIS in HER2-positive IBC and to assess the potential influence of clinicopathological variables in a nationwide cohort.

Methods All women diagnosed with HER2-positive IBC, treated with NST and surgery between January 2010 and December 2019, were selected from the Netherlands Cancer Registry (NCR). Of these patients, all pre-NST biopsy and postoperative specimen pathology reports were obtained from PALGA, the Dutch Pathology Registry, and assessed for presence of DCIS. Response of DCIS was defined as absence of DCIS in postoperative pathology when a DCIS component was present in the pre-NST biopsy. Clinicopathological factors associated with DCIS response were assessed using logistic regression analyses. **Results** In total, 5834 patients were included, of whom 1443 (24.7%) had a DCIS component in the pre-NST biopsy. Mastectomy rates were higher in IBC with adjacent DCIS compared to IBC without adjacent DCIS in the pre-NST biopsy (53.6% versus 41.0%, $p < 0.001$). Of these 1443 patients, 743 (51.5%) showed complete response of the DCIS component. Complete response of DCIS occurred more frequently in patients who also had a complete response of IBC (63.4% versus 33.8%, $p < 0.001$). Multivariable logistic regression analysis showed ER negative IBC (OR 1.79; 95% CI 1.33-2.42) and treatment with HER2-targeted therapy (OR 5.97; 95% CI 1.82-19.55) to be independently associated with complete response of DCIS. **Conclusion** More than half of HER2-positive IBC patients with adjacent DCIS in the pre-NST biopsy showed a complete response of the DCIS component to NST. Complete response of DCIS should be considered, especially in ER-negative HER2-positive IBC and in case of complete response of IBC. Future studies should investigate the evaluation of DCIS response by imaging and the possibility of increasing breast-conserving surgery rates.

Disclosure(s):

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7:00 AM - 8:15 AM

P4-06-03

Pathological complete response (ypCR) in early and locally advanced breast cancer (LABC) patients treated with neoadjuvant chemotherapy in a middle-income country. Results from a real-world historical cohort.

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Introduction

Breast cancer (BC) is the most frequent neoplasm in Colombia, with mortality rate increasing in past decade. The expected 5-year overall survival (OS) is < 80%, being the Latin American country with the worst prognosis. 2 factors related to this are higher frequency of advanced stages and higher frequency of aggressive tumor subtypes.

Neoadjuvant chemotherapy (NACT), and ypCR, have demonstrated impact on the risk of relapse and death.

This trial describes the characteristics, treatment patterns, clinical outcomes, and ypCR after NACT in a cohort of Colombian BC patients.

Methods

We included BC adult patients treated with NACT in 3 institutions in Colombia. Clinical, sociodemographic, and outcome variables were retrieved retrospectively from clinical charts. Univariate, bivariate and time-to-event analyses were performed. A partition survival tree was performed to explore interactions between variables. Statistical analyses were done in R software.

The protocol was approved by the IRC and EC of Fundación Cardioinfantil and Hospital Militar Central.

Results

We included 312 patients treated between 2013 and 2019. 50.9% were ER and/or PgR positive, 28.5% HER2 positive and 20.5% triple negative breast cancer (TNBC). 75.9% of the patients had a LABC. TNBC patients were younger (median age 46 years), premenopausal (58%), had higher Ki67 index (Ki67 \geq 20%= 91%), and a higher tumor grade (Grade 3= 56.7%). Most of the patients (91.7%), received Doxorubicin + Cyclophosphamide, and Taxanes (97.8%), 76.6% of TNBC patients received Carboplatin. Breast conserving surgery was performed in 53.7% of the patients, and only 38.9% received immediate breast reconstruction. 88.5% of the patients were treated with adjuvant radiotherapy.

The ypCR rate was 34.6% and was achieved more frequently in HER2 positive subtype. The ypCR rates in TNBC were higher in patients treated with carboplatin (55% vs 20%, $p=0.02$). Other factors related to ypCR were high Ki67 ($p= 0.0005$) and higher tumor grade ($p= 0.0034$). Most of the relapses were distant (14.1%), with only 1.9% of local relapse rate. Table No 1 summarizes clinical outcomes.

With a median follow up of 4.9 years, the 5 year OS was 88.2%. Clinical stage at diagnosis ($p= 0.01$); node involvement ($p= 0.0014$); ER ($p= 0.0032$); PgR ($p= 0.0069$); HER2 ($p= 0.0334$); phenotype ($p=0.0145$); type of surgery ($p< 0.0001$); ypCR ($p=0.003$); and relapse ($p= < 0.00001$) were related with OS. We did not found differences in the 5 year OS between stage II and III patients (87.8% vs 88%). The 5 year OS did not differ between ypCR and ypCR-IS (94.2% vs 93%).

The relapse rate was 3.7% in ypCR vs 22.1% in non ypCR patients ($p< 0.00001$). The 5 year OS rate was 94.3% for ypCR and 85% for non ypCR patients ($p= 0.0059$). When analyzed by phenotype, ypCR was only related to risk of death among TNBC ($p= 0.011$).

We perform a partition survival tree, identifying 6 subgroups with different OS behaviors: TNBC and non TNBC; low proliferative and high proliferative; early stage and locally advanced stage.

Discussion

We found an increased number of LABC. The ypCR rate was higher than described elsewhere, explained by higher proportion of TNBC and HER2 enriched tumors and differences in treatment selection in subgroups. In the TNBC subgroup the use of carboplatin was associated with higher ypCR.

ypCR was related with risk of death and relapse, but with statistical significance for OS only in the TNBC population.

This study offers a baseline characteristic of NACT BC cohort, that will allow us to design and implement strategies to improve outcomes in early and LABC.

Table No 1: Treatment outcomes by phenotype.

Variable	Luminal A (n= 59) (% 95% CI)	Luminal B HER2 negative (n= 100) (% 95% CI)	Luminal B HER2 positive (n= 67) (% 95% CI)	HER2 enrich (n= 22) (% 95% CI)	TNBC (n= 64) (% 95% CI)	All (n= 312) (% 95% CI)
ypCR	6 (10.2%) (3.8 – 20.8)	19 (19%) (11.8 – 28.1)	37 (55.2%) (42.7 – 67.4)	16 (72.7%) (49.8 – 89.2)	30 (46.9%) (34.3 – 59.7)	108 (34.6%) (29.3 – 40.2)
ypCR-IS	13 (22%) (12.3 – 34.7)	32 (32%) (23 – 42.1)	38 (56.7%) (44 – 68.9)	16 (72.7%) (49.8 – 89.2)	34 (53.1%) (40.2 – 65.7)	133 (42.6%) (37.1 – 48.3)
Mastectomy	30 (50.8%) (37.5 – 64.1)	45 (45%) (35 – 55.3)	28 (41.8%) (29.8 – 54.5)	8 (36.4%) (17.2 – 59.3)	32 (50%) (37.2 – 62.7)	143 (46%) (40.2 – 51.5)
Relapse	10 (16.9%) (8.4 – 28.9)	16 (16%) (9.4 – 24.7)	7 (10.4%) (4.3 – 20.3)	2 (9%) (1.1 – 29.1)	14 (21.8%) (12.5 – 33.9)	49 (15.7%) (11.8 – 20.2)
Death (n=305)	5 (8.8%) (2.8 – 18.7)	11 (11%) (5.6 – 18.8)	4 (6.2%) (1.7 -14.6)	1 (4.8%) (0.1 – 22.8)	16 (25%) (15 – 37.4)	37 (12.1%) (8.5 – 15.9)

Disclosure(s):

William Mantilla, n/a: AMGEN: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Speakers burrow, Research funding (Ongoing); Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); BMS: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Terminated, March 1, 2022); Novartis: Consulting Fees (e.g., advisory boards) (Terminated, July 15, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, July 15, 2022); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Research Funding, Speakers bureau, Advisory Board (Ongoing); Roche: Advisory Board, Research Founding, Speakers bureau (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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12/8/2022

7:00 AM - 8:15 AM

P4-06-04

Clinical outcomes of loco-regional HER2-positive invasive lobular carcinoma of the breast

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Background: HER2-positive invasive lobular carcinoma (ILC) of the breast is a rare entity. Treatment decisions for HER2-positive lobular breast cancer are often extrapolated from the HER2-positive ductal subtype of breast cancer but the clinical outcomes and prognostic factors are not well defined. Methodology: Women with a diagnosis of stage I to III HER2-positive ILC or invasive ductal carcinoma (IDC) of the breast between 2010 and 2018 were identified from the National Cancer Database. Baseline characteristics were compared between ILC and IDC using Chi-square test for categorical variables and the Mann-Whitney U test for continuous variables. Five-year overall survival (OS) was estimated by the Kaplan Meir method. Multivariate cox proportional hazards regression model including age, race, ethnicity, Charleston Deyo score, grade, TNM stage, and treatment modalities such as type of surgery, chemotherapy, and radiation was used to identify factors associated with OS in HER2-positive ILC. In a subset of patients receiving neoadjuvant chemotherapy, the odds of achieving a complete pathological response were compared between women with ILC and IDC in a multivariate logistic regression model adjusting for age, race, ethnicity, Charleston Deyo score, grade, and clinical stage. Results: A total of 4,197 women with HER2-positive ILC and 116,984 women with HER2-positive IDC were included in the final analysis. The median age at diagnosis was 63 years for women with HER2-positive ILC and 56 years for women with HER2-positive IDC ($p < 0.001$). The five-year OS among women with HER2-positive ILC was 93.1%, 90.8%, and 78.8% in TNM stages I, II, and III respectively. In multivariate analysis, a significant difference in overall survival was not observed between women with HER2 positive ILC and IDC (Hazard Ratio [HR]: 1.0, 95% Confidence Interval [CI]: 0.9 - 1.1, $p = 0.55$). Among women receiving neoadjuvant chemotherapy, a complete pathological response was observed in 31.7% of women with HER2-positive ILC and 42.7% of HER2-positive IDC. In multivariate analysis, there was no difference in odds of achieving a complete pathological response to neoadjuvant chemotherapy between HER2-positive ILC and IDC (Odds Ratio [OR]: 0.8, 95%CI: 0.7 - 1.0, $p = 0.12$). Higher odds of complete pathological response in HER2-positive ILC were observed for women with estrogen-receptor negative (OR: 2.0, 95% CI: 1.1- 3.8), $p = 0.02$) and progesterone-receptor negative (OR 2.4, 95%CI: 1.5- 3.7), $p < 0.001$) tumors. The

five-year OS for women with a complete pathological response, partial response, and no response after neoadjuvant chemotherapy in HER2-positive ILC were 89.6%, 84.9%, and 77.3% respectively (p=0.01). Conclusion: This study demonstrates that HER2-positive ILC has comparable clinical outcomes to HER2-positive IDC and response to neoadjuvant chemotherapy correlates with OS in HER2-positive ILC. These findings lend support to the current practice of treating HER2-positive ILC and IDC in a similar manner.

Disclosure(s):

Suman Gaire, MD: No financial relationships to disclose

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Grace M. Choong, M.D.: MJH Life Sciences: Consulting Fees (e.g., advisory boards)
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12/8/2022

7:00 AM - 8:15 AM

P4-06-05

Response to neoadjuvant chemotherapy among women with triple-negative breast cancer by HER2 expression status

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Background: - Low levels of HER2 expression among women with HER2-negative breast cancer is an emerging target. In addition, prior studies have suggested that low levels of HER2 expression might confer resistance to chemotherapy among women with triple-negative breast cancer (TNBC). In this study, we assess the response to neoadjuvant chemotherapy among women with TNBC with varying degrees of HER2 expression. Methodology: - Utilizing the National Cancer Database, we identified adult women treated with neoadjuvant chemotherapy for a diagnosis of clinical TNM stage I to III triple-negative invasive ductal carcinoma of the breast between the years 2010 and 2018. Baseline characteristics were compared between HER2 immunohistochemistry (IHC) scores of 0, 1+, and 2+ (Women with HER2 2+ expression had to be negative for amplification in the HER2 gene by FISH) using Chi-square for categorical variables. The odds of achieving a complete pathological response were compared among women with different HER2 expression statuses in a multivariate logistic regression model adjusting for age, race, ethnicity, grade of the tumor, and clinical TNM stage at diagnosis. A multivariate cox proportional hazards regression model was used to identify the prognostic effect of HER2 expression on overall survival (OS) adjusting for age at diagnosis, race, ethnicity, grade of tumor, and clinical TNM stage at diagnosis. Results: - A total of 11,038 women with HER2 IHC score of 0, 8,718 women with a score of 1+ and 2,700 women with a score of 2+ were included in the final analysis. The median age at diagnosis was 52 for women with a HER2 IHC score of 0, 53 for women with a HER2 IHC score of 1+ and 54 for women with an IHC score of 2+/FISH negative. The rates of complete pathological response among women with HER2 IHC scores of 0, 1+, and 2+ were 39.5%, 38.1%, and 36.1% respectively. In multivariate analysis, a significant difference in the odds of achieving complete pathological response was not observed for women with HER2 1+ (OR: 1.1, 95% CI: 0.95-1.20, p = 0.3) or HER2 2+ (OR: 0.9, 95% CI: 0.7-1.0, p = 0.1) tumors compared to women with HER2 IHC score of 0. In multivariate Cox regression analysis, women with TNBC with HER2 IHC score 2+ were found to have a better OS (Hazard Ratio [HR]: 0.88, 95% CI: 0.80-0.97, p = 0.01) compared to women with HER2 IHC score of 0 whereas a significant difference in OS was not observed between women with HER2 IHC scores of 0 and 1+ (HR: 0.95, 95% CI: 0.89-1.01, p = 0.1). Conclusion: - This study demonstrates that HER2 expression status does not influence the rates of complete pathological response to neoadjuvant chemotherapy in women with TNBC.

However, women with HER2 IHC score of 2+ were found to have a favorable prognosis, which needs to be evaluated further in future studies.

Disclosure(s):

Pravash Budhathoki, MD: No financial relationships to disclose

Anish Shah, MD: No financial relationships to disclose

Suman Gaire, MD: No financial relationships to disclose

Utsav Joshi, MD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-06-06

Neoadjuvant B27 protocol in Triple-Negative Breast Cancer: Evaluation response rate, pathological complete response rates ,toxicity ,and the prognosis of Adolescent and Young Adult (AYA) age group compared to older population

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Background: Neoadjuvant chemotherapy (NACT) is the standard early-stage triple-negative breast cancer (TNBC) treatment. Achieving pathological complete response (pCR) is considered an essential prognostic factor with favorable long-term outcomes. Younger patients have with poorer prognosis in breast cancer. To date, few studies are comparing the prognosis of AYA and older women (≥ 40) with breast cancer subtypes, specifically Triple-negative breast cancer (TNBC), as AYAs had higher proportions of this subtype. Method: Retrospective review was performed on female patients who received NACT at a King Hussien Cancer Center from January 2014 to June 2020. Data were collected from patients' electronic medical records. TNBC was histopathologically confirmed. Logistic regression analysis of predictors of pathologic complete response (pCR). Survival curves were estimated with the Kaplan-Meier method. Multivariate analysis for EFS was performed using Cox's proportional hazards regression model, covariates included age at diagnosis (AYA vs. ≥ 40), tumor size, nodal status LVI and pCR Result: We analyzed 211 women with stage I-III TNBC, including 62 (29.4%) women aged 18 to 39 years (AYA) and 149 (70.6%) ≥ 40 years. 138 (68.3%) were node positive, and 71 (34.8%) were T3/4 disease. Median follow-up was 28.1 months, median number of ER visit during NAC is 1 (0-11) , 23 (10.9 %) patients had admission during neoadjuvant chemotherapy, most commonly due to febrile neutropenia 13 (56.9%). 37 (17.5%) patients did not complete NAC, due to disease progression in 22 (10.4%), and toxicity in 15

(7.1%) patients. 195 (92.4%) patients had surgery, including 75 (35.5%) had breast-conserving surgery (BCS). 166 (76.3%) patients had objective response, and 64 (30.3%) had pCR. 170 (80.6%) received adjuvant radiotherapy, and 38 (18%) received adjuvant capecitabine. No significant differences between the AYA and the ≥ 40 group in terms of clinicopathological, toxicity, pCR rate, and the rate of BCS. In univariate analysis, the LVI, nodal status, pCR, and age group were significant predictors of DFS. In multivariate analysis, only PCR and age are the only independent predictor of DFS. The median DFS was worse in the AYA population 47.8 (31.21-64.39) months vs. NR in ≥ 40 (p-value 0.013). In patients who achieved pCR, the estimated 5-years DFS for the AYA group was 56.1% versus 86.8% for the ≥ 40 group, (p-value 0.71). In patients with residual disease, PFS for AYA was 34.2 (95%CI 11.5-57) months vs. 59.5 months in the ≥ 40 group, (p 0.009). Conclusion: Although there is no difference in pCR between the AYA age group patient treated with NACT for TNBC and the older age group, the DFS is significantly worse in the AYA than the ≥ 40 age group in patients with residual disease. As well, DFS is numerically worse in the AYA age vs. the ≥ 40 age group in patients who achieved pCR.

Disclosure(s):

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7:00 AM - 8:15 AM

P4-06-07

Preliminary indications of safety and efficacy of neoadjuvant chemotherapy plus chemokine-modulating regimen (rintatolimod, IFN- α 2b, celecoxib) in triple negative breast cancer

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BACKGROUND: Pathologic complete response (pCR) or microinvasive residual breast cancer (ypTmic) following neoadjuvant chemotherapy (NAC) is critical for good long-term outcomes in triple negative breast cancer (TNBC) patients (pts) but is achieved only in 40-50% of pts. Its combination with pembrolizumab, the new standard of care in TNBC, increases the pCR rate to 65% but is associated with significant immune-related and permanent toxicities. Higher intratumoral levels of CD8+ cytotoxic T-lymphocytes (CTLs) and low levels of regulatory T-cells (Treg) and myeloid derived suppressor cells (MDSC) predict improved relapse-free survival (RFS), overall survival (OS) and higher probability of pCR, a surrogate marker for RFS. Locally produced chemokines CCL5, CXCL9, CXCL10 and CXCL11 are critical for local infiltration with CTLs, while CCL22 is responsible for Treg attraction, with high CXCL9 expression being associated with a 3-fold higher rate of achieving pCR in response to NAC. Our preclinical data show that Chemokine-modulatory (CKM) regimen, combining rintatolimod (TLR3 agonist), interferon (IFN)- α 2b and celecoxib (COX-2 inhibitor), selectively induces CTL-attractants but decreases MDSC- and Treg-attractants in the tumor microenvironment (TME). We hypothesized that the combination of CKM with paclitaxel will promote selective CTL infiltration into TNBC, and along with doxorubicin/cyclophosphamide (AC), will result in higher rate of pCR, translating into improved RFS and OS. **METHODS:** In the phase I study NCT04081389, 9 pts with stage I-III TNBC were enrolled with median age of 47 (37-55) years. All patients were treated with paclitaxel 80 mg/m² IV weekly for 12 weeks, and for first 3 weeks days 1-3 also

received CKM regimen consisting of rintatolimod 200 mg IV and celecoxib 200 mg oral twice daily. IFN- α 2b was administered in an accelerated titration design at doses 0 or 5 million units (MU)/m² [Dose Level (DL) 1,2 respectively] in first 2 pts (no intra-patient dose escalation), then 10 MU/m² [DL 3] in 4 patients and then 20 MU/ m² [DL 4] in 3 patients. Pre- and 3 week-on treatment biopsies were performed at DL 3 and DL 4 (5 patients). This was followed by standard dose-dense AC and surgery. Dose-limiting toxicity (DLT) was defined as grade 3 or higher toxicity within the first 3 weeks of treatment. The primary endpoint was safety and tolerability, to determine the recommended phase II dose (RP2D) of CKM for extended efficacy study. The secondary endpoints included the efficacy (pCR), along with RFS and OS. Tumor and blood biomarkers were analyzed in exploratory studies. RESULTS: Treatment was well-tolerated with mostly grade 1 or 2 treatment-related adverse events (TRAEs) and no DLTs. Grade 3 TRAE were neutropenia (3/9), attributed to CKM (1/9) or paclitaxel (3/9), pneumonia (1/9) and anemia (1/9) attributed to AC. Two additional severe adverse events (pneumonia and squamous cell carcinoma of skin in situ) were observed, unrelated to study treatment. Paclitaxel- or AC-related toxicities were not higher than expected. There was no evidence of delayed or immune-related toxicities 90 days post-treatment. 5/9 (56%) pts attained pCR, and 1 additional pt had ypTmic at the time of surgery. There were no patients with progressive disease. All patients were able to get planned surgery with no additional delays observed. There was consistent (p=0.07) selective increase in CD8 α (CTL marker) in on-treatment tumor biopsies with concomitant decrease in CD8 α in the blood (p=0.04). CONCLUSIONS: The treatment was well-tolerated and no DLTs were observed and we determined RP2D for future studies. We observed promising clinical activity with pCR + ypTmic rate of 66%, comparable to pembrolizumab combination with NAC. A larger phase II study is being designed to confirm the observed efficacy and to determine if CKM regimen would be a safer short-term alternative to pembrolizumab or if CKM can overcome the resistance to the standard pembrolizumab/NAC therapy.

Disclosure(s):

Shipra Gandhi, MD: Astrazeneca: Consulting Fees (e.g., advisory boards) (Ongoing)
Mateusz Opyrchal, MD PhD: AZ: Consulting Fees (e.g., advisory boards) (Terminated, April 1, 2020); Bayer: Contracted Research (Terminated, May 1, 2018); Crisper Theurapeutics: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Eli Lilly: Contracted Research (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Terminated, May 1, 2019)
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12/8/2022

7:00 AM - 8:15 AM

P4-06-08

HER2-protein expression is a predictive marker for treatment response in patients with HER2-positive breast cancer who received neoadjuvant chemotherapy with dual HER2-blockade

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Background In HER2-positive breast cancer, pathologic complete response (pCR) has been known to be a surrogate marker for favorable prognosis after neoadjuvant chemotherapy. We aimed to identify the clinico-pathologic factors related to pCR in patients with HER2-positive breast cancer treated with neoadjuvant dual HER2-targeted therapy. **Methods** Two-hundred ninety-five patients with HER2-positive breast cancer who received neoadjuvant chemotherapy with docetaxel, carboplatin, trastuzumab, and pertuzumab (TCHP) were included in this retrospective analysis. We assessed the association between age, clinical T, N stage, pathologic factors such as histologic grade, hormone receptor (HR), tumor-infiltrating lymphocytes, the membranous expression of HER2 protein evaluated by immunohistochemistry (IHC) and pCR. The fluorescent in situ hybridization (FISH) was performed in a tumor with HER2 score of 2+. **Results** Of the 295 patients, 195 (66.1%) achieved pCR (ypT0/is and ypN0). Besides, 240 (81.4%) patients were HER2 score of 3+, and 55 (18.6%) patients were HER2 score of 2+. The pCR was frequently observed in patients with HER2 score of 3+ (64 of 176 [73.3%]) than in those with HER2 score of 2+ (19 of 55 [34.5%]), regardless of HR status. After adjusting other clinicopathologic factors, the high HER2 protein expression was only an independent factor for pCR (adjusted OR 3.85, 95% CI, 1.66-8.91, p=0.002). **Conclusions** Our results suggest that high expression of HER2 protein assessed by IHC is important in predicting neoadjuvant TCHP response in HER2-positive breast cancer.

Disclosure(s):

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7:00 AM - 8:15 AM

P4-06-09

A phase 1b study of neratinib with THP in metastatic and locally advanced breast cancer, and phase II study of THP followed by AC in HER2 + primary inflammatory breast cancer (IBC), and neratinib with taxol followed by AC in HR+ /HER2- IBC

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Background: The pathologic complete response (pCR) rate in inflammatory breast cancer (IBC) patients is worse than in non-IBC patients; new drug combinations are warranted to improve pCR rates across all IBC molecular subtypes. Based on our preclinical data, we added neratinib to standard neoadjuvant chemotherapy in both HER2+ (synergy) and HER2-/hormone receptor (HR)+ (high frequency of ERBB2 mut) untreated IBC, as a single-center, non-randomized phase I/II trial. Patients and Method: This study enrolled three cohorts: Cohort I phase Ib (C1P1B), Cohort I Phase II (C1P2) and Cohort II (C2). In C1P1B to determine the recommended phase 2 dose (RP2D), we enrolled patients with HER2+ metastatic or locally advanced breast cancer. Patients received paclitaxel/trastuzumab/pertuzumab (THP) + neratinib x 4 cycles (up to 8 cycles per physician's discretion). For C1P2 and C2, we enrolled Stage III – IV primary IBC patients. In C1P2, patients with HER2+ IBC received neratinib (RP2D) combined with THP x 4 cycles followed by doxorubicin/cyclophosphamide (AC) x 4 cycles. Per stage I design, 11 patients were enrolled with plan to enroll 20 more patients in Stage II if at least 6 had a pCR. In C2, patients with HER2-/HR+ IBC received neratinib 200 mg/day combined with paclitaxel x 4 cycles followed by AC x 4 cycles. Stage I design planned for enrollment of 16 patients with enrollment of 15 more patients on stage II, if at least 2 Stage I patients had pCR. In all three cohorts, patients initiated prophylactic anti-diarrheal medication (loperamide & budesonide) with the first dose of neratinib. Results: From 2018 to 2022, thirty-

four patients were enrolled and treated (n=4 C1P1B, n=14 C1P2, n=16 C2). In C1P1B, observed DLTs (dose limiting toxicities) were Grade (Gr) 2 Diarrhea, n=2 (50%); Gr3 diarrhea, n=2 (50%); 2 patients had a serious adverse event (SAE); 3 patients (55%) had Gr2 nausea. The RP2D was established at 80 mg/day (dose level 0). For patients in C1P2, the most frequently occurring adverse events (AEs) included Gr2 Alopecia, n=14 (100%); Gr2&3 Diarrhea, n=14 (100%); Gr2/3 Nausea, n=12 (86%); Gr2/3 Anemia, n=7 (50%); Gr2/3 Fatigue, n=8 (57%); Gr2/3 Hypokalemia, n=6 (57%); and Gr2/3 Neutrophil count decreased, n= 7 (50%). 6 patients had an SAE. Of the first 11 patients, 5 (46%) had pCR, 1 (9%) RCB-1, 1 (9%) RCB-II and 1 (9%) RCB-III. Three patients stopped study treatment for toxicity (27%), were non-evaluable and replaced. Of these, one had RCB-III (33.3%), one progression of disease (PD) (33.3%), and one came off study for toxicity (33.3%). Rather than replacing additional non-evaluable patients, the study was closed to new patient accrual. In C2, the most frequently occurring AEs were Gr2 diarrhea, n=7(44%); Gr3 diarrhea, n=8 (50%); Gr2 alopecia, n=14 (88%); Gr2/3 Anemia, n=10 (63%); Gr2/3 Nausea, n=7 (44%); Gr2/3 Neutropenia, n= 7 (44%). 3 patients had an SAE. Of 16 patients in this cohort, 1 had pCR (6%), 5 RCB-II (31%), 4 RCB-III (25%), 3 came off study for toxicity (19%) and 3 had PD (19%). C2 also closed to new patient accrual given the high toxicity profile. Conclusion: The addition of neratinib did not improve the pCR rate in HER2+ or HER2-/HR+ subtypes of IBC, and increased toxicities were observed. The trial closed to new patient entry March 2022. However, some patients achieved significant response. Biomarker analysis is ongoing. Evaluable participants will continue long-term follow-up per protocol. Acknowledgments: This study is supported by PUMA Biotechnology.

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P4-06-10

Is Anthracycline Chemotherapy Essential in the Treatment of Women with Breast Cancer? – A Real World Comparison in the Neoadjuvant Setting

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Background: Breast cancer is the second most commonly diagnosed cancer in North American women. The administration of neoadjuvant chemotherapy (NAC) is the mainstay of treatment

for individuals with high risk disease in an effort to reduce the extent of surgery, evaluate the role of additional adjuvant therapies (based on pathologic response to NAC), and improve disease-free and overall survival (OS). Anthracyclines have been shown to increase response rates leading to a greater likelihood of pathologic complete response compared to non-anthracycline regimens. However, for some individuals anthracyclines are omitted from the NAC regimen due to toxicities including greater immunosuppression, cardiac toxicity and risk of acute leukemia. We established a population-based cohort of individuals treated with NAC for breast cancer. We report the outcomes of women selected for treatment with non-anthracycline NAC compared to those treated with anthracyclines. Methods: This is a retrospective population-based cohort study using linked health administrative data held at the Institute for Clinical Evaluative Sciences (ICES) in Ontario, Canada. We identified adult women diagnosed with stage I-III breast cancer (ICD-10 C50^A) between 2012 and 2020 who received NAC. Administration of at least 50% of the planned chemotherapy regimen was required. We excluded patients with bilateral breast cancer, previous malignancy and male sex. NAC regimens were classified as anthracycline and non-anthracycline-containing regimens. To address confounding between those receiving anthracycline and other regimens, we built a propensity score model including patient and disease characteristics. The association with OS was calculated using Cox proportional hazards models, and breast cancer-specific survival (BCSS) was calculated using cause-specific Cox proportional hazards models. Models were adjusted for the propensity score, radiation treatment as a time-varying covariate, age, socioeconomic status, breast cancer stage and receptor sub-type, as well as Charlson comorbidity index. Results: A total of 4,180 women were identified with a median follow up of 62 months (IQR 44 – 85). Of these, 279 (6.7%) were treated with non-anthracycline regimens compared to 3,901 treated with anthracycline. Patients who received non-anthracyclines were older (median 62 years vs. 50 years; $p < 0.001$), and less likely to have stage III disease (33.0% vs. 48.7%; $p < 0.001$), and harbor triple-negative breast cancer (TNBC) (14.0% vs. 24.4%; $p < 0.001$). They were more likely to have no recorded comorbidities (89.2% vs. 96.5%; $p < 0.001$), undergo mastectomy (82.1% vs. 71.9%; $p < 0.001$), and sentinel lymph node biopsy (44.4% vs. 32.3%; $p < 0.001$). After propensity score and multivariable adjustment, women selected for treatment with non-anthracycline regimens had similar OS (HR 0.85, 95% CI 0.60-1.21) and BCSS (cause-specific HR 0.76, 95% CI 0.46-1.25) compared to those treated with anthracyclines. When stratified by stage, women treated with non-anthracycline regimens did not have significantly higher incidences of breast cancer death or death from any cause (stages I, II, and III Gray's Test p -value all > 0.1). The mean OS was 7.2 years for women who received non-anthracycline regimens (95% CI 7.0 – 7.4) compared to 7.9 years for those who received anthracycline (95% CI 7.9 – 8.0) (log-rank $p = 0.100$). Conclusions: Women with stage I-III breast cancer treated with non-anthracycline NAC regimens are a highly selected population. These patients were older and healthier, with earlier stage disease and more favorable subtype (i.e. non-TNBC) when compared to those treated with anthracycline NAC. Our results demonstrate that women were well selected to omit anthracyclines and did not have worse survival outcomes. Further research is needed to better understand in whom anthracycline can be safely omitted.

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7:00 AM - 8:15 AM

P4-06-11

Pathologic Complete Response in Triple Negative Breast Cancer of Black vs White Patients in the Post-Keynote 522 Era

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Pathologic Complete Response in Triple Negative Breast Cancer of Black vs White Patients in the Post-Keynote 522 Era Melanie Sheen MD, Victoria Chung DO, Ruby Maini MD, Michael Duggan BS, Julia Levy BS Background Triple-negative breast cancer (TNBC) is an aggressive form of breast cancer that lacks estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER-2) gene amplification. Women with TNBC have worse survival outcomes and increased rates of relapse and distant metastasis as compared to women with non-TNBC. Treatment of TNBC has recently been focused on neoadjuvant chemotherapy (NACT) with a goal of achieving a pathologic complete response (pCR) which is associated with longer event-free survival and overall survival. The KEYNOTE-522 trial was presented at the San Antonio Breast Cancer Symposium in December 2019 and found that patients who received pembrolizumab, an anti-programmed death 1 (PD-1) monoclonal antibody, plus NACT were more likely to achieve pCR than women who received placebo plus NACT. On July 26, 2021, the FDA approved the use of pembrolizumab in combination with NACT for high risk, early stage TNBC. KEYNOTE-522 did not collect race as a baseline demographic characteristic, and since TNBC disproportionately affects younger women and Black women, confirming the efficacy of achieving pCR in these groups is essential. Further investigation of the factors that may contribute to achieving pCR in women treated with pembrolizumab for TNBC is warranted. We set out to perform a retrospective analysis examining the rates of pCR in Black versus White patients with TNBC since the initial revelation of the KEYNOTE-522 data. Methods This retrospective chart review of a regional health care network included patients who had been diagnosed with Stage II/III TNBC, documented race as Black/African-American or White, and received treatment with pembrolizumab in the NACT setting. Exclusion criteria included ER-positivity, PR-positivity, HER2-positivity, or unknown receptor status, no pembrolizumab in the neoadjuvant setting, absence of documented race, and age < 18 years-old. Data was collected using Epic

SlicerDicer program. Results 118 patients met inclusion criteria. 59 (50.0%) were Black/African American, 59 (50.0%) were white. There were 57 (48.3%) patients who had pCR status identified through pathology reports while the remaining 61 (51.7%) are still undergoing NACT awaiting surgery. 34 Black women and 17 white women have not had surgery yet. Of women who underwent surgery, 12 Black women achieved pCR compared to 15 White women. 13 Black women and 16 White women did not have pCR Discussion Analysis of the data demonstrates an equal number of Black and White women receiving NACT with pembrolizumab. Of those women, there was relatively equal number of pCR between Black and White women. This data shows no appreciable difference in outcomes of Black and White women in terms of response to therapy. Conclusion Given the known association of pCR with increased survival, pembrolizumab should be considered in the treatment regimen for both Black and White women with stage II/III TNBC. This retrospective study is limited by a small patient population. Continued data collection is underway and will be updated.

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P4-06-12

Decision of Neoadjuvant Therapy in Younger vs. Older Breast Cancer Patients: A Real-World Data Analysis

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Background: The incidence of breast cancer among younger patients (age ≤ 40) is higher in Latin America than in other regions. The multidisciplinary approach of breast cancer cases has been related with better survival, and the knowledge about specific clinicopathological features of this population is needed to optimize the therapeutic approach. The aim of our study was to describe the clinicopathological characteristics of breast cancer in younger (Y) compared with older patients (O), and to determine which characteristics were associated with the use of primary systemic therapy.

Methods: A retrospective cohort study was designed. Clinicopathological data of consecutive invasive non-metastatic breast cancer patients diagnosed between Jan 2015 to Dec 2019 in two private oncological centers in Lima, Perú were collected. Logistic regression analysis was performed to obtain models to predict primary systemic therapy as first treatment.

Results: We included 503 cases (mean age 49.8 years [SD 11.8]), 30.6% younger (n = 109) and 69.4% O (n = 394). No significant differences were found for ductal histology (89% Y vs. 87.7% O, p = 0.49) and HER2-overexpression (28.4% Y vs. 23.9% O, p = 0.39). Significant differences were found for stage III (37.6% Y vs. 20% O, p < 0.01), grade 3 (44.4% Y vs 33% O, p = 0.04) and HR-positive (64.2% Y vs. 75.1% O, p = 0.03). Univariate analysis showed significant OR = 2.1 to receive primary systemic therapy for Y (95%CI 1.37 – 3.24; p < 0.01), however, multivariate analysis adjusted for age, hormone receptors (HR), HER2, grade and stage showed non-significant OR = 1.5 to receive primary systemic therapy for Y (95%CI 0.90 – 2.50; p = 0.12) as detailed in the table below:

Conclusions: In our series we found a greater proportion of young breast cancer patients than previously reported. Clinical-pathological characteristics of breast cancer were different between younger and older patients, showing more aggressive phenotypes for younger patients with greater proportion of stage III, grade 3 and non-expression of hormone receptors.

Decision of using primary systemic therapy in our series was based on anatomic and biologic characteristics and not on age.

Univariate analysis (Primary Systemic Therapy)			
	OR	95%CI	p-value
Age ≤ 40	2.10	1.37 – 3.24	< 0.01
Multivariate analysis (Primary Systemic Therapy)			
	OR	95%CI	p-value
Age ≤ 40	1.50	0.90 – 2.50	0.12
HR-positive	0.41	0.25 – 0.68	< 0.01
HER2-positive	3.91	2.38 – 6.51	< 0.01
Grade 3	1.52	0.96 – 2.40	0.08
Stage III	7.05	4.24 – 12.04	< 0.01

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Neoadjuvant paclitaxel/olaparib in comparison to paclitaxel/carboplatinum in patients with HER2-negative breast cancer and homologous recombination deficiency – long-term survival of the GeparOLA study

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Background: The GeparOLA study was designed to evaluate the efficacy and safety of the combination of paclitaxel (P) plus olaparib (O) as part of neoadjuvant chemotherapy (NACT) in patients with human epidermal growth factor receptor 2 (HER2)-negative, either hormone receptor (HR)-positive or HR-negative and homologous recombination deficiency (HRD) defined as having a g/tBRCA mutation and/or a high HRD score. Primary analysis showed a pCR rate of 55.1% (90% CI 44.5%-65.3%) with PO and 48.6% (90% CI 34.3%-63.2%) with P plus carboplatinum (Cb). The PO combination could not exclude a pCR rate of $\leq 55\%$ in the PO arm but was significantly better tolerated. Analysis on the stratified subgroups showed higher pCR rates with PO in the cohorts of patients < 40 years and HR-positive tumors (Fasching Ann Oncol 2020). Here, we report long-term data. Methods: GeparOLA (NCT02789332) was a non-comparative, multicenter, prospective, randomized, open-label, phase II trial. Patients with primary HER2-negative breast cancer, HRD and indication for chemotherapy (cT2-cT4a-d or cT1c and cN+ or cT1c and pNSLN+ or cT1c and TNBC or cT1c and Ki-67 >20%) were randomly assigned to receive either P 80 mg/m² weekly plus O 100 mg twice daily for 12 weeks or P plus Cb area under the curve 2 (AUC2) weekly for 12 weeks, both followed by four cycles of either 2-weekly or 3-weekly epirubicin 90 mg/m² plus cyclophosphamide 600 mg/m². Primary endpoint was pCR (ypT0/is ypN0) rate after NACT with PO followed by EC. Long-term efficacy endpoints included invasive disease-free survival (iDFS), distant disease-free survival (DDFS) and overall survival (OS). The time-to-event endpoints analysis is planned with median follow-up of at least 4 years and a follow-up completeness of at least 80%. Results: Between

September 2016 and July 2018, 274 patients were screened, of whom 107 were randomized and 106 (PO N=69; PCb N=37) started treatment. The median age was 47.0 years (range 25.0-71.0); 32 patients were aged < 40 years; 36.2% of patients had cT1 tumors and 31.8% were cN-positive; the majority (86.8%) had grade 3 tumors and a Ki-67>20% (89.6%). Seventy-seven patients (72.6%) had TNBC. After a median follow-up of 49.8 months (range 0.1-69.1), 18 (15 in PO; 3 in PCb) iDFS events and 7 (6 in PO; 1 in PCb) deaths were reported. The 4-year survival rates are shown in the table below. iDFS (HR PO to PCb=2.86 [95%CI 0.83-9.9], log-rank p=0.081), DDFS (HR =3.03 [95%CI 0.67-13.67], log-rank p=0.129), and OS (HR=3.27 [95%CI 0.39-27.2], log-rank p=0.244) tended to be inferior with olaparib. Patients without g/tBRCA mutation seem to benefit from the use of carboplatinum (7/30 iDFS/DDFS events in PO; 0/16 in PCb, log-rank p=0.037, HR n.a.). Conclusions: In patients with HER2-negative and HRD breast cancer the use of olaparib instead of carboplatinum although showing comparable pCR rates, tended to result in an overall inferior outcome. This was mainly driven by the patients without a g/tBRCA mutation. In patients with a g/t BRCA mutation no difference between olaparib and carboplatinum was seen. Key words: Olaparib, HER2-negative breast cancer, HRD, survival Funding: The study was financially supported by AstraZeneca

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-07-01

Overall survival with locoregional surgery in de novo metastatic breast cancer

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Background: Breast cancer remains the most frequent type of cancer in women, with de novo metastatic breast cancer (dnMBC) accounting for approximately 6-10% of patients. Advances in treatment of dnMBC have led to an increase in overall survival (OS), but the role of locoregional surgery remains unclear. Aim: To determine the value of locoregional surgery compared with no surgery on OS of women with dnMBC Settings and design: This study was designed as a randomized clinical study and was approved by the Ethics Committee of the Ethics Committee of Cangzhou Clinical College of Integrated Traditional Chinese and Western Medicine of Hebei Medical University (NO.20200212). Methods: Patient characteristics were previously reported in ASCO2022. Eighty-six patients with dnMBC were randomised to surgery of the primary tumor followed by systemic therapy (surgery group) or to primary systemic therapy without surgery (non-surgery group), by a computer generated block randomisation sequence. Randomisation was stratified by site of distant metastases, number of metastatic lesions, and molecular subtypes. Follow-up visits were conducted during treatment, monthly in first year, every 3 months thereafter. The primary endpoint was overall survival analysed by intention to treat. The stratified log-rank test and Cox proportional hazards model were used to compare OS between groups. The level for significance was set at $p < 0.05$. All analyses were performed with STATA 17. Results: Between Jan 3, 2019, and Mar 29, 2021, of the 103 women presenting with dnMBC, we randomly assigned 86 patients: 44 to surgery of the primary tumor followed by systemic therapy and 42 to primary systemic therapy without surgery. At data cut-off of Dec 1, 2021, median follow-up was 27 months with 44 deaths (surgery group $n=21$, non-surgery group $n=23$). The 2-year OS was 45.2% without and 52.3% with locoregional surgery (hazard ratio=0.59; 95% CI, 0.32 to 1.12; $p = 0.11$). The median OS was 25.5 months (95% CI, 23.52 to 29.38) in non-surgery group and 33 months (95% CI, 27.43 to 34.53) in surgery group. Conclusions: Our prospective randomized trial showed that compared with non-surgery counterparts, locoregional surgery does not improve OS of patients with dnMBC. Large, well-designed studies involving a large number of cases, multi-institution trials and longer follow-up are needed to verify the finding.

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7:00 AM - 8:15 AM

P4-07-02

Toxicity profile of single agent trastuzumab deruxtecan in solid tumors: A meta-analysis

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Background: Trastuzumab deruxtecan (T-DXd) has been evaluated in numerous solid tumors and has been approved for metastatic HER2-positive breast and gastric/gastroesophageal cancers. We aimed to provide a precise estimate of toxicity of T-DXd observed in clinical trials. Methods: A systematic literature search was performed in PubMed and supplemented by review of abstracts from ASCO and ESMO. Eligible studies were clinical trials (dose-expansion phase 1, phase 2, and phase 3) investigating single agent T-DXd. The search was performed in June 2022. For single-arm trials, meta-analysis comprised one-sample proportions to obtain the random effects estimates of toxicity and respective 95% confidence intervals (CI) for T-DXd, while for randomized trials, the Mantel-Haenszel odds ratio method was utilized. Results: Fifteen trials comprising 1566 participants were evaluable for toxicity. ECOG Performance Status (PS) was reported in 11 studies and was ≥ 2 in only a single patient. The median age at enrollment was reported for 13 studies and was 57.5 years. Seven trials comprising 1023 (65.3%) participants evaluated T-DXd for breast cancer. From available data, 1209/1440 (84%) of participants were female and 735/1551 (47%) were from East Asia. The median follow-up time was 11.1 months (13 studies) and median previous lines of treatment were 3 (12 studies). All-grade toxicity rate of $\geq 10\%$ was reported for most toxicities; however, grade ≥ 3 toxicity rate of $\geq 10\%$ was reported only for neutropenia and anemia; 17.4% (95%CI 12-22.8) and 14.8% (95%CI 8.6-21), respectively (Table 1). Interstitial lung disease / pneumonitis (ILD) was reported in 203 (12.4%) patients, including 160 (9.41%) grade 1-2, and 23 (1.1%) grade 3-4. Treatment-related death was reported in 20 (1%) patients, and all were due to grade 5 ILD. No significant difference in ILD was identified in subgroup analysis of trials conducted in east

Asia vs. the rest of the world, breast vs. other solid tumors, 5.4mg/kg vs. other doses, median follow-up < 12 months vs. ≥12 months or median previous lines ≥3 vs. < 3. In the three randomized clinical trials, grade ≥3 toxicity was significantly higher for nausea (OR: 9.32, 95%CI: 2.53-34.32), ILD (OR: 5.35, 95%CI: 0.97, 29.48), fatigue (OR:2.5, 95%CI: 1.11-5.66), and anemia (OR:1.77 95%CI: 1.14-2.74). Conclusions: T-DXd was associated with infrequent grade ≥3 toxicities across clinical trials. Grade 1-2 ILD was more common; however, grade 3-4 ILD occurred in 1.1%. This may be related to active monitoring of this toxicity in clinical trials and discontinuation of treatment in participants with G2 ILD. There is lack of evidence for the safety of T-DXd in patients with ECOG PS ≥ 2.

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12/8/2022

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P4-07-03

The impact of HIV on non-adherence for tamoxifen among women with breast cancer in South Africa

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Abstract Introduction HIV-positive women with breast cancer (BC) have worse overall survival than HIV-negative women with BC, and poor adherence to prescribed tamoxifen is known to contribute to poor survival. We, therefore, investigated the association of HIV infection with adherence to adjuvant tamoxifen among women with localized hormone receptor (HR)-positive breast cancer in South Africa. Methods Among 4,097 women diagnosed with breast cancer at six hospitals in the prospective South African Breast Cancer and HIV Outcomes (SABCHO) cohort study between July 2015 and December 2020, we focused on women with stages I-III HR-positive breast cancer who were prescribed 20mg of adjuvant tamoxifen daily for ≥ 3 months during the study period. We collected venous blood once from each participant during a routine clinic visit and analyzed concentrations of tamoxifen and its metabolites using a triple quadruple mass spectrometer. We defined non-adherence as a tamoxifen level $< 60\text{ng/mL}$ after 3 months of prescribed daily tamoxifen use. We compared socio-demographic, lifestyle factors, tamoxifen-related side effects, and concurrent medication use among women with and without HIV and developed multivariable logistic regression models of tamoxifen non-adherence. Results Among 369 participants, 78 (21.1%) were HIV-positive and 291 (78.9%) HIV-negative. After a median (interquartile range) time of 13.0 (6.2-25.2) months since tamoxifen initiation, the tamoxifen serum concentration ranged between 1.54 and 943.0ng/mL, with a median of 52.3ng/mL. In the full cohort, 208 women (56.4%) were non-adherent to tamoxifen; only 161 (43.6%) were adherent. Women < 40 years of age were less likely to adhere to tamoxifen than women > 60 years (73.4% vs 52.6%, odds ratio (OR)=2.49, 95% confidence interval (CI)=1.26-4.94); likewise, HIV-positive women (70.5% vs 52.6%, OR=2.16, 95% CI=1.26-3.70) were less

likely to adhere than HIV-negative women. In an adjusted model, only HIV was associated with non-adherence; HIV-positive women had twice the odds of non-adherence to tamoxifen, compared to HIV-negative women (OR=2.40, 95% CI=1.11-5.20). Conclusion Non-adherence to tamoxifen may limit the overall survival of women with HR-positive breast cancer; in our study, especially in HIV-positive women.

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7:00 AM - 8:15 AM

P4-07-04

STX-478, a mutant-selective PI3K α H1047X inhibitor clinical candidate with a best-in-class profile: Pharmacology and therapeutic activity as monotherapy and in combination in breast cancer xenograft models

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PI3K α is highly mutated in cancer resulting in hyperactivation of lipid kinase activity and downstream AKT signaling. H1047 is the most common site of oncogenic mutation and occurs in ~14% of all breast cancers. Initial therapeutic benefit of targeting PI3K α was established with alpelisib, an alpha-selective PI3K inhibitor that is equipotent against wild-type and mutant forms. However, wild-type PI3K α inhibition results in frequent dose-limiting toxicities including hyperglycemia, restricting the full potential of this drug. Selective targeting of H1047X-mutant PI3K α is expected to both improve anti-tumor activity and reduce toxicity. STX-478 is an allosteric, CNS-penetrant, selective PI3K α H1047X inhibitor, having excellent drug-like properties and exceptional kinome selectivity. STX-478 demonstrated minimal inhibition of CYP enzymes in vitro, supporting the potential for combinations with a wide range of therapeutics in breast cancer and a variety of other tumor types. STX-478 selectivity extended to the inhibition of other activating kinase domain mutations in biochemical assays. In a diverse panel of PI3K α H1047X mutant cell lines, STX-478 selectively reduced the cellular levels of pAKT (S473) with a strong correlation between pAKT inhibition and cell viability (R = 0.8). In a high-throughput viability screen of 467 cancer cell lines, the presence of PIK3CA H1047X and other kinase domain mutations were the single strongest predictor of STX-478 sensitivity with potency superior to alpelisib. STX-478 also selectively inhibited the proliferation of cell lines with PI3K α helical domain mutations, potentially due to the selective dependency of these cells on mutant PI3K α . When combined with fulvestrant, lapatinib, or abemaciclib, STX-478 demonstrated synergistic anti-proliferative activity in cell lines with relevant ER/HER2 status. Unlike alpelisib, STX-478 did not impair glucose metabolism or cause insulin resistance at efficacious doses. In the T47D (PI3K α H1047R) breast cancer model, STX-478 (100 mg/kg) monotherapy caused tumor regression whereas alpelisib caused only stasis. STX-478 combination with fulvestrant was well-tolerated, with more consistent and deeper tumor regression. Similar results were observed in a PI3K α H1047R mutant ER+/HER2- PDX model, where fulvestrant monotherapy showed minimal activity, while combination with STX-478 yielded tumor regressions. In an ER+/HER2+ PDX model (PI3K α H1047R/R108H), palbociclib and STX-478 (100 mg/kg) monotherapy resulted in similar efficacy while the combination was well tolerated and yielded tumor regression. Together these data indicate robust STX-478 monotherapy activity that was well tolerated and improved when dosed in combination with fulvestrant or CDK4/6 inhibitors. Finally, we investigated the effect of STX-478 treatment in an ER+ PDX model carrying a helical domain mutation. STX-478 treatment resulted in tumor growth inhibition at doses that did not result in metabolic dysfunction, suggesting that STX-478 may also be efficacious in treating PIK3CA mutant tumors with helical domain mutations. In summary, STX-478 efficacy was superior to alpelisib at a dose level that exceeds the clinically relevant exposure in mice without causing metabolic dysfunction. STX-478 has a predicted low human dose, CNS exposure, low risk of DDI, and a predicted long half-life with minimal variation in peak-to-trough plasma concentrations which further supports a favorable therapeutic index. STX-478 has the potential to provide a best-in-class profile to improve outcomes in patients harboring tumors with prevalent PI3K α H1047X mutations as well as other kinase and helical domain mutant tumors. The significant CNS exposure of STX-478 is expected to enable this treatment for patients with brain tumors and brain metastases not afforded by existing options. STX-478 is currently in IND enabling studies and is expected to enter human clinical trials in 2023.

Disclosure(s):

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P4-07-05

Real world data of adjuvant endocrine therapy for breast cancer in very young women. A Chilean 20-year experience

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BACKGROUND: Breast cancer (BC) is the most common cancer diagnosed in premenopausal women with an increasing incidence for age 35 or less. Although proportionally less frequent, hormone receptor (HR)-positive BC still remains the main subtype for this group, but given tumor characteristics and suboptimal adjuvant endocrine therapy (ET), present inferior long-term outcomes when compared to HR-positive BC in older women. Both Tamoxifen and Exemestane Trial (TEXT) and Suppression of Ovarian Function Trial (SOFT) have helped to optimize ET strategies for premenopausal women, identifying which patients benefit from ovarian function suppression (OFS). In Chile, we have scarce data on very young BC patients and limited access to proper OFS treatment specially in our public health system. Thus we aim to characterize a cohort of very young women regarding treatment strategies and survival, plus as an exploratory analysis evaluate Regan Score in our cohort.

METHODS We conducted a retrospective population-cohort study involving women under 36 years of age, with early HR-positive/human epidermal growth factor receptor 2 (HER2)-negative BC, treated both at a community hospital and at an academic private hospital between 2001 and 2021. We did a descriptive analysis including stage distribution and treatment strategies (chemotherapy (CT), ET of choice and OFS use). We evaluated prognosis for the entire population. Survival analysis was carried out using the Kaplan-Meier method.

RESULTS A total of 143 patients were included. Median age at diagnosis was 33 (19 - 36); 15.4% percent of patients were diagnosed in stage I, 51.4% stage II and 30.1% stage III. Eighty six percent received CT, 35.0% neoadjuvant. Ninety three percent received endocrine adjuvant treatment: 81.2% TAM alone, 6.8% TAM/OFS and 10.5% IA/OFS. Regarding OFS strategies only 38.5% received gonadotropin-releasing hormone (GnRH) agonists while the rest were oophorectomized. Regan median composite score was 2.77 (2.61 - 2.93) for the entire cohort. Rising to 2.95 (2.79 - 3.11) for patients treated with CT plus ET compared to 1.91 (1.55 - 2.27) for those treated with ET exclusively (p=0.0001). Patients that received TAM alone had a median Regan Score of 2.72 (0.77-4) compared to 3.14 (2.07-4.0) for patients that had OFS added (p=0.04).

With a median follow-up of 59 months, 5-year Disease Free Survival (DFS), Distant DFS and Overall Survival (OS) for the entire cohort were 63.5%, 66.9% and 88.7%, respectively.

CONCLUSION. To our knowledge this is one of the largest cohorts considering very young women BC in Latinamerica. We confirm their elevated overall risk with markedly higher Regan scores compared to SOFT and TEXT populations for both CT and ET exclusively treated patients. Due to access difficulties very few patients received OFS and when used, surgical oophorectomy was the main strategy of choice, with all the potential long term consequences it conveys. Thus OFS use was restricted to very high risk women, meaning that a large group of only TAM users were undertreated according to nowadays standards. This could explain the elevated recurrence risk observed in our population when compared to other under 35 years of age cohorts.

TABLE 1. Cohort characteristics

Table 1.

	n	%
Total of patients	143	100
Age - Median (range)	33	(19-35)
TNM		
I	22	15,4
II	72	50,3
III	43	30,1
Unknown	6	4,2
Chemotherapy	119	83,2
Neoadjuvant	42	35,3
Adjuvant	74	62,2
Adjuvant Endocrine Treatment (AET)	133	93,0
TAM	108	81,2
TAM+OFS	9	6,8
AI+OFS	14	10,5
OFS	1	0,8
Unknown	1	0,8
Ovarian Function Supression (OFS)	26	18,2
Oophorectomy	16	61,5
GnRH analogs	10	38,5

TABLE 2. Regan risk score

Table 2.

Composite Risk Assessment of the Cohort (Regan Score)		
Total patients of the cohort	143	
Patients with information to calculate (%)	82 (57.3%)	
Median Regan Score (CI 95%)	2.77	(2.61 - 2.93)
Risk according to Regan Score	Median RS	CI 95%
High Risk	3.44	3.34 - 3.56
Intermediate Risk	2.34	2.21 - 2.47
Low Risk	1.11	0.35 - 1.86
Median Regan Score according to treatment	Median RS	CI 95%
Neo/adjuvant CT + ET	2.95	2.79 - 3.11
ET exclusively	1.91	1.55 - 2.27
TAM alone	2.72	0.77 - 4.0
TAM + OFS	3.14	2.07 - 4.0
Survival data of the entire cohort	5-years (%)	
Disease Free Survival	63.5	
Distance Disease Free Survival	66.9	
Overall Survival	88.7	

CT: chemotherapy; ET: endocrine therapy; TAM: tamoxifen; OFS: ovarian function suppression; RS: Regan Score.

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P4-07-06

Implementation of A Bone Modifying Agent Pathway at UChicago Medicine for Metastatic Breast Cancer Patients

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Background: In 2019, a quality improvement (QI) research project was conducted at UChicago Medicine (UCM) to evaluate bone modifying agent (BMA) use for skeletal-related event (SRE) prevention in patients with metastatic breast cancer and metastatic castration-resistant prostate cancer. Denosumab was the preferred BMA agent at UCM in this setting. Compared to zoledronic acid (ZA), denosumab was associated with higher drug cost and lower adherence rate mainly due to the difficulty of maintaining the 4-weekly frequency. Studies have shown that ZA can be de-escalated from 4-weekly to 12-weekly for SRE prevention. There is still no convincing evidence to show that this de-escalated schedule can be applied to denosumab. One study evaluated the noninferiority of 12-weekly compared with 4-weekly denosumab suggested that the health-related quality of life was non-inferior (Clemons et al., 2021). However, the study was not powered to evaluate the statistical difference in SRE rates. Based on the results of the 2019 QI project, a BMA pathway was generated at UCM in September 2020 with the purpose of guiding physician prescribing patterns, improving adherence rate, and reducing drug costs. This pathway recommended using ZA as the preferred agent for SRE prevention instead of denosumab. Methods: This was a retrospective study that included 198 patients who had metastatic breast cancer and received at least one dose of ZA or denosumab from UCM outpatient oncology clinic for SRE prevention. All included patients must have bone metastases. 107 patients from the pre-implementation study period (July 1st, 2018 to June 30th, 2019) and 91 patients from the post-implementation study period (November 10th, 2020 to November 10th, 2021) were included. Patients were divided into four groups based on study time (pre- or post-implementation period) and BMA agent (ZA and denosumab). The primary outcome was BMA therapy adherence rate, which was defined by those who received greater than or equal to 80% of appropriately scheduled doses. Secondary outcomes included the percentage of patients on ZA or denosumab, SREs, BMA-associated adverse effects, and BMA cost. Descriptive statistics were used SREs and BMA-associated adverse effects. Results: The percentage of patients on ZA significantly increased from 12% to 64% after BMA pathway implementation ($P < 0.0001$). Denosumab use decreased from 88% to 36% ($P < 0.0001$). The overall BMA adherence rate including both ZA and denosumab patients during the post-implementation period was 68%, which was not significantly different compared to the overall adherence rate of 74% during the pre-implementation period ($P = 0.5461$). The adherence rates in denosumab groups (63% in pre and 30% in post) were lower than in ZA groups (100% in pre

and 90% in post). The most common reason for the lower adherence rates in denosumab groups was scheduling convenience. During the study period, there were 2, 0, 3, and 3 patients who had SREs in the above four groups respectively. The predominant adverse events among all groups were hypocalcemia and hypophosphatemia. The cost analysis showed using ZA as the primary BMA agent saved 1.1 million dollars of drug costs during the post-implementation study period at UCM. Conclusion: Implementing a BMA pathway encouraged the providers to choose ZA as the preferred agent for SRE prevention in metastatic breast cancer patients with bone metastasis, which dramatically reduced drug costs. The overall BMA adherence rate was not significantly improved with the implementation. The difficulty of maintaining a 4-weekly denosumab frequency continued to exist.

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7:00 AM - 8:15 AM

P4-07-07

Impact on overall survival according to sites of metastasis: Real-world data

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Background Metastatic breast cancer, has a heterogeneous presentation and management, therefore its overall survival ranges from 2 to 3 years. Despite advances in breast cancer screening, diagnosis, and treatment, nearly 12-30% of early stage breast cancer patients

eventually develop metastatic disease. In Ecuador, breast cancer is the most common malignancy among women, and the leading cause of newly diagnose cancer in the general population (Globocan 2020). This study aims to determine the frequency of metastatic sites and its impact in overall survival. Methods: An observational, retrospective, descriptive, single-center study was carried out. All patients with Metastatic breast cancer who had been treated at the National Oncology Institute SOLCA Guayaquil, in the period from 2016 to 2020 were included in the analysis. All statistical analyses were performed using SPSS for Windows (version 25.0;SPSS). The Kolmogorov-Smirnov test was used to test for the normality of distribution. Correlations were determined with Spearman correlation coefficients. The number of metastatic sites were recorded and their impact on overall survival was calculated by the Kaplan-Meier method and compared by the long-rank test, multivariable adjusted hazard ratios (HR) were estimated by Cox regression models. Results: A total of 1113 patients were included in the analysis, of which 84 patients (7.5%) were metastatic disease. The distribution of metastatic sites at diagnosis were: bone 64% (n=53), lung 51% (n=42), liver 30% (n=25), soft tissues 23% (n=19) , and the least frequent were metastases to the central nervous system 17% (n=14), mediastinal lymph node 5% (n=4), peritoneal lymph node 1% (n=1). Regarding metastatic sites, 41% (N: 35) had only 1 metastatic site, 33,7% (N: 28) had 2 metastatic sites, and 25.3% (N:21) has 3 or more sites. A multivariable analysis was performed which takes into account all the metastases in the analysis. All have a higher risk of mortality vs not having any metastasis (all are greater than 1). But the only significant one is CNS with a RR 1,31 (1,08 - 1,61) P=0,005. Three or more sites of metastasis have RR 1,22 (0.95-1.57) p: 0.11. Relative Risk (RR) according to the different sites of metastasis are shown in the table#1. The association between 3 or more sites of metastasis showed a negative impact on overall survival (15 months +/-2.3 SD vs 36 months +/- 3.7 SD) compared to 1 site of metastasis. Conclusions: Approximately half of the women (N:49) with metastatic breast cancer in our population presented 2 or more sites of metastasis, which significantly decreases overall survival. The central nervous system is the site of metastasis with the highest relative risk of mortality, generating functional deterioration, adding morbidity, and only 64% (9 out of 14) of the patients access to radiotherapy as palliative treatment. Thus, better strategies for early diagnosis and adequate treatment of metastatic disease should be developed.

Disclosure(s):

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P4-07-08

**IMPACT ON OVERALL SURVIVAL ACCORDING TO BREAST CANCER
IMMUNOPHENOTYPES: REAL-WORLD DATA IN METASTATIC BREAST CANCER IN
ECUADOR**

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Background: Breast cancer immunohistochemistry subtype classification by hormone receptor has become the standard practice for therapeutic decision making. The subtype is one of the crucial factors affecting breast cancer prognostic. Despite the progress in understanding of complex mechanisms in progression of breast cancer, the treatment is a global challenge health around the world, the 5-year survival rate is 26%. Currently in develop countries, in the metastatic stage, a gain in survival in the HR+ / HER2+ subtype has been evidenced, likely attributable to major advances in HER2-targeted treatment (1). However, although in developed countries there is access to targeted therapy, in the Ecuadorian health system, difficulties complicate patients access to health care and treatment. Methods: We conducted a retrospective study about survival data in breast cancer metastatic according immunohistochemistry subtype. We analyzed all primary invasive breast cancer cases in the period from 2016 to 2020 in an oncology institute of Ecuador, the final study sample consisted for 83 patients. The overall survival was calculated by the Kaplan-Meier method and compared by the long-rank test. Multivariable adjusted hazard ratios (HR) were estimated by Cox regression models. Results: There were 31 patients (37.1%) with a HR(+)/HER2(-) breast cancer subtype, 15 patients HR(+)/HER2(+), 5 patients HER2 (+), 18 patients HR(-)/HER2(-) and 14 patients without breast cancer subtype identified. Most patients were treated with different chemotherapy protocols; additional, in the group of women with HR(+)/HER2(+) subtype and HER2 (+) subtype only 15.87% were treated with HER2-targeted treatment, the vast majority in the last year. The best survival pattern was observed among women with HR(+)/HER2(-) breast cancer subtype with 35 months (IC 95% = 14,9 – 55), followed by HR(+)/HER2(+) with 27 months (IC 95% = 13,21 – 40,79), HER2 with 24 months (IC 95% = 4.4 – 32), and 14 months (IC 95% = 0 – 29.7) for HR(-)/HER2(-), however the difference wasn't significant ($p = 0.08$). Hazard ratio of HR(+)/HER2(-) breast cancer subtype for breast cancer specific mortality risk was 1.61 (IC 95% = 0.64 – 4.19 $p = 0.29$). Conclusions: Hormone receptor subtype wasn't s a significant independent prognostic factor in female metastatic breast cancer patients in a single center of Ecuador. However, there is a trend that subtype HR(+)/HER2(-) breast cancer subtype, has a better survival than the rest of the subtypes. These results differ from those of the rest of the world, probably access to target medicine and difficulties in access to health care system are the cause. Thus, better strategies for early access to adequate chemotherapy protocols should be developed

Disclosure(s):

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7:00 AM - 8:15 AM

P4-07-09

Identifying Drivers of First-Line HR+/HER2- Metastatic Breast Cancer Treatment Choices

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Background: Despite demonstrated clinical benefits of first line (1L) cyclin-dependent kinases 4/6 inhibitors (CDK4/6i) and their preferred status in the NCCN guidelines, many appropriate patients with hormone receptor positive (HR+)/human epidermal growth factor receptor 2 negative (HER2-) metastatic breast cancer (mBC) in the United States (US) may still receive chemotherapy or endocrine monotherapy. US oncologists may consider treatment expectations, patient clinical characteristics, and non-clinical factors (e.g., cost, anticipated adherence) when selecting 1L mBC treatment regimens. However, little is known about how prevalent these decision factors are among US oncologists. Comprehensively understanding the decision-making process in 1L treatment selection is a critical step towards ensuring equitable care for patients with HR+/HER2- mBC.

Objective: To describe self-reported clinical and non-clinical factors considered by US oncologists in selection of 1L treatment for HR+/HER2- mBC.

Methods: Data were collected through from an anonymous cross-sectional online survey from a convenience sample of US oncologists from August-October 2021. Eligible oncologists were board certified, in practice 2-30 years, ≥50% of time spent in direct patient care, and managed ≥5 1L patients with HR+/HER2- mBC in past 3 months. Respondents were sampled from a national research database of physicians sourced from multiple databases (e.g., American Medical Association Physician Masterfile). The survey captured self-reported demographic and

practice characteristics and reported importance of the following factors in selecting 1L treatment for patients with HR+/HER2-mBC: anticipated treatment efficacy and safety, patient demographics, and clinical and non-clinical characteristics. Study variables were summarized via descriptive statistics. Correlation analyses evaluated associations between patient demographics, clinical characteristics, treatment expectations, and non-clinical characteristics and oncologists' self-reported 1L prescribing rates of CDK4/6i, aromatase inhibitor (AI) monotherapy, and chemotherapy.

Results: 250 oncologists participated; 67% from community practice and the remainder from academic institutions (Table 1). Anticipated treatment efficacy and safety/tolerability were ranked as the most important factor considered by oncologists when selecting 1L treatments. 1L CDK4/6i prescribing was most strongly correlated with patient Medicare eligibility ($r, 0.54, p < 0.05$) and postmenopausal status ($r, 0.67, p < 0.05$). 1L chemotherapy prescribing was most strongly correlated with patient premenopausal status ($r, 0.42, p < 0.05$) and perimenopausal status ($r, 0.31, p < 0.05$), and physician consideration for patient symptom burden ($r, 0.31, p < 0.05$). 1L AI monotherapy prescribing was most strongly correlated with concerns with expected patient compliance to treatment ($r, 0.42, p < 0.05$) and patient cost/logistical challenges ($r, 0.41, p < 0.05$).

Conclusion: This study found a variety of patient, clinical, and non-clinical factors may underlie US oncologists' selection of 1L treatment for HR+/HER2- mBC. Anticipated efficacy and safety/tolerability were reported as the most important factors in 1L treatment decisions. Patient demographics, clinical characteristics, and considerations for cost and compliance challenges varied in association with 1L CDK4/6i, chemotherapy, and AI monotherapy prescribing patterns among US oncologists.

Table 1. Oncologist Demographic and Practice Characteristics

Table 1. Oncologist Demographic and Practice Characteristics			
		Total Sample (N=250)	
		%	n
Primary Specialty	Medical Oncology	45.2%	113
	Hematology Oncology	54.8%	137
Practice Setting	Academic	32.8%	82
	Community	67.2%	168
Region of Practice	Northeast	24.8%	62
	Midwest	17.6%	44
	South	37.6%	94
	West	20.0%	50
Gender	Male	71.6%	179
	Female	20.8%	52
	Other	0.4%	1
	Prefer not to answer	7.2%	18
Practice Location	Major metropolitan area	33.2%	83
	Urban area	30.4%	76
	Suburb of a large city	28.0%	70
	Small city	5.6%	14
	Rural or small town	2.8%	7
Has Onsite Multidisciplinary Breast Clinic		52.4%	131
Has Onsite Infusion Clinic		91.2%	228
		Mean (SD)	Median
Oncologist Age		48.69 (9.67)	47.00
% of Patients with Commercial Insurance		37.70 (16.88)	40.00
% of Patients with Medicare		34.41 (14.71)	33.50
% of Patients with Medicaid		14.06 (11.77)	10.00
% Patients with Health Insurance Marketplace/State Exchanges Insurance		8.80 (12.13)	5.00
% of Patients with Cash/Self-Pay		4.74 (7.17)	0.00
% of Patients with Other Insurance Type		0.32 (1.60)	0.00
Years in Practice		15.45 (6.74)	16.00
% of Time Spent in Direct Patient Care		91.72 (7.42)	90.00
# of Patients with BC Seen/Treated in Past 3 Months		107.05 (106.03)	80.00
# of Patients with HR+/HER2- BC Seen/Treated in Past 3 Months		54.88 (56.25)	40.00
# of Patients with HR+/HER2- BC Treated with 1L Therapy in Past 3 Months		35.69 (39.44)	20.00
Note. 1L: first line, BC: breast cancer, HER2-: human epidermal growth factor receptor 2 negative, HR+: hormone receptor positive, SD: standard deviation.			

Disclosure(s):

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7:00 AM - 8:15 AM

P4-07-10

Effect of acupuncture and exercise therapy on muscular strength, lymphedema and quality of life in breast cancer survivors: randomized clinical trial

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Introduction: The continuous advance in the early detection and treatment of breast cancer has significantly reduced mortality and, consequently, increased the number of survivors with treatment side effects that act on the quality of life, such as lymphedema, loss of upper limb strength, shoulder dysfunction, decreased functional capacity, flexibility, and joint mobility. Exercise therapy is a recognized practice for the rehabilitation of these disorders; however, acupuncture needs to be better evaluated to compare its equivalence with classical therapy. **Objective:** To compare three distinct rehabilitation treatments (exercise therapy, acupuncture and Stiper®) in women undergoing breast cancer surgery, assessing strength, lymphedema and quality of life. **Methods:** Seventy-nine women with pain above 3 on the visual analogue pain scale (VAS) and with more than 90 days of surgery were included. They were divided into three groups that received weekly treatment for 10 weeks: group I (G1) treated with standard, pre-defined exercise therapy, based on stretching of the cervical muscles, shoulder girdle and shoulder ROM exercises with a duration of 30 minutes, group II (G2) treated with 30 minutes of acupuncture using predefined points and group III (G3) treated with the same acupuncture points as group II, however, using the Stiper® (silicon oxide micronized quartz pellet) in place of needles. **Results:** Sixty-seven patients completed the treatment, being 26 from G1, 23 from G2 and 18 from G3. There was an improvement in upper limb muscle strength over time in all groups, except for abduction and internal rotation movements. During treatment, there was no increase in the number of patients with lymphedema and there was no statistical difference between the groups. Regarding the EORTC QLQ-C30 quality of life questionnaire, nine of the fifteen factors analyzed showed significant differences between sessions. The factors that did not have significant differences between the three groups were Social Function, Nausea and Vomiting, Dyspnea, Loss of Appetite, Constipation and Diarrhea. **Conclusion:** The rehabilitation of physical dysfunctions in women who survived breast cancer through exercise therapy, acupuncture and Stiper® in upper limb muscle strength, lymphedema and quality of life, proved

to be effective, without difference between groups, which leads to the conclusion that acupuncture didn't show superiority of results when compared with exercise therapy, thus being an effective approach for the rehabilitation of these women.

Disclosure(s):

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Disparities in the uptake of telemedicine and implications for clinical trial enrollment in breast cancer patients

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Purpose/Objectives: Since the COVID-19 pandemic, telemedicine has become an attractive alternative to office visits in routine radiation oncology practice. The purpose of this study was to identify factors associated with patient preference for an initial consult telemedicine visit and correlation with clinical trial enrollment. Materials/Methods: We evaluated breast cancer patients seen during the open enrollment of a prospective randomized controlled non inferiority trial evaluating radiation fibrosis with five versus three fractions from 07/13/2020 to 05/13/2021. Univariate and multivariate logistic regression models were used to identify factors associated with virtual vs in-person initial consultation and enrolled vs not enrolled patients. All statistical tests were two-sided and the null hypothesis was rejected for $p < 0.05$. Results: We identified 476 patient consultations with 259 office visits and 217 telemedicine visits. On multivariate analysis, increased age, unemployment, chemotherapy receipt and radiation at NYU were associated with decreased usage of telemedicine for consultation visit. Out of 217 patients who underwent a telemedicine initial consultation, 10% were eligible to enroll on the trial and of those eligible, 76% enrolled. Out of 259 patients who underwent office visit initial consultation, 14% were eligible to enroll on the trial and of those eligible, 53% enrolled. Among eligible patients, there was no statistically significant difference in clinical trial enrollment between telemedicine and office visits. There was no statistically significant difference in patient characteristics between enrolled vs not enrolled patients. Conclusion: Though patient and disease characteristics remained similar between patients undergoing telemedicine and office visits consultations, increased age, unemployment and receipt of chemotherapy were associated with lower usage of telemedicine. Those who underwent in person initial consultation were also more likely to subsequently receive their radiation at our clinic. Further studies are needed to better define underlying reasons for patient selection and impact on care and trial enrollment in order to ensure equal access and benefit from telemedicine, especially in already vulnerable patient populations.

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P4-07-12

Development of Triple-negative breast cancer (TNBC) syngeneic models and TROP2-directed antibody-drug conjugate (ADC) surrogate to model therapeutic combinations

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Background: Sacituzumab govitecan (SG, Trodelvy®) is a human trophoblast cell surface antigen 2 (TROP-2) directed antibody drug conjugate (ADC) coupled to an active form of irinotecan (SN-38) via our novel hydrolyzable linker (CL2A). SG is the only FDA-approved ADC treatment for TNBC patients in the second-line setting. TROP-2 is a transmembrane protein encoded by the tumor-associated calcium signal transducer 2 (TACSTD2) gene and highly expressed in TNBC, an aggressive type of cancer accounting for approximately 15% of all

breast cancers. TROP-2 overexpression is associated with poor survival and relapse, but its biological function in TNBC remains poorly understood. Hypothesis/rationale: To better understand TROP-2 and TROP-2-directed ADC biology, we developed and characterized TROP2^{high} vs TROP2^{low} TNBC syngeneic tumors and an SG surrogate directed to murine TROP-2. Experimental design: We established 2 syngeneic TNBC models with differential TROP-2 expression: 4T1 cells were flow sorted into high (>95%) vs low (< 7%) TROP-2 expressors and EMT6 cells were transduced with a murine TACSTD2-encoding lentivirus. Balb/c mice were subcutaneously implanted with 0.5 x 10⁶ TROP-2^{high}, TROP-2^{low}, or parental tumor cells (4T1 or EMT6). Tumor immunophenotyping and transcriptomic analyses were performed 15 and 24 days after implantation. An SG mouse surrogate was engineered to mimic SG, using an anti-TROP-2 antibody (Rab64) that cross-reacts with human and murine TROP-2 covalently attached to SN-38 by the CL2A linker. SG surrogate activity was characterized in vitro and in 4T1 syngeneic models. Results: SG surrogate demonstrated high affinity for human and mouse TROP-2 (K_D=1.1 and 1.4 nM, respectively) with SN-38 release rates and PK similar to that of SG. Flow cytometry analysis after bulk cell sorting of 4T1 or lentivirus transduction of EMT6 confirmed high TROP2 expression after at least 3 in vitro passages. Fifteen days after subcutaneous implantation, flow cytometry analysis of tumor single-cell suspensions revealed significant differences in immune infiltrates between 4T1-derived tumor groups (n=5/group; mean percentages in TROP2^{high} vs TROP2^{low} 4T1-derived tumors of cells expressing CD45: 65% vs 10%, P < 0.0001; CD8: 5.5% vs 1%, P = 0.0033; CD4: 22% vs 4%, P = 0.0055; macrophages: 12.5% vs 2.5%, P = 0.0002; myeloid cells: 52% vs 75%, P = 0.0066). In addition, TROP2^{high} 4T1-derived tumors were smaller and had significantly less necrosis than TROP2^{low} and unsorted 4T1-derived tumors 25 days after implantation. Finally, transcriptomics analyses of TROP2^{high} vs TROP2^{low} 4T1-derived tumors demonstrated the association of TACSTD2 expression levels with regulation of distinct molecular pathways. Conclusion: Syngeneic tumors derived from 4T1 cells with differential TROP2 expression levels are associated with differential cellular states and tumor microenvironment composition. In contrast, no significant phenotypic changes were observed in tumors derived from TACSTD2-transduced compared with mock-transduced EMT6 cells. Taken together, these results suggest that expression of the TACSTD2 gene is associated with, but not causative of, different tumor phenotypic states. Additional studies to investigate TROP-2 expression as a correlative marker of patient prognosis and the antitumor immune response are warranted. The effects of in vivo treatment with an SG surrogate on 4T1 tumor growth and immune phenotype will be discussed at the time of the presentation.

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P4-07-13

Satisfaction of patients after implant-based subpectoral reconstruction with a titanized polypropylene mesh (TiLOOP® Bra) compared to prepectoral reconstruction with a titanized polypropylene pocket (TiLOOP® Bra Pocket)

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Introduction Patients' satisfaction after breast reconstruction can be evaluated with validated questionnaires as the Breast-Q questionnaire. The Breast-Q questionnaire includes different domains; one of them is "satisfaction with the result". Material and methods: In the multicentre, prospective studies PRO (patient related outcome)-BRA (clinicaltrials.gov: NCT01885572) and PRO-Pocket (clinicaltrials.gov: NCT03868514), patient satisfaction was assessed using the Breast-Q questionnaire. In the PRO-Bra study, 269 patients underwent subpectoral surgery using the TiLOOP® Bra polypropylene mesh (pfm medical ag, Germany). In the "PRO-Pocket" study, 311 patients underwent prepectoral surgery using the TiLOOP® Bra Pocket polypropylene mesh. For the evaluation, those patients from the PRO-Bra and PRO-Pocket studies who completed a Breast-Q questionnaire 6 and/or 12 months after surgery were included. The BreastQ score is measured from 0 to 100, with a score of 100 corresponding to "very satisfied". Satisfaction with the result of the breast reconstruction was evaluated. Results: In the PRO-Bra study, a total of 221 and 203 patients completed a Breast-Q at 6 months and/or 12 months FU, respectively. The mean age and BMI of the patients with completed Breast-Q were comparable between the two studies (PRO-Bra: 49.3 [\pm 11.6] years, 22.9 kg/m² [\pm 3.5]; PRO-Pocket: 47.7 [\pm 11.7] years, 24.5 kg/m² [\pm 4.3]). In the PRO-Pocket study, a total of 258 and 266 patients completed a Breast-Q at 6 months and/or 12 months FU, respectively. In the PRO-Bra study the mean score of satisfaction with the result at 6 months follow-up (FU) was 74.5 (\pm 19.9), in the PRO-Pocket 79.1 (\pm 19.1), at 12 months FU the mean scores were 76.3 (\pm 18.9) for PRO-Bra and 78.2 (\pm 20.4) for PRO-Pocket. Furthermore, stratification according to age (cutoff 50 years) or BMI (cutoff 25 kg/m²) did not reveal any differences between the subgroups or the two studies (see Table). PRO-Bra PRO-Pocket mean score (\pm SD) 6 months 12 months 6 months 12 months BMI \leq 25 75.1 (\pm 19.7) 76.4 (\pm 17.8) 77.7 (\pm 19.9) 78.9 (\pm 19.8) BMI > 25 72.1 (\pm 20.7) 76.1 (\pm 22.9) 82.1 (\pm 16.9) 76.8 (\pm 21.8) age \leq 50 76.4 (\pm 18.7) 77.0 (\pm 18.9) 80.1 (\pm 18.7) 78.1 (\pm 19.6) age > 50 71.5 (\pm 21.5) 75.3 (\pm 19.0) 77.5 (\pm 19.5) 78.4 (\pm 21.8)

Conclusion: Our data so far show high patient satisfaction with overall outcome of the surgery. In addition, patients' satisfaction with the result was comparable after subpectoral as well as prepectoral implant placement. This is particularly important in the PRO-Pocket study, as approximately 60% of the operations and the follow-up period took place during the COVID-19 pandemic.

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7:00 AM - 8:15 AM

P4-07-14

Long-term Outcomes After 1 or 2-3 Lines of Neoadjuvant Therapy in Stage III Inflammatory Breast Cancer

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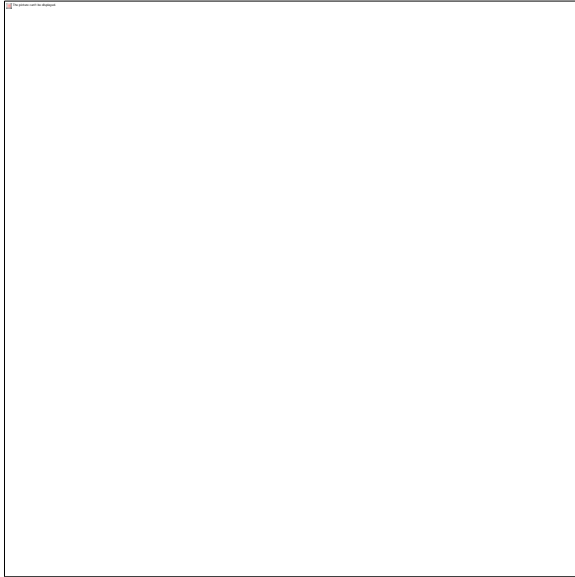
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Background: Inflammatory breast cancer (IBC) is associated with a poor prognosis. While many stage III IBC patients (pts) experience a sufficient response to first-line (1L) neoadjuvant chemotherapy (NAC) to permit subsequent surgical therapy, the prognostic significance of requiring additional NAC to enable resectability is unknown. We sought to describe the pathologic complete response (pCR) rates, breast cancer-free survival (BCFS) and overall survival (OS) among pts requiring 1 vs >1 lines of NAC prior to surgery. Methods: Upon IRB approval, pts with stage III IBC from 2 academic institutions (Dana-Farber Cancer Institute and MD Anderson Cancer Center) who received 1L or 2-3 lines (2-3L) of NAC prior to surgery were identified. Standard NAC regimens containing different drugs, such as AC-T or TCHP, were considered as 1L. Pts with locoregional progression or metastatic disease prior to surgery were excluded. Hormone receptor (HR), HER2 status, grade, and pCR, defined as no residual invasive cancer in the breast and the axilla, were evaluated. BCFS, defined as time from surgery to locoregional and/or distant recurrence, and OS, defined as time from surgery to death, were evaluated by the Kaplan-Meier method. Multivariable Cox models stratified by institution and containing the covariates pCR and tumor subtype were utilized to estimate the HR of 2-3L vs. 1L of therapy. Results: 808 eligible pts diagnosed between 1997 and 2020 were identified. 733 (91%) had 1L and 75 (9%) had 2-3L of NAC, and the median age was 50 years. 295 (37%) had HER2+, 282 (35%) HR+HER2-, 211 (26%) had HR-HER2- disease and for 20 (2%) pts, the receptor status was unknown. The median time from diagnosis to surgery was 6 months. Grade III disease, triple-negative and HER2-positive disease were more prevalent in pts receiving 2-3L of therapy (table). pCR was achieved in 178 (24%) pts receiving 1L of NAC, and in 14 (19%) pts receiving 2-3L of NAC. At 68 months of median follow-up, 417 (52%) pts experienced a recurrence with 376 in the 1L group and 41 in the 2-3L group. The 5-year BCFS was shorter for the 2-3L group compared to the 1L group (33% v 46%, HR=1.37; 95% CI:0.99-1.91). However, in 192 pts with a pCR, BCFS was similar, regardless of the number of NAC lines. There were 38 recurrences among 178 1L pts, and 3 recurrences among 14 2-3L pts,

resulting in BCFS of 76% and 83% in 1L and 2-3L pts, respectively. Overall, there were 308 deaths, 276 deaths among 1L pts and 32 among 2-3L pts. The 5-yr OS estimate in 1L versus 2-3L pts was 60% versus 53% (HR=1.32, 95% CI: 0.91-1.93). Conclusion: Among pts with stage III IBC, pCR was observed among 24% who had 1L and 19% of pts who required 2-3L of NAC. BCFS and OS were comparable among pts with pCR after 1L and 2-3L. Our results suggest the need to continue to optimize current treatment strategies in IBC to improve pCR rates across all disease subtypes regardless of the number of lines of NAC required.



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12/8/2022

7:00 AM - 8:15 AM

P4-07-16

B-IMMUNE final analysis: a phase Ib/II study of durvalumab combined with dose-dense EC in a neoadjuvant setting for patients with locally advanced luminal B HER2(-) or triple negative breast cancers.

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Background: Neoadjuvant association of immune checkpoints inhibitors (ICI) and dose dense chemotherapy is promising for triple negative breast cancers (TNBC). However, response rates vary from one study to another. Timing, best chemotherapy partner and efficacy in less immunogenic breast cancer (BC), like luminal B tumors, should be further investigated. This study evaluates for TNBC and luminal B HER2(-) BC the neoadjuvant treatment with paclitaxel followed by a short combination of an anti-PD-L1 antibody with anthracyclines. Method B-IMMUNE (NCT03356860), a multicentric phase Ib/II prospective trial, included patients with stage I to III luminal B HER2(-) or TNBC treated with paclitaxel 80mg/m² weekly from week 1 to 12 followed by 4 cycles of epirubicine 90mg/m² and cyclophosphamide 600 mg/m² (EC) Q2W in a neoadjuvant setting. Phase Ib evaluated a single infusion of durvalumab (anti-PD-L1) combined with the 3rd cycle of EC. Phase II evaluated infusions of durvalumab with the 1st and 3rd EC cycles. Surgery was planned 3 weeks after the last EC cycle. Primary objectives were safety and pathological complete response (pCR) rate compared to a historical control. Secondary endpoint was the overall response rate (ORR) based on breast MRI. Eleven patients were enrolled in a control arm without durvalumab, exclusively for translational research purposes. Based on a 2-stage Simon design with an $\alpha = 0.1$ and $\beta = 0.1$, 22 TNBC patients were needed in the phase II to test a null hypothesis of 30% pCR rate against a one-side alternative of 60%, and 24 luminal B BC patients to test a null hypothesis of 15% pCR rate against a one-side alternative of 40% (including an additional accrual margin of 10% for eventual dropouts). At least 9 pCRs had to be observed among the first 20 evaluable TNBC patients and 6 among the first 22 evaluable luminal B patients to rule out the null hypothesis. Results This analysis concerns the 50 patients treated with the experimental treatment, 3 from the phase Ib and 47 from the phase II part. Median age was 51 y-old (31 to 72y), tumor subtypes were 24 TNBC, 25 Luminal B and one sarcoma excluded from the efficacy analysis. Seven (14%) patients had a stage I tumor, 17 (34%) a stage IIA, 13 (26%) a stage IIB, 8 (16%) a stage IIIA, 4 (8%) a stage IIIB and 1 (2%) a stage IIIC. Concerning safety, 232 AEs were reported on 39/50 patients and 34 (14,6%) were graded ≥ 3 . The 5 most frequent all-grade AEs were fatigue (8,2%), diarrhea (5,6%), neutropenia (5,2%), anemia and nausea (4,3%). Most frequent grade 3 AEs were anemia and neutropenia (14,7%). Among 4 immune-related adverse events, all were thyroid disorders. One patient died 10 months after the end of

treatment due to progressive disease in the liver. Forty-six of the 47 phase II patients were evaluable for efficacy. pCR was reported in 12/22 TNBC patients (55%) and 8/24 luminal B HER2(-) patients (33%). Subgroup analyses based on PD-L1 expression and TILs score are planned. Conclusions The B-IMMUNE study met its primary objective showing a significant improvement in pCR versus the historical control in both TNBC and in Luminal B HER2(-) BC cohorts with the addition of only 2 doses of durvalumab to the anthracyclines. The safety profile is comparable to those previously described with reported immune related adverse events limited to thyroid endocrine disorders.

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7:00 AM - 8:15 AM

P4-07-17

Follow-up in breast cancer care: guidelines and individual risks

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The aim of this study was to investigate how breast cancer follow-up in the Netherlands changed during the COVID-19 pandemic, compared to 2018-2019, and to what extent follow-up during the pandemic corresponded to the patient risk of recurrence. During the early phase of the pandemic the Dutch Society for Surgical Oncology (NVCO) issued a report with recommendations on how follow-up could be postponed, as a guidance for the pandemic, based on a low, intermediate or high risk of recurrence. In this study we investigated to what extent this advice was followed. A dataset of 33160 women diagnosed with primary invasive breast cancer between January of 2017 and July of 2021 was selected from the Netherlands Cancer Registry (NCR) and Dutch Hospital Data (DHD). The pandemic, 2020 and weeks 1-32 of 2021, was divided into six periods (A to F), based on the number of hospitalized COVID patients in the Netherlands. The five-year risk of locoregional recurrence (LRR) was determined for each patient with the INFLUENCE nomogram. The LRR risk was compared to the risk groups from the NVCO report with a Kruskal-Wallis test. The percentage of patients who received a mammogram during period A to F was compared to the same periods of 2018-2019 with a chi-squared test. Correlation between the LRR risk, and if patients had a mammogram, was investigated with logistic regression. This analysis was repeated separately for the risk groups. Correlation between the LRR risk, and time intervals between surgery and the first and second mammogram was analyzed using cox proportional hazard models, this was also repeated for the risk groups. There was a significant difference in LRR risk between the NVCO risk groups. In the low-risk group (n=7673), 86 patients (1.1%) had a risk >5%. In the intermediate risk group (n=19197), 18364 patients (95.7%) had a risk of < 5%, and 65 patients (0.34%) had a risk of >10%. In the high-risk group (n=2674), 2365 patients (88.4%) had a risk <

10%. The percentage of patients who received a mammogram was significantly lower in periods B to F of the pandemic. Logistic regression showed a negative correlation between the risk of LRR and if patients had a mammogram in 2020 (OR 0.93) and 2021 (OR 0.93). There was also a negative correlation between the risk groups and mammography in 2020 (OR 0.92 for intermediate and 0.80 for high), and for the risk groups and mammography in 2021 (OR 0.98 for intermediate and 0.95 for high). There was no significant impact of LRR risk, or risk group, on time intervals between mammograms. During the pandemic, patients with a higher LRR risk, or a higher risk according to NVCO advice, had lower odds of having a mammogram. If the advice would have been followed, in 0.5% of the patients scheduled for follow-up, the recommendation was to postpone in contrast to a high estimation of the individual risk. For 62.7%, a follow-up was recommended, despite a low estimated individual risk. Because the number of high-risk patients is relatively low, individual risk prediction could be supportive, in case of future restrictions. This way the high-risk patients can be identified and prioritized for follow-up, and can also be encouraged to come to the hospital.

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P4-07-18

FerOX, an anthracyclines nanoformulation to lead toward immuno-mediated cancer remission, preserving T-cell immune competence

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Background Chemotherapy with anthracyclines, such as doxorubicin (DOX), still remains a mainstay in cancer treatment. DOX kills tumor cells by direct interference with DNA replication, thus it is very effective against highly proliferating cells. Since DOX is not cell-specific drug, it displays severe side effects that limit its clinical use. Besides its direct cytotoxicity, it enhances also tumor immunogenicity, since DOX-induced immunogenic cancer cell death facilitates tumor antigens presentation. However, the generation of an adaptive immune response is one of the most highly- proliferative processes, thus it may be affected by DOX cytotoxicity, paradoxically preventing the establishment of a proper adaptive antitumor immune response. Therefore, the effect of DOX on dividing T-cells urges investigation. Methods We explored the phenotypic and functional effects of DOX on lymphocytes from healthy donors and from breast cancer (BC) patients. Purified peripheral blood mononuclear cells (PBMC) were subjected to an uptake assay and to a CFSE-based proliferation assay in vitro. Characterization of lymphocytes was made by flow cytometry (FC) and confocal microscopy. Innovative DOX nanoformulation with proved efficacy in cancer cell line, BC Patient-derived Organoids (PDO) and murine model of BC, has been assessed in parallel to liposomal DOX, evaluating both DOX uptake and their capability to preserve proliferation potential in different PBMC subpopulation. Results PBMC

incubated in vitro with DOX displayed a dose-dependent DOX uptake that results in a dramatic proliferative impairment. The same behavior has been observed in BC patient-derived PMBC, isolated immediately after the end of first cycle of chemotherapy, which show a prompt DOX internalization coupled with a dramatic impairment of proliferative potential in comparison to the match-paired PMBC isolated before the treatment. Interestingly, FC characterization showed that DOX internalization is higher in CD8+ than CD4+ T-cells and mainly affects central memory, effector memory and terminal differentiated effector. Since pivotal to every adaptive immune response is the activation and massive proliferation of T cells from their resting state, we have exploited a DOX formulation in ferritin nanocages (FerOX), that displays a TfR1-mediated tumor specific homing in order to circumvent drug internalization in those immune cells. FerOX efficacy has been proved in BC-PDO, evidencing an inverse correlation between TfR1 expression and HF_n-DOX IC₅₀. HF_n nanoformulation protects immune cells from DOX toxic effects, reducing DOX uptake and proliferative impairment, mainly preserving Naïve T-cells. The capability of FerOX to preserve T-cells competence to generate an immune response has been corroborated by an in vitro experiment aimed to mimic what could happens to patient's PBMCs if they could be treated with FerOX. Conclusions As a whole, our data indicate that preventing T-cells chemotherapy-related toxicity through FerOX could allow the host adaptive immune system to fully benefit from the DOX-induced immunogenic cell death to vaccinate against cancer. This strategy could be promising for complete tumor eradication and might generate a long-term immunosurveillance of recurrences and metastases.

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7:00 AM - 8:15 AM

P4-07-19

Eribulin enhances STING-dependent induction of type I interferons in immune and triple-negative breast cancer cells

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Triple-negative breast cancer (TNBC) is a heterogenous subtype of breast cancer that lacks effective targeted treatment options. However, TNBC typically has a higher mutational burden and greater degree of immunogenicity than other breast tumors, making immunotherapy a viable strategy for effective treatment of this disease. Strategies to improve the response of TNBC patients to immunotherapy include the upregulation of the cGAS-STING innate immune sensing pathway and STING agonists are in clinical development for the treatment of TNBC. We demonstrate that eribulin, a microtubule destabilizer currently used in the treatment of TNBC, functions as an indirect STING agonist because it promotes the release of mitochondrial DNA into the cytoplasm. Eribulin also enhances type I interferon expression induced by STING agonists through a second TBK1-dependent mechanism downstream of STING activation that is shared by the RIG/MAVS RNA sensing pathway. Both mechanisms of eribulin-mediated activation of interferon expression occur in immune and TNBC cells and are shared with other microtubule destabilizers, including vinorelbine, but not with the microtubule stabilizing agent paclitaxel. These effects of eribulin on innate immune sensing pathways in vitro prompted further evaluations of the impact of eribulin on the in vivo immunological response to mammary tumors. We found that eribulin, but not paclitaxel, promotes the activation of CD4+ T-cells in the spleens and draining lymph nodes of tumored animals. This activation required tumor priming but was independent of any direct effect on tumor growth inhibition, demonstrating a specific role of eribulin as a tumor immune modulator. These data contribute to accumulating evidence that there are important mechanistic differences between the microtubule targeted chemotherapeutics currently used in the treatment of TNBC and suggest that eribulin elicits a more favorable innate immunological signature than paclitaxel. Research supported by Eisai Inc.

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P4-07-20

Effect of prior treatments on post-CDK 4/6 inhibitor overall survival in hormone receptor positive breast cancer

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Purpose:

There are multiple treatment options for patients with metastatic breast cancer (MBC); however, there is minimal data on the optimal sequencing. Furthermore, limited information is available to understand the influence of prior treatment duration and class on novel therapies in real-world settings, such as cyclin-dependent kinase 4/6 inhibitors (CDK 4/6i) for patients with hormone receptor-positive, human epidermal growth factor receptor 2- negative (HR+ HER2-) MBC. Our study sought to identify the effect of prior treatments on post-CDK 4/6i survival.

Methods:

This retrospective study used the nationwide, de-identified electronic health record-derived Flatiron Health database of women with HR+ HER2- MBC who received at least one CDK 4/6i between 2011 and 2020. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated for the association between duration and class of all cancer treatments prior to receipt of CDK 4/6i and overall survival (OS) adjusting for age at diagnosis, race and ethnicity, site of metastasis, and metastatic diagnosis year. Time dependent HRs were used to compare the OS for patients receiving one versus multiple CDK 4/6i.

Results:

Of 5,363 patients, most were aged 55-64 (29%), White (69%), and had visceral metastasis (70%). The median survival from receipt of first CDK 4/6 inhibitor was 3.3 years. When compared to patients with no prior treatments, patients with up to one year of prior treatments had a 30% increased hazard of death ((HR, 1.30; 95% CI 1.15-1.46; Table 1). Similarly, patients with one to less than three years of prior treatment had a 68% increased hazard of

death (HR 1.68; 95% CI 1.49-1.88) and those with three or more years had a 55% increased hazard of death (HR 1.55; 95% CI 1.36-1.76). Furthermore, patients who received prior endocrine therapy alone experienced a 29% increased hazard of death (HR, 1.29; 95% CI 1.16-1.44), while patients receiving prior chemotherapy experienced a 72% increased hazard of death (HR, 1.72; 95% CI 1.54-1.93) when compared with patients who did not receive a prior treatment. Finally, patients who received a different CDK 4/6i after their first had a 17% decreased hazard of death compared to patients who received subsequent endocrine or chemotherapy after their first CDK 4/6i (HR, 0.83; 95% CI 0.71-0.96).

Conclusion:

Prior treatment duration and class are associated with a decreased overall survival after CDK 4/6 inhibitor administration. However, patients receiving more than one CDK 4/6 inhibitor in their sequence saw survival benefits. This highlights the importance for clinicians to consider prior treatment and duration in treatment decision-making and for trialists to stratify by these factors when reporting results of future studies.

Table 1. The association between OS and treatment duration and class before CDK 4/6 inhibitor initiation (N=5,363)

Prior treatment characteristics	Adjusted hazard ratio	95% Confidence interval
Treatment Duration (years)		
0	-	-
<1 year	1.30	1.15 to 1.46
1 to <3 years	1.68	1.49 to 1.88
3 or more	1.55	1.36 to 1.76
Prior cancer Treatment class		
No prior cancer treatment	-	-
Chemotherapy	1.72	1.54 to 1.93
Endocrine therapy	1.29	1.16 to 1.44

Abbreviations: OS, Overall survival; CDK, cyclin-dependent kinase

All patients were diagnosed with metastatic breast cancer in 2011 – 2020. Prior treatments included those for early-stage and metastatic

Hazard ratios and 95% confidence intervals obtained by Cox proportional hazard models
Model adjusted for age at diagnosis, race, site of metastasis

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Jeffrey Franks, MSPH: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

P4-07-21

Neo-adjuvant chemotherapy in various breast cancer subtypes in the 21st century.

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Introduction

Breast cancer is a complex, heterogeneous disease encompassing a spectrum of subtypes with distinct biological features, each having unique responses to various treatment modalities and different clinical outcomes. The type of neoadjuvant chemotherapy (NAC) for locally advanced breast cancer is decided based on breast cancer subtype, which includes triple negative breast cancer (TNBC), hormone receptor positive breast cancer (HR+BC), HER2+ breast cancer (HER2+BC) and triple positive breast cancer (TPBC). Multiple NAC regimens exist but have not been directly compared to determine the optimal treatment regimen in patients with various stages (I-III) and subtypes of breast cancer. The objective of this study was to assess pathological complete response (pCR) rates in patients treated with various types of NAC and analyze associated clinical factors in our diverse patient population.

Methods

This study included 297 patients treated with NAC for breast cancer between 2015 and 2021 at LCMC Health, New Orleans, Louisiana. The tumor, lymph node, metastasis (TNM) system was used for clinical and pathological staging. Biologic subclassification using estrogen receptor (ER), progesterone receptor (PR), HER2 were performed. Response to NAC was documented as pCR when there was no evidence of residual invasive tumor in the breast or axillary lymph nodes. Categorical variables were summarized by reporting counts and percentages, while continuous variables were summarized by reporting means and standard deviations. Fisher exact tests were used to compare pCR status by each chemotherapy status or demographic factor. Wilcoxon Rank-sum tests were used to compare continuous variables across pCR groups. Multivariable linear regression was performed to predict overall tumor shrinkage %.

Results

Among all patients, median age was 54.75 years (min-max: 22-78). 30 (10%) patients were stage I, 175 (58.9%) were stage II, 89 (29.9%) were stage III and 3 (1%) were stage IV with oligometastatic disease. 171 (57.6%) were African American (AA), 82 (27.6%) were Caucasians and 41 (13.8%) were other race. Table 1. shows chemotherapy and pCR rates among different breast cancer subtypes. Patients with carboplatin (57.3 vs 35.3; $p < 0.001$), had a higher likelihood of complete remission than non-users. After multivariable linear regression adjustment, Paclitaxel increased the % reduction in tumor size significantly (EST= 39%, CI 2% – 77%; $p=0.042$) compared to non-users. In the subset of TNBC patients this held in terms of pCR rates (47.1% vs 25%, $p=0.036$). In TPBC, pCR was higher in younger ($p=0.028$) and non-AA ($p=0.0023$) patients.

Conclusion

Multiple NAC regimens for breast cancer exist and optimization of regimens is key. We explored the use of several different chemotherapy agents and found the use of carboplatin beneficial, while doxorubicin, cyclophosphamide and cisplatin had a decreased likelihood of achieving a pCR; however, this may be due to the intrinsic nature of the subtypes that would be treated with these NAC regimens. We plan to explore by subtype and treatment regimen in future analysis.

Interestingly, AA have significantly less pCR in TPBC, compared to non-AA, although this finding was not seen in other subtypes. Future studies are needed to investigate this further.

Table 1. Chemotherapy and pCR rates among different breast cancer subtypes.

	TNBC	HR+BC	HER2+BC	TPBC
Total number of patients	119 (40%)	77 (25.9%)	50 (16.8%)	51 (17.1%)
Median age	55.15	54.35	56.16	53.06
African Americans	79 (66.4%)	40 (51.9%)	29 (58%)	26 (51%)
Patients with pCR	4 (35%)	9 (11%)	33 (66%)	27 (53%)
100% absolute reductions in primary mass size	47 (39%)	12(15%)	38 (76%)	28(54%)
Most common chemotherapy received	ACT	ACT	TCHP	TCHP

Abbreviations: ACT (doxorubicin/cyclophosphamide/paclitaxel); TCHP (docetaxel/carboplatin/Herceptin Perjeta);

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- Aneesha Ananthula, MD:** No financial relationships to disclose
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Clinical decision support systems for multidisciplinary team decision-making in patients with solid cancer: an implementation model based on a scoping review

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Background

Clinical decision-making by multidisciplinary teams (MDTs) is getting more complex as treatment advice for the individual patient must be based on an increasing amount of patient and tumor characteristics, and scientific evidence on treatment efficacy. Clinical decision support systems (CDSSs) can make an important contribution to assist but also optimize MDT decision-making. However, implementation of CDSSs in clinical practice is challenging.

Aim & methods

The aim of our study is to set up a CDSSs implementation model for multidisciplinary decision-making in solid cancer. It is based on a scoping review of the currently reported CDSSs for MDT decision-making in solid cancers with identification of reported barriers and facilitators for implementation of these CDSSs. For this we systematically searched the Cochrane Library, MEDLINE (accessed through PubMed) and Scopus up to September 1st 2021.

Results

Of the 710 screened abstracts, 38 papers met the inclusion criteria (table 1). Sixteen different CDSSs were identified. For implementation of CDSSs, 87 barriers and 73 facilitators were reported. The reported barriers could be categorized in the same categories as those of the facilitators (a factor can be reported as a barrier if the factor is not addressed well, and as a facilitator if the factor is properly addressed).

The most frequently reported barriers for CDSS implementation for MDT decision making

mainly concerned CDSS maintenance (e.g. not incorporating guideline updates), loco-regional feasibility of the CDSS recommendation (e.g. no access to diagnostics or treatment), validity, not incorporating patient preference in decision making, data accuracy, noncoverage of certain patient subpopulations, lack of an information standard, usability, data availability and no interoperability of the CDSS with the electronic health record. The most frequently reported facilitators included, besides the categories as mentioned above, the category shared decision making (reporting of alternative treatment options) and technical skills (involvement of a computer scientist). Table 2 shows the most frequently reported categories of barriers and facilitators, and scores for each included study the number of reported barriers (B) and facilitators (F) in each category.

Conclusion

Based on the identified barriers and facilitators, we developed a CDSS implementation model to guide more successful CDSS integration in the clinical workflow to support MDTs (the model will be shown at the congress). The usability of this theoretical model should be explored in future studies.

Table 1. Characteristics of 38 included articles

Paper	decisions (n)	patients (n)	study period	cancer type	country	setting	CDSS
Alkermu, 2021		250	2017 - 2018	colorectal cancer	China	M- & M+	WFO
Choi, 2019		65	2017 - 2017	gastric cancer	Korea	M- & M+	WFO
Kim, 2019		69	2016 - 2017	colorectal cancer	Korea	M- & M+	WFO
Kim, 2020		405	2018	lung cancer	Korea	M- & M+	WFO
Lee, 2020		295	2018	breast, colorectal, gastric, other	Korea	M- & M+	WFO
Lee, 2018		656	2009 - 2016	colorectal cancer	Korea	M- & M+	WFO
Liu, 2018		149	2017	lung cancer	China	M- & M+	WFO
Simashekar, 2018		638	2014 - 2016	breast cancer	India, USA, UK	M- & M+	WFO
Tian, 2020		235	2016 - 2018	gastric cancer	China	M- & M+	WFO
Zhao, 2020		382	2016 - 2018	breast cancer	China	M- & M+	WFO
Zhou, 2010		382	2017	lung, breast, other	China	M- & M+	WFO
Zou, 2020		246	2016 - 2018	cervical cancer	China	M- & M+	WFO
Bouaud, 2014		557	2009 - 2010	breast cancer	France	M-	OncoDoc2
Bouaud, 2012		199	2007 - 2009	breast cancer	France	M-	OncoDoc2
Bouaud, 2011		109	2007 - 2009	breast cancer	France	M-	OncoDoc2
Bouaud, 2015		384	2009 - 2010	breast cancer	France	M-	OncoDoc2
Seroussi, 2007		467	2005 - 2000	breast cancer	France	M-	OncoDoc2
Seroussi, 2013		1624	2007 - 2009	breast cancer	France	M-	OncoDoc2
Seroussi, 2012		1624	2007 - 2009	breast cancer	France	M-	OncoDoc2
Seroussi, 2013		825	2009 - 2010	breast cancer	France	M-	OncoDoc2
Redjal, 2020		1861	NA	breast cancer	France	M-	GL-DSS, OncoDoc
Redjal, 2021		1861	NA	breast cancer	France	M-	GL-DSS, OncoDoc
Seroussi, 2017			NA	breast cancer	France	M-	GL-DSS
Hendriks, 2019			NA	breast cancer	Netherlands	M-	OncoGade
Hendriks, 2020		394	2012 - 2015	breast cancer	Netherlands	M-	OncoGade
Keikes, 2021		158	2016 - 2017	colorectal cancer	Netherlands	M- & M+	OncoGade
Arisobola, 2021		640	2018 - 2020	lung cancer	France	M- & M+	PhSciOUS
Cyplik, 2017			not reported	laryngeal cancer	Germany, Poland, USA	M- & M+	Kernel for Workflow, Knowledge & Decision Management
Eccher, 2014		61	2008 and 2012	breast cancer	Italy	M-	OncoCure
Epstein, 2006		102	not reported	breast cancer	Hong Kong	M-	AdvanT!
Daouk, 2017			NA	breast cancer	USA	not reported	not reported
Heden, 2015			NA	breast, colon, prostate cancer	Germany	M- & M+	Health Case Management Platform
Liu, 2019		1065	2007-2015	breast cancer	Australia	M-	
O'Reilly, 2008		98	2004	colorectal cancer	UK	M+	OncoSurge
Prebet, 2018			NA	breast cancer	France	M-	
Russale, 2005			NA	breast cancer	France, Canada	M-	
Sesen, 2014		4020	2006 - 2010	lung cancer	UK	M- & M+	Lung Cancer Assistant
Shekarriz, 2020		126	2008 - 2017	pancreatic cancer	Germany	M-	MEBKAStB

Table 2. Overview of the most frequently reported categories of barriers and facilitators. For each included study the number of reported barriers (B) and facilitators (F) are scored for each category.

CDSS	first author	year	Healthcare		CDSS utility		Healthcare feasibility		Usability		Data accuracy		Interoperability		Information shared		Patient & clinician preferences		Patient participation		Healthcare decision-making		Other usability		Technical risks			
			B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F
WFO	Alkerm	2021																										
WFO	Choi	2019																										
WFO	Kim	2019																										
WFO	Kim	2020																										
WFO	Lee	2020																										
WFO	Lee	2018																										
WFO	Liu	2018																										
WFO	Sureshchek	2018																										
WFO	Tian	2020																										
WFO	Zhao	2020																										
WFO	Zhou	2019																										
WFO	Zhu	2020																										
OncoDec2	Bouaud	2014																										
OncoDec2	Bouaud	2012																										
OncoDec2	Bouaud	2011																										
OncoDec2	Bouaud	2015																										
OncoDec2	Sérusiaux	2007																										
OncoDec2	Sérusiaux	2013																										
OncoDec2	Sérusiaux	2012																										
OncoDec2	Sérusiaux	2013																										
GL-DSS	Rogstad	2020																										
GL-DSS	Rogstad	2021																										
GL-DSS	Sérusiaux	2017																										
OncoGuide	Hendriks	2019																										
OncoGuide	Hendriks	2020																										
OncoGuide	Kelkers	2021																										
PreSciOUS	Ansorbeto	2021																										
Kernel for WorkFlow, Knowledge & Decision Managem	Czytko	2017																										
OncoCure	Egger	2014																										
AdjuvantF	Epstein	2006																										
NR	Guyalaco	2017																										
Health Care Management Platform	Hedden	2015																										
NR	Lin	2016																										
OncoSurge	O'Reilly	2008																										
NR	Priest	2018																										
NR	Rossale	2005																										
Lung Cancer Assistant	Sesen	2014																										
MEEDIASB	Stokarr	2020																										

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7:00 AM - 8:15 AM

P4-07-23

Results of a Phase 2 Trial of Combination Immunotherapy with Concurrent Nelipepimut-S + GM-CSF and Trastuzumab in High-risk HER2+ Breast Cancer Patients

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INTRODUCTION: The HER2-targeted peptide vaccine nelipepimut-S + GM-CSF (NeuVax) has been shown to be safe, immunogenic, and potentially synergistic with trastuzumab. Here we present the results of a randomized phase 2 trial assessing the ability of nelipepimut-S/GM-CSF versus GM-CSF alone, added to the standard adjuvant Trastuzumab, to prevent recurrences in high-risk HER2-positive breast cancer patients. **METHODS:** The study was a multi-center, prospective, randomized, controlled, single-blinded, phase 2 trial. Enrolled patients had high risk HER2+ breast cancer defined by the presence of residual disease post neoadjuvant therapy or by the presence of positive lymph nodes after upfront surgery. Eligible patients had completed an approved trastuzumab-chemotherapy containing regimen and they were receiving adjuvant Trastuzumab monotherapy. Enrollment was limited to patients with HLA-A2, A3, A24, and/or A26 alleles. Patients received intradermal injections of nelipepimut-S + GM-CSF or placebo + GM-CSF every three weeks for six total vaccinations with concurrent, standard monotherapy with iv trastuzumab. After completion of the primary vaccine series, booster inoculations were administered every six months for four doses. The primary outcome measure was invasive disease-free survival (iDFS) at 36 months. Secondary outcome measures were distant recurrence-free survival (DRFS), toxicity assessment, and evaluation of immune response. **RESULTS:** 100 patients were enrolled and randomized 1:1 to nelipepimut-S/GM-CSF or GM-CSF alone. There were no significant clinicopathologic differences between the groups. There was no difference in related local ($p=0.49$) or systemic toxicities ($p=0.41$). Kaplan-Meier estimates of iDFS at 36 months were 79% in the nelipepimut-S arm and 92% in

the placebo arm (log rank, $p=0.11$). DRFS at 36 months was estimated to be 90% in the nelipepimut-S arm and 95% in the placebo arm (log rank, $p=0.40$). Delayed type hypersensitivity (DTH) response to nelipepimut-S was measured and considered positive if there was more than 5 mm induration after 48 hours. DTH response converted from negative to positive in 11% of patients in the vaccine group versus 5% of patients in the placebo group ($p=0.36$). In both groups, iDFS at 36 months was 100% for those with a positive DTH response post-inoculation and 88% for those with a negative DTH response post-inoculation (log rank, $p=0.29$). CONCLUSION: Combination immunotherapy with concurrent nelipepimut-S + GM-CSF and trastuzumab is safe, however there was no difference in iDFS or DRFS among high-risk HER2+ breast cancer patients who received nelipepimut-S + GM-CSF compared to GM-CSF alone. We observed a trend towards improved iDFS in patients with a positive DTH response to nelipepimut-S, though it was not statistically significant.

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12/8/2022

7:00 AM - 8:15 AM

P4-07-24

Circulating tumor cells enumeration and Health Related Quality of Life of patients treated with first-line chemotherapy for HER2 negative metastatic breast cancer

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Background: In patients with metastatic breast cancer (mBC), Circulating Tumor Cells (CTC) counts have a strong prognostic impact on progression free survival (PFS) and overall survival (OS). Changes 4 weeks after the start of a new line of therapy, inform on treatment efficacy. Despite improvements in systemic treatment, metastatic BC remains mainly incurable with alteration of health-related quality of life (HRQOL) during the course of the disease. The aim of this work was to assess impact of clinical factors and biological factors as CTC on HRQOL. Methods: The French cohort COMET is a prospective study including first line HER2 negative patients receiving weekly paclitaxel and bevacizumab according to EMA approved combination. The aim of this cohort was to evaluate clinical, biological and radiological parameters associated with patients' outcome (CTC, CEC, serum markers, ctDNA, pharmacogenomic polymorphisms, metabolomic parameters, visceral fat assessed by initial CTscan, serum estradiol level, and quality of life). HRQOL was assessed at baseline, at every cycle until progression and then every 3 months up to death using the EORTC QLQ-C30 questionnaire and its breast cancer specific module, the EORTC QLQ-BR23. Five dimensions of HRQOL were analyzed for the primary analyses: Global health status (GHS), physical functioning (PF), Emotional functioning (EF), fatigue (FA) and pain (PA). Time until definitive deterioration (TUDD) in HRQOL was defined as the interval between inclusion and the first decrease in HRQOL score ≥ 5 compared to baseline HRQOL score with no further improvement or in case of death. CTC counts were determined using the standard CellSearch system [Menarini Silicon Biosystems]. Results: Out of 510 patients included in COMET study, 432 patients with available HRQOL data were analyzed in this study. At baseline, patients reported a mean score for GHS of 57.6 (SD=22.7), for PF of 75.8 (23.2), for EF of 62.2 (25.8), for FA of 42.2 (29.60) and for PA of 38.1 (31.5). The Median TUDDs for the 5 targeted dimensions was 10.1 months [7.5-16.9] for GHS, 6.1 months [4.1-8.9] for PF, 21.6 [18.7-31.2] for EF, 10.8 [6.2-16.6] for FA and 13.6[10.1-22.5] months for PA. CTC counts were available in 261 patients at base line and in 229 patients after 4 weeks of treatment, before second cycle of chemotherapy. CTC high count was independent of main clinical and biological characteristics except lobular subtype. We confirmed the poor outcome of patients with high CTC count at base line and after one cycle of

treatment with the threshold of > 4CTC/7.5 ml of blood. Out of the 5 dimensions of HRQOL, TUDD of EF was significantly correlated with a high CTC level at base line ($p=0.0262$) and even more with still an elevated count of CTC after one cycle of chemotherapy($p=0.0137$). There was no association of CTC with the other dimensions of HRQOL. Conclusion: This is the first study ever reporting an analysis of QoL and CTC. We observed an association of high CTC count with one component of HRQOL scale. This suggests that CTC could be complementary to clinical factors that could influence HRQOL in HER2 negative metastatic BC treated with first line chemotherapy.

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7:00 AM - 8:15 AM

P4-07-25

Performance of Sentinel Lymph Node Biopsy after Neoadjuvant Chemotherapy in Clinically Node Positive Breast Cancer Patients: Systematic Review and Meta-analysis

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Background There is an increase in the use of neoadjuvant chemotherapy (NACT) to downstage breast cancer. Sentinel lymph node biopsy (SLNB) has replaced Axillary lymph node dissection (ALND) as a standard of care for the treatment of breast cancer patients with negative axilla at presentation. However, the reliability of SLNB after NACT in patients with initially node-positive breast cancer is still controversial and debatable. This meta-analysis was conducted to investigate the accuracy and feasibility of SLNB after NACT in patients presented

with positive axillary lymph nodes. Methods A comprehensive literature search was conducted using Medline, PubMed, Embase, Central, and SCOPUS for studies from their date of inception till April 2021 on the performance of SLNB following NACT in clinically node-positive breast cancer patients. We included prospective studies including breast cancer patients with positive lymph nodes at diagnosis, receiving neoadjuvant chemotherapy before undergoing an SLNB, irrespective of their molecular subtypes or breast cancer stage. We excluded retrospective studies, case reports, review articles, and letter to editors. The main outcomes of interest were the false negative rate (FNR) and the identification rate (IR). We also aimed to investigate the accuracy, negative predictive value (NPV), positive predictive value (PPV), specificity, and sensitivity of the SLNB procedure. Results An aggregate of 33 studies were included in this meta-analysis enrolling 4624 patients. The pooled identification rate (IR) was 88% (95% CI: 86-90; heterogeneity I²: 80.93 %) and the false negative rate (FNR) was 13% (95% CI: 11-15; heterogeneity I²: 72.31%). The pooled accuracy, NPV, PPV, specificity and sensitivity were 91.8% (95% CI: 69.39 -114.3), 82.8% (95%CI: 60.19-105.52), 98.2% (95%CI: 65.86 -130.63), 93.7% (95 CI%: 32.4 -155.03), 82.1% (95%CI: 58.38- 107.24) respectively. Conclusion In this comprehensive meta-analysis, we were able to review the largest number of studies (N=33) and patients (N=4624). We carried out this study with the intention to overcome the limitations of previously conducted meta-analyses such as including retrospective studies and a mixed population of clinically node-positive and node-negative breast cancer patients. Based on current findings, the usage of SLNB instead of ALND for the treatment of node-positive breast cancer patients is acceptable. However, further analysis is needed for the improvement of SLNB performance. Keywords: Sentinel lymph node biopsy; Breast cancer; Node positive; Neoadjuvant chemotherapy.

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7:00 AM - 8:15 AM

P4-07-26

Development of CDCP1-targeting antibody-drug conjugate for Triple negative and metastatic breast cancer

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Introduction: CUB-domain containing- protein 1 (CDCP1) is a transmembrane receptor involved in the progression of several cancers. Recent studies demonstrate that CDCP1 is a rational target for the development of innovative targeted therapies for cancer including theranostics agents and antibody-drug conjugates. Objective/Methods: To determine the therapeutic potential of CDCP1 in breast cancer, we investigated its expression in multiple cohorts of breast cancer tissues by immunohistochemistry, as well as in various preclinical models including cell lines, primary cells and patient-derived xenografts using flow cytometry, western blot and immunofluorescence staining. Then, we evaluated the capacity of the CDCP1-targeting chimeric antibody ch10D7 to specifically accumulate in breast cancer lesions in in vivo preclinical models including patient-derived xenografts and breast cancer metastasis models. Finally, we determined the efficacy of the ch10D7-MMAE antibody-drug conjugate to kill breast cancer cells in vitro and breast tumours ex-vivo and in vivo. Results: The CDCP1 receptor is expressed at targetable level in a significant proportion of breast cancer cases with high/intermediate expression detected in ~30% of localized ER-positive cases, ~50% of metastatic ER-positive cases and >70% of Triple negative or HER2-positive cases. Similar proportion of expression was detected in cellular models. We demonstrated that ch10D7 antibody labelled with the radionucleotide Zircodium-89 specifically accumulates in breast cancer lesions in vivo allowing the detection of mammary-fat pad implanted patient-derived xenografts and of breast cancer metastasis by PET/CT imaging. Finally, we confirmed that the ch10D7-MMAE antibody-drug conjugate is very efficient at inducing cell death in vitro as well as controlling primary tumour and metastatic tumour burden in pre-clinical models, conferring a significant survival advantage compared to classical therapy. Conclusion: Our work

demonstrates that CDCP1 is a potential target to detect and limit the progression of breast tumours and that biomolecules specifically recognising this receptor are promising agents which could improve survival of patients.

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P4-07-27

Clipped lymph nodes for cN+ patients decrease false negative rate and lead to potential changes in surgical and oncological management after clinical complete response following neoadjuvant chemotherapy

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Introduction

Targeted axillary dissection (TAD) after neoadjuvant chemotherapy (NAC) is a new axillary staging technique that consists of surgical removal of biopsy-proven, positive, clipped axillary nodes (CLN) in addition to the sentinel lymph node biopsy (SLNB), and provides for more conservative axillary surgery¹. A question was recently raised whether clipping a positive node for later assessment indeed leads to a management change². The purpose of our study is to report the feasibility of TAD and to evaluate false negative rate (FNR), impact on surgical and oncological management.

Materials and methods This retrospective, single-institution, study included 73 consecutive women operated between 2019 and 2021 after NAC for cN+ disease confirmed by cytology or histology, whose diseased lymph-node was marked with a clip before therapy. At surgery, in case of clinical-radiological complete response, patients underwent TAD (dual mapping with radiocolloid and blue dye + CLN) (n=43), or TAD plus ALND if any residual disease (n=30). The chemotherapeutic regimen were anthracycline/taxane based, with trastuzumab in case of HER2+ tumors. Patients were routinely evaluated with a breast MRI both before and after NAC.

Results Clinical and pathological details of the 73 enrolled patients are listed in Table 1. The mean age at diagnosis was 49.53±10 years. Pathologic complete response was achieved in 32 out of 73 patients (43.8%) with the greatest rate in HR-/HER2+ tumors (n=10/12; 83.3%). The identification rate of the CLN was 91.8% (68/73), and it was one of SLNs in 68.5% (50/73) of the cases. In cases in which one, two or three or more SLNs were identified, the CLN was in the SLN specimen in 42.9%, 77.8% and 81.8% of cases, respectively. The FNR of the SLN was 18.5% (CI: 4.9-38.1). In 18 cases the CLN was not in the SLN specimen; eleven out of 18 CLNs were positive, leading to ALND, and three of them had additional positive LNs. Only in one case the CLN was negative and the SLN was positive. In 3 cases (4.1%), the CLN was positive in the absence of residual tumour in the breast leading a potential change in the oncological management.

Conclusions Removal of CLN after NAC is feasible, allowing de-escalation of surgical management of cN+ women in case of clinical-radiological complete response, as 59% of women avoided a formal ALND. The CLN coincides with SLN in about 70% of cases (more than 80% if three or more SLNs are identified) and reflects the overall status of the axilla in 97.3% of the cases. Adding CLN to SLNB contributes to reduce significantly the FNR of the latter from 18% to 0% (FNR for SLNB =18.5% vs FNR for TAD=0%). Potential changes in surgical (CLN+/SLNs-) and oncological management (CLN+/SLNs- and absence of residual tumor in breast) occurs in 15.1% (11/73) and 4.1% (3/73) of cases, respectively.

References

- 1.Swarnkar PK et al. The Evolving Role of Marked Lymph Node Biopsy (MLNB) and Targeted Axillary Dissection (TAD) after Neoadjuvant Chemotherapy (NACT) for Node-Positive Breast Cancer: Systematic Review and Pooled Analysis. *Cancers (Basel)* 2021 Mar 26;13(7):1539.
- 2.Weiss A et al. How Often Does Retrieval of a Clipped Lymph Node Change Adjuvant Therapy Recommendations? A Prospective, Consecutive, Patient Cohort Study. 2022 Jun. *Ann Surg*

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Table1. Clinicopathologic characteristics in the cN+ breast cancer patients before NAC and clipped Lymph Node after NAC	
	n (%)
Imaging T-stage before NAC	
cT1	14 (19.2)
cT2	51 (69.9)
cT3	7 (9.6)
Receptor-based subtype	
HR+/HER2-	21 (28.8)
HR+/HER2+	24 (32.9)
HR-/HER2+	12 (16.4)
HR-/HER2-	16 (21.9)
CLN in SLNs specimen	50 (68.5)
CLN not in SLNs specimen	18 (24.7)
CLN+/SLNs-	11 (15.1)
CLN+/SLNs-, without residual cancer in breast	3 (4.1)

NAC: neoadjuvant chemotherapy; LN: lymph node; SLN: sentinel lymph node; CLN: Clipped Lymph Node

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7:00 AM - 8:15 AM

P4-07-28

Prognostic Impact of Delaying Multimodality Treatment in HER2 Positive Breast Cancer

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Objective: Multimodality treatment in breast cancer is a key to the improved survival outcomes. The effects of delays in multimodality treatment in HER2 amplified breast cancer were studied. Patients and Methods: Of the patients with primary HER2 amplified breast cancer who were treated between 2009 and 2018 in a single institution, 1,075 patients met the inclusion criteria. The patterns of the multimodality treatments and the prognostic effects of treatment delays were studied. Kaplan-Meier method was used to estimate the relapse free survival (RFS) and overall survival (OS). Hazard ratio (HR), their 95% confidence interval (CI) and p value were computed using the Cox proportional-hazards model adjusting for 11 covariates including age, ethnicity, clinical T stage, clinical N stage, ER, PR, Ki67, LVI, histologic grade, surgery type (mastectomy versus lumpectomy), neoadjuvant versus adjuvant chemotherapy. The Harrell's C statistics were used to determine the Cox model accuracy. Adjusted multivariate analyses of recurrence/death and death were computed using Cox proportional-hazards model. Delays in treatment were defined as starting treatment beyond 60 days after diagnosis or after the completion of the leading treatment. Results: Of the patients included, 49% received neoadjuvant chemotherapy/HER2 target treatment and surgery, 43% had adjuvant treatments and surgery and 8% had surgery only without chemotherapy. Timely commencement of treatment in the 3 groups were 85.7% , 72.1% and 78.4% respectively. The 5-year RFS was 88.7% and OS was 98.2%. Patients who received neoadjuvant and adjuvant chemotherapy were combined, and six treatment groups with delays in various treatments were compared: no delay in chemotherapy/target treatment and surgery (1); surgery delay (2); chemotherapy delay (3); delays in both treatments (4) and surgery only groups with (5) or without delays (6). Concordance statistics showed that the covariate adjusted Cox proportional-hazards model had a better accuracy than the unadjusted. Compared to those without delays, patients with both chemotherapy and surgery delayed had worse recurrence/death (adjusted HR = 4.11, 95% CI: 1.39-12.5, p= 0.0161). Delays in either surgery or chemotherapy also increased recurrence/death, although to a lesser magnitude. The adjusted death in surgery delay, chemotherapy delay and delays in both had HR 2.91; 2.22; and 2.29 respectively when compared to the group without delays in either treatment although not significant at p < 0.05.

Adjusted recurrence/death and death were similar between neoadjuvant and adjuvant groups (HR 0.99 & HR 0.85 respectively). The group that received surgery only without chemotherapy was associated with worse recurrence/death (adjusted HR=1.78, 95% CI: 0.19 – 16.9)
Conclusion: Delays in any treatment adversely impacted recurrence and death and chemotherapy/target treatment is a critical component in treating patients with operable HER2 positive breast cancer.

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P4-07-29

**Olaparib plus Trastuzumab in HER2[+] BRCA-Mutated Advanced Breast Cancer Patients:
The OPHELIA Study**

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Background: Olaparib (O) is approved for the treatment of HER2[-] patients (pts) with early or metastatic breast cancer and a germline BRCA mutation. Nevertheless, there is no evidence that HER2[+] tumors are resistant to PARPi. Preclinical data support that HER2[+] cells are sensitive to PARPi and strongly suggest that PARP inhibition augments the efficacy of trastuzumab (T). To test whether PARPi is synergistic with anti-HER2 therapy, the OPHELIA study has assessed the efficacy and safety of O in combination with T in pts with HER2[+] germinal BRCA-mutated advanced breast cancer (ABC). Methods: OPHELIA (NCT03931551)

is an open-label, multicenter, single-arm, phase II trial. The study enrolled pts aged ≥ 18 years diagnosed of HER2[+] ABC with germinal deleterious mutations in BRCA1 or BRCA2 who had received at least one prior systemic regimen for advanced disease (including a pertuzumab- or trastuzumab emtansine based regimen). Pts received O (300 mg oral, twice daily) plus T (either loading dose of 8 mg/kg IV infusion, and subsequent 3-weekly doses of 6 mg/kg IV infusion; or 600 mg SC injection, on day 1 of every 21-day cycle) until disease progression, unacceptable toxicity, or consent withdrawal. Primary endpoint was investigator-assessed clinical benefit rate (CBR) for at least 24 weeks as per RECIST v.1.1. Secondary endpoints included overall response rate (ORR), duration of response (DoR), progression-free survival (PFS), overall survival (OS); and safety and tolerability as per NCI-CTCAE v.5.0. The primary analysis evaluated CBR ($H_0: \leq 5\%$; $H_1: \geq 30\%$) based on exact binomial test. Sample size was designed to attain a 90% power at 10% one-sided alpha level. Results: From Mar 25, 2019, through Mar 2, 2022, 5 pts (from a total of 42 pts evaluated) were enrolled at 17 sites in Spain. Median age was 37.0 (range 32–54) years, 1 (20.0%) patient was male, 4 (80.0%) pts carried germinal BRCA2 mutations, 4 (80.0%) pts had received ≥ 3 advanced disease treatments lines, and 4 (80.0%) pts presented ≥ 2 metastatic sites. At data cutoff (Mar 2, 2022), with a median follow-up of 18.7 months (min: 11.7; max: 22.1), 40.0% of pts remained on therapy. CBR at 24 weeks was 80.0% meeting the primary endpoint (4 of 5 pts; 95% CI, 28.4% to 99.5%, $p < 0.001$). ORR (1 complete and 2 partial responses) was 60.0% (95% CI, 17.4% to 94.7%), and median DoR was 3.8 months (95% CI, 2.5 to 8.3 months). Two (40.0%) pts had PFS events due to disease progression at 5.2 and 1.2 months, respectively. Rest of pts were treated for 5.5, 11.2, and 19.0 months. There were 2 (40.0%) deaths at 14.0 and 18.5 months. The most common non-hematological treatment emergent adverse events (TEAEs) of any grade (G) were fatigue (60.0%; 0% $G \geq 3$), nausea (60.0%; 0% $G \geq 3$), vomiting (40.0%; 0% $G \geq 3$), and back pain (40.0%; 0% $G \geq 3$). Anemia (40.0%; 20.0% $G \geq 3$) and lymphopenia (40.0%; 20.0% $G \geq 3$) were the most frequent hematological TEAEs. One (20.0%) patient discontinued treatment because of a drug-related TEAE (leukopenia). A dose reduction of O was reported in 1 (20.0%) patient. No treatment-related deaths were reported. Conclusions: HER2 overexpression in germline BRCA-mutated ABC is infrequent. The activity observed in these 5 pts indicates that O+T combination might be of help in this group of pts. We strongly believe that randomized data are not needed, and RWE studies might help us to understand the real activity of this combination. Toxicity was as expected.

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Features and survival outcomes of HER2-low patients from a prospective registry of unresectable locally advanced or metastatic breast cancer: GEICAM/2014-03 (RegistEM)

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Background: HER2-low breast cancer (BC) is a new therapeutic entity, but it is uncertain if this subgroup of BC differs from HER2-negative tumors in clinical characteristics, prognosis, and response to therapy. The objective is to describe the clinical characteristics and outcomes of 422 patients (pts) with HER2-low BC documented before 1st line, having been diagnosed with advanced BC (ABC) before 2019 and included in the RegistEM study (n=1,663).

Methods: In this analysis (cut-off date 08/April/2022; database is ongoing), two subgroups of pts have been considered based on HER2 results: HER2-low (n=422) (immunohistochemistry [IHC] 1+ or IHC 2+ and in situ hybridization [ISH] negative) and HER2-IHC 0 (n=590), as reference. Hormone Receptor (HR) expression has also been considered for subgroup analysis.

Results: At first ABC diagnosis, < 1% pts had unresectable locally advanced BC (ULABC) in both groups, 31% de novo metastatic BC in HER2-low and 20% in HER2-IHC0 groups. Less than 1% were male, 99% Caucasian and ~71% postmenopausal. Median age was 60 years, being similar between both groups (range 26-96). Family history of BC and/or ovarian cancer was reported in 32% pts in HER2-low and 29% in HER2-IHC0. Germline BRCA1/2 mutation was higher in HER2-low (14/40=35%) in reference to HER2-IHC0 (14/64=22%) (p=0.14).

Relevant information summarized by HR expression and HER2 status are detailed in the table below. Visceral disease was similar in both total groups (58% in HER2-low vs HER2-IHC0 56%), but slightly higher in HR- HER2-low pts (81% vs 64%), and 84% and 90% pts had ≤3 metastatic locations, in HER2-low and HER2-IHC0 groups, respectively. Distribution of 1st-line therapies was also similar between both groups, being endocrine therapy (ET) plus biological therapy (BT) (HER2-low 39% vs HER2-IHC0 36%) and ET (HER2-low 30% vs HER2-IHC0 28%), while chemotherapy (CT) (HER2-low 13% vs HER2-IHC0 16%) and CT plus BT (HER2-low 9% vs HER2-IHC0 10%) were more frequent in HR- pts. A 2nd-line therapy was reported in 70% HER2-low pts and 67% HER2-IHC0 pts. The median time to progression (TTP) at 1st-line therapy in HER2-low pts was 11 mo (0-66), being similar in HER2-IHC0 pts, but the higher difference was observed in relation to HR expression. Treatments in 2nd-line were similar in both groups, CT and ET/BT were the most frequent totally. Median duration of 2nd-line therapy was ~6 mo; progressive disease (PD) was reported in 85% pts. A 3rd-line therapy was reported in 74% HER2-low and 69% HER2-IHC0 pts. The median time to progression (TTP) to 3rd-line therapy was 6 mo, being similar in HER2-low and HER2-IHC0 pts. The most frequent 3rd-line therapies were CT and ET/BT in both groups, as in 2nd-line. Median duration of 3rd-line therapy was 4 mo; PD was reported in 84% HER2-low pts and 82% HER2-IHC0 pts. Median (95% confidence interval [CI]) PFS at 1st, 2nd and 3rd lines (mo) were 14 (12-16), 6 (5-7) and 6 (5-6) in HER2-low pts, being similar in HER2-IHC0. OS was comparable in all subgroups analyzed, however, differences were observed regarding HR status.

Conclusions: Our results show that HER2-low BC pts have similar characteristics than HER2-IHC0 BC pts. There are differences in therapy outcomes in terms of survival and prognosis, particularly in HR- tumors, being better in HER2-low BC pts. It could be related to the fact that these tumors have a specific biology, but more evidence is needed.

	HER2-IHC0 N = 590 (2 HR unknown)				HER2-low (IHC 1+ or IHC 2+ (HR-)) N = 522 (18 HR unknown)			
	HR+ n= 494 (84%)		HR- n= 87 (15%)		HR+ n= 399 (83%)		HR- n= 123 (24%)	
BC extension at first diagnosis, n (%)	304 (29)		77 (89)		347 (88)		55 (66)	
Ductal in situ	159 (22)		9 (10)		133 (33)		18 (24)	
Invasive lobular carcinoma BC	145 (15)		68 (78)		214 (55)		37 (46)	
Time to ABC >= 24 mo, n (%)	303 (32)		77 (89)		351 (89)		55 (66)	
Location of metastatic sites, n (%)								
Bone	263 (89)		88 (102)		245 (61)		34 (29)	
Lung	113 (23)		36 (41)		98 (25)		10 (8)	
Liver	109 (24)		36 (41)		88 (22)		10 (8)	
Lymph nodes	159 (32)		49 (56)		140 (35)		24 (20)	
Soft tissue	71 (8)		17 (20)		70 (18)		10 (8)	
Brain	14 (1)		1 (1)		15 (4)		9 (7)	
Liver	1	2	1	2	1	2	1	2
n	489	303	81	57	395	247	104	48
Pts who reach next line, n (%)	328 (67)	224 (74)	149 (87)	87 (70)	247 (62)	158 (64)	143 (60)	26 (53)
Overall n	36 (2)	4 (1)	46 (13)	18 (20)	10 (6)	16 (4)	15 (12)	6 (6)
Therapies by line, n								
1st	206 (42)	139 (37)	53 (24)	-	185 (46)	89 (36)	42 (23)	-
ET	157 (32)	98 (26)	15 (7)	3 (3)	132 (34)	54 (23)	11 (6)	-
CT/BT	23 (5)	36 (10)	4 (2)	-	18 (5)	1 (0)	1 (1)	-
CT/BT	32 (7)	25 (7)	9 (4)	25 (21)	17 (5)	16 (7)	21 (9)	6 (6)
CT/BT	24 (5)	16 (5)	4 (2)	-	12 (3)	11 (5)	9 (5)	-
CT	46 (9)	34 (10)	13 (6)	54 (47)	30 (8)	29 (12)	15 (8)	25 (26)
BT	3 (1)	3 (1)	7 (3)	-	1 (0)	1 (0)	2 (1)	2 (2)
The most frequent therapies, n (%)								
Aromatase inhibitor (AI) + CDK4/6	118 (24)	37 (8)	4 (2)	-	107 (28)	37 (15)	7 (4)	-
Fulvestrant + CDK4/6	58 (12)	19 (5)	16 (7)	-	38 (10)	16 (7)	1 (1)	-
AI	81 (16)	17 (5)	4 (2)	1 (1)	81 (21)	18 (8)	4 (2)	-
Fulvestrant	53 (11)	36 (10)	5 (2)	-	38 (10)	15 (6)	6 (3)	-
Endocrine + Everolimus	21 (4)	21 (6)	-	-	2 (1)	1 (0)	-	-
CDK4/6 (monotherapy)	2 (1)	1 (1)	1 (1)	-	2 (1)	1 (0)	-	-
Capitablin (monotherapy)	22 (4)	46 (13)	15 (7)	15 (13)	15 (4)	21 (9)	11 (6)	4 (4)
Capitablin + Bicalutamide	7 (1)	4 (1)	1 (1)	4 (3)	2 (1)	-	1 (1)	3 (3)
Toremifene (monotherapy)	8 (2)	10 (3)	1 (1)	4 (3)	6 (2)	15 (6)	4 (2)	1 (1)
Toremifene + Bicalutamide	13 (3)	9 (3)	1 (1)	1 (1)	9 (3)	4 (2)	-	4 (4)
Sequential Toremifene and Capitelablin	2 (1)	2 (1)	2 (1)	1 (1)	1 (1)	2 (1)	1 (1)	-
Paltrifosfamide CT	8 (2)	4 (1)	14 (12)	13 (11)	1 (1)	1 (1)	4 (2)	4 (4)
Eribulin (monotherapy)	1 (1)	4 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)
Vorinostat (monotherapy)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)
Median duration of treatment, mo	13 (10-20)	6 (0-41)	5 (0-20)	4 (0-27)	1 (0-34)	14 (0-44)	6 (1-20)	6 (1-21)
Median TTP, mo (range)	13 (10-20)	6 (0-41)	5 (0-20)	4 (0-27)	1 (0-34)	14 (0-44)	6 (1-20)	6 (1-21)
Median PFS, 95% CI, mo	14 (12-16)	6 (5-7)	5 (4-6)	5 (4-7)	14 (12-16)	6 (5-7)	6 (5-6)	6 (5-6)
Median OS, 95% CI, mo	41 (35-46)	40 (37-42)	40 (37-42)	37 (34-40)	41 (35-46)	40 (37-42)	39 (37-41)	39 (37-41)

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7:00 AM - 8:15 AM

P4-07-31

A whole food, plant-based (WFPB) dietary intervention to improve cardiometabolic and cancer-related outcomes in women with breast cancer

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Background: With dramatically rising obesity rates in the US, obesity at breast cancer diagnosis is common; further compounding the problem is that breast cancer treatment often results in additional weight gain. Among women undergoing breast cancer treatment, both obesity at diagnosis and post-diagnosis weight gain are associated with increased all-cause mortality and increased breast cancer mortality. We tested a WFPB dietary intervention in metastatic breast cancer patients to improve cardiometabolic and cancer-related outcomes, as it has been shown to reduce weight and improves cardiometabolic health in overweight and obese individuals.

Methods: Women with stage 4 breast cancer receiving treatment were randomized 2:1 into 2 arms: 1) a WFPB diet (N=21) or 2) usual diet (N=11) for 8 weeks with assessments at baseline, 4, and 8 weeks. Our WFPB diet consisted of an ad libitum whole food, plant-based diet; 3 meals/day were provided to WFPB subjects, which included fruits, vegetables, whole grains,

nuts and seeds, and excluded meat, dairy, eggs, and added oils/solid fats. WFPB subjects received weekly education regarding diet. Subjects in the usual care group were asked to continue their usual diet for the next 8 weeks. Outcomes include cardiometabolic risk factors, related sex hormones, and cancer progression markers. Effects of the WFPB diet on the outcomes were assessed by comparing marginal means by arm estimated at 8 weeks from the analysis of covariance model controlling for the baseline value.

Results: Of the 32 subjects randomized, 30 subjects (20 WFPB and 10 usual care) completed all 3 assessments. Reductions in weight, BMI, total cholesterol, and LDL cholesterol were statistically significant as well as clinically meaningful, both within the WFPB group and between the groups. In the WFPB group, subjects lost a mean of 6.2% of their body weight versus 0.7% body weight loss in the control group ($p < 0.01$). LDL cholesterol was reduced by a mean of 20.0% in the WFPB subjects versus a 10.6% increase in control subjects ($p < 0.01$). Reductions in insulin and HOMA-IR, a measure of insulin sensitivity, were statistically significant within the WFPB group and trended towards significance between the groups. Sex hormone binding globulin (SHBG) levels increased significantly both within the WFPB group and between groups. There was a significant decrease in both IGF-1 and free testosterone within the WFPB group from baseline to week 8.

Conclusions: Our WFPB intervention resulted in improvements in several cardiometabolic and hormonal markers. The intentional weight loss, which was clinically large given the duration of the trial, was accompanied by reduced cholesterol, insulin resistance, free testosterone, and IGF-1. Given the moderate to large effect sizes noted, further study is warranted to evaluate the sustainability of benefits over time and to assess their potential impact on cancer-related outcomes.

Cardiometabolic and Cancer-Related Outcomes

<u>Outcome</u>	<u>WFPB Diet</u>		<u>Usual Diet Control</u>		<u>Between group differences in change (adjusted for baseline value)</u>		
	<u>Baseline n = 21</u>	<u>Final n = 20</u>	<u>Baseline n = 10</u>	<u>Final n = 10</u>	<u>Diff.</u>	<u>Cohen's d Effect size</u>	<u>p-value</u>
Weight (lbs.)	178.5	165.7*	159.9	158.8	-8.8	-0.21	<0.01
BMI	30.2	27.8*	28.4	28.2	-1.6	-0.25	<0.01
<u>Cardiometabolic Outcomes</u>							
Total Cholesterol (mg/dL)	194.9	159.4*	174.6	181.4	-36.4	-0.97	<0.01
LDL Cholesterol (mg/dL)	106.1	82.2*	92.3	97.9	-23.8	-0.76	<0.01
Systolic BP (mmHg)	113.5	110.3	111.0	113.3	-4.1	-0.35	0.34
Diastolic BP (mmHg)	72.2	69.8	65.3	66.7	-1.8	-0.16	0.57
Glucose (mg/dL)	101.5	93.8	114.4	117.3	-11.9	-0.45	0.16
Insulin (mU/L)	16.7	11.2*	11.4	12.1	-3.7	-0.39	0.08
HOMA-IR	4.6	2.7*	3.2	3.5	-1.3	-0.44	0.08
<u>Cancer Progression and Hormonal Markers</u>							
CA 27.29 (log ₂ [U/mL])	4.94	4.84	5.45	5.54	-0.14	-0.09	0.23
CA 15-3 (log ₂ [U/mL])	4.74	4.73	5.39	5.46	-0.01	-0.01	0.93
CEA3	3.0	3.2	7.9	10.2	-0.9	-0.01	0.91
IGF-1	173.3	156.4*	150.5	144.7	-6.7	-0.14	0.48
Sex Hormone Binding Globulin (nmol/L)	72.5	98.2*	89.0	78.9	30.5	0.83	<0.01
Free testosterone	0.47	0.32*	0.23	0.27	0.0	0.00	1.00
*p < 0.05 for within-group change							

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12/8/2022

7:00 AM - 8:15 AM

P4-07-32

Prognostic factors among elderly patients with operable non-metastatic breast cancer treated with primary endocrine therapy

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Background: The growing population of elderly patients with breast cancer imposes challenges for treatment when frailty and comorbidities may coexist. Age alone should not be a cutoff for cancer treatment decisions: benefit and risk should be taken into account, considering comorbidities burden, functionality, life expectancy and patient preferences. Primary endocrine therapy (PET) represents an alternative when primary surgery or neoadjuvant chemotherapy would not be adequate treatment choices for patients with hormonal receptor positive (HR+) non-metastatic breast cancer. We aimed to evaluate the prognostic factors associated with survival among elderly patients treated with PET with or without surgery. Methods: We retrospectively reviewed electronic medical records of a cohort of patients who were 70 years of age or older and were treated with PET for operable non-metastatic breast cancer in an academic cancer center from 2009 to 2021. Study endpoints were progression-free survival (PFS), overall survival (OS), and factors associated with PFS and OS. For PFS, the events considered were disease progression in patients treated with PET alone, disease recurrence in those who underwent surgery, or death from any cause. Survival was estimated using the Kaplan-Meier method and compared with the log-rank test. Prognostic factors evaluated were age, histological type, grade, Ki67 index, stage, ECOG-performance status (ECOG-PS) and comorbidities burden, according to Charlson index. Univariate and multivariable analysis were performed using Cox regression. Results: PET was the first treatment for 197 pts aged 70 years or older. The median age was 81 years (range 70-101). Most patients had ductal (N=149; 75%) or lobular carcinomas (N=22; 11%), grade 1 (N=48; 24%) or grade 2 (N=114; 58%), and stage II (N=67; 34%) or stage III (N=94; 48%) disease. Half of the patients had an ECOG-PS 3 (n=65) or 4 (n=35); 165 pts (83%) had an Charlson index < 6. Seventy-two pts (36%) underwent surgery. Thirty pts (15%) had a disease recurrence or progression and 60 pts (30.5%) died; most deaths (n=38; 63%) were not related to breast cancer. In a multivariable analysis, pts with grade 3 disease had higher risk of recurrence/progression/death (HR 3.31, 95% CI 1.45-7.58, P=0.005), while those treated with surgery had a decreased risk (HR 0.37, 95% CI 0.21-0.65; P=0.001). Median PFS was 55.2 mo for pts treated with PET alone and 99.7 mo in those treated with ET followed by surgery. Median OS was 63 mo and 111.9 mo, respectively. Conclusion: In this cohort, deaths observed were mostly unrelated to breast cancer, suggesting that PET is an appropriate choice for selected pts. Nevertheless, patients with grade 3 disease and those who were not treated with surgery after PET had a higher risk of disease progression/recurrence or death. Prognostic factors can be useful to select candidates for PET.

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7:00 AM - 8:15 AM

P4-07-33

Differences in Treatment Outcomes Between Patients with HER2-Low versus HER2-Zero, Hormone Receptor-Positive Advanced-Stage Breast Cancer Treated with CDK4/6 Inhibitors

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Background: The cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors transformed the care of patients with hormone receptor-positive (HR+), human epidermal growth factor receptor-2 (HER2)-negative (HR+/HER2-) advanced-stage breast cancer (aBC). Breast cancers with no expression of HER2 are recently classified into two groups: HER2-Zero subtype which include those with HER2-immunohistochemistry (IHC) score of 0 (IHC-0) and "HER2-low", defined as HER2-IHC score of 1+ or (2+ with negative in situ hybridization (ISH) assay). There is increasing interest in the HER2-low subtype which is becoming a new distinct entity with promising data from recently reported clinical trials using novel anti-HER2 antibody-drug conjugates (ADC) in this subgroup. This study investigates the differences in treatment outcomes between patients with aBC with HER2-low versus those with HER2-Zero (IHC-0) disease treated with CDK4/6 inhibitors and endocrine therapy (ET). Methods: We retrospectively reviewed patients with (HR+/HER2-) aBC who received CDK4/6 inhibitors with an aromatase inhibitor (AI) or fulvestrant from June 2017 to May 2020 at a single cancer center. Data was extracted from patients' electronic medical records and from our institutional cancer registry. Progression-free survival (PFS), defined as the time from the initiation of CDK4/6 inhibitors to the date of radiological or clinical progression or death, and was estimated by the Kaplan-Meier method and compared by the log-rank test. Multivariate Cox regression modeling was performed with covariates including progesterone receptor (PR) status, prior

chemotherapy, site of metastasis (visceral versus bone-only disease), line of treatment (first-line or beyond), menopausal status, age (less than or \geq 45) and number of metastatic sites (< or \geq 3). P-value < 0.05 was considered statistically significant. Results: During the study period, a total of 256 patients with advanced-stage breast cancer who received ET and CDK4/6 inhibitors (ribociclib in all patients) were included, median age was 48 (22-87) years. Majority (n=162, 63.3%) received ribociclib as a first-line therapy while the others had it as a second line and beyond. 136 (53.1%) patients had de novo metastatic disease, and 122 (47.7%) were premenopausal. In total, 114 (44.5%) of the patients were HER2-Zero (IHC-0), while 142 (55.5%) others had HER2-low disease as defined above. The overall response rate (ORR) for the HER2-Zero group was 52% versus 39% for the HER2-low group (P= 0.005). The median PFS was 23.0 (95% confidence interval [CI], 19-40) months for HER2-Zero versus 17.0 (95% CI 14-20,) months for HER2-low; P= 0.0035. In multivariate analysis, HER2-low expression remained significant determinant of inferior PFS after adjusting for other factors including the line of treatment (aHR:2.10, 95% CI 1.03-4.27, P=0.041) , age (aHR 2.20, 95% CI 1.29-3.77, P=0.004) , number of metastasis (aHR:1.96, 95% CI 1.32-2.91, P=0.001), and site of metastasis (aHR:1.64, 95%CI 1.058-2.55, P=0.027). Conclusion: In patients with advanced-stage breast cancer treated with CDK4/6 inhibitors and ET, level of HER2 negativity may affect treatment outcomes; patients with HER2-Zero had better PFS compared to those with HER2-low disease. These findings, if confirmed in larger studies, should help oncologists select patients with HER2-low for better treatment options including a combination of anti-HER2 therapy and CDK4/6 inhibitors.

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7:00 AM - 8:15 AM

P4-07-34

CO2 laser, radiofrequency, and promestriene in treatment of genitourinary syndrome of menopause in breast cancer survivors. Clinical and histological aspects of a randomized control trial

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Background: 74% of women have urogenital symptoms classified as Genito-urinary Syndrome of menopause (GSM) during breast cancer treatment. Promestriene is effective and safe in the treatment of GSM. However, some women and oncologists are not comfortable with long-term use. Therefore, new options for and alleviating GSM have been considered, such as microablative fractional CO2 laser (CO2L) and microablative fractional radiofrequency (RF).

Objective: To compare the effect of promestriene, CO2L, and RF treatments of GSM in women with breast cancer in the use of antiestrogens therapy, concerning clinical and histological

findings of vulvar vestibule.

Methods: This is a secondary analysis of a Multi-arm randomized controlled trial (NCT04081805). Were eligible for the study 100 women with breast cancer using adjuvant endocrine therapy referring moderate to severe symptoms of GSM (itching, dyspareunia, fissures, thinning of vaginal rugae, and tropism reduction). After providing written informed consent, they were evaluated according to pre and post-treatment protocol by filling the VAS of GSM and by clinical evaluation including a standardized gynecological exam with vestibular biopsy. Women were then randomized to either CO2L, RF or promestriene groups. The CO2L and RF groups received 3 consecutive monthly outpatient vulvovaginal energy applications. The CT was oriented for domiciliary use of promestriene, 1g/d for 21 days and, subsequently, twi4 month seek for 4 months. The follow-up visit was performed 120 days after interventions and also included an evaluation of global patient impression of improvement (5 points Likert scale).

Results: 94 women were randomized as follows: 32 in the CO2L group, 32 in the RF and 30 in the promestriene. 70 patients concluded the treatment and had adequate pre and post-treatment material to analyze, 23 CO2L, 21 RF and 26 promestriene. Pre-treatment demographic and clinical data are presented on table 1.

The evolution of GSM according to each treatment is demonstrated on table 2. Was also reported a high satisfaction after the treatment protocol in all groups evaluated by Likert Scale: CO2L 4,783 (□0,518), RF 4,150 (□0,813) , CT 4,280 (□1.13), p=0,055.

The histological parameters were presented on table 3. Histological atrophy was surprisingly identified in only 4 women (5.7%), pre-treatment. No injuries to the histological structure of the vulvar vestibule or relevant clinical adverse events were identified post-treatments.

Conclusion: CO2L, RF, and promestriene provided significant and similar improvement of GSM in women with breast cancer using anti-estrogens. The use of energies did not cause structural tissue damage or relevant clinical complications.

Table 1. Clinical and demographic parameters before treatment

Table 1. Clinical and demographic parameters before treatment

Parameter	Laser (n=23)	Radiofrequency (n=21)	Promestriene (n=26)	P value
Age, mean (SD), y	52.43 (±8.14) ^{a,b}	51.00 (±5.18) ^a	56.65 (±9.17) ^b	0.039
Time since menopause, mean (SD), y	7.22 (±8.46) ^a	4.28 (±3.77) ^b	10.77 (±8.55) ^a	0.015
BMI, mean (SD), Kg/m ²	26.44 (±3.32)	28.85 (±5.37)	27.25 (±5.73)	0.361
Tamoxifen, n (%)	8 (34.78%)	7 (33.33%)	10 (38.46%)	0.930
Anastrozole, n (%)	15 (65.22%)	14 (66.67%)	16 (61.54%)	0.930
Sexual active, n (%)	17 (73.91%)	12 (57.14%)	19 (73.08%)	0.402
Smokers, n (%)	1 (3.84%)	1 (4.34%)	2 (9.52%)	

Mean (±standard deviation); BMI body mass index, Tukey test: Similar letters (a, b) mean similar results. Chi-Square

Mean (standard deviation); BMI body mass index, Tukey test: Similar letters (a, b) mean similar results. Chi-Square

Table 2. Evolution of GSM (VAS) after treatment with CO2L, RF, and promestriene

		CO ₂ L (n=23)	Radiofrequency (n=21)	Promestriene (n=26)	P value
Fissures	Pre	2.45 (±3.99)	3.0 (±3.93)	3.154 (±3.49)	group=0.431 time<0.000 group*time=0.711
	Post	0.318 (±1.12)	1.684 (±3.48)	0.783 (±1.85)	
Pruritus	Pre	1.54 (±3.26)	3.61 (±3.89)	2.61 (± 3.33)	group=0.037 time<0.001 group*time=0.909
	Post	0.27 (±0.76)	2.21 (±3.34)	0.95 (± 1.96)	
Dispareunia	Pre	7.27 (±3.65)	7.70 (± 3.78)	6.95 (± 3.45)	group=0.49 time<0.000 group*time=0.893
	Post	2.71 (±3.40)	4.07 (±4.08)	2.88 (±3.14)	
Tropism reduction	Pre	5.50 (± 2.87)	5.57 (± 3.24)	5.11 (± 3.41)	group=0.66 time<0.000 group*time=0.524
	Post	4.00 (±3.05)	3.31 (±2.33)	3.17 (± 3.14)	
Thinning of vulvar rugae	Pre	5.18 (±2.98)	5.52 (±3.28)	5.15 (± 3.40)	group=0.92 time<0.000 group*time=0.568
	Post	3.61 (±2.99)	3.26 (±2.55)	3.17 (±3.14)	

Mixed ANOVA. VAS - Visual Analog Scale of GSM Symptoms, values expressed in mean (SD)

Table 3. Histological parameters according groups and pre and post-treatment

Parameter	Treatment condition	CO ₂ L (n=23)	RF (n=21)	Promestriene (n=26)	P value
Epithelium					
1. Reduction of cell maturation n (%)	Pre	0/23 (0.00)	2/21 (9.52)	1 (3.85)	2.244 [#]
	Post	1/23 (4.55)	1/21 (4.76)	3/26 (11.54)	1.144 [#]
Comparison (pre and post)		-	1.00	0.625	
2. Medium thickness µm	Pre	2.35(±0.87)	2.52(±0.79)	2.55 (±1.10)	Group= 0.74 [§]
	Post	2.67(±0.94)	2.74 (±1.25)	2.31 (±0.75)	Time=0.46
					Group x time = 0.195
3. Presence of papillae n (%)					
Enhanced n (%)	Pre	16/23 (69.57)	11/21 (52.38)	18/26 (69.23)	0.396 [#]
	Post	13/23 (56.52)	8/21 (38.10)	12/26 (46.15)	0.470 [#]
Normal n (%)	Pre	7 (30.43)	10 (47.62)	8 (30.77)	0,396
	Post	10 (43.48)	13 (61.90)	14 (53.85)	0,470
Reduced n (%)	Pre	0 (0)	0 (0)	0 (0)	
	Post	0 (0)	0 (0)	0 (0)	
Comparison (pre and post)		0.508 [§]	0.581 [§]	0.146 [§]	
4. Hiperqueratosis n (%)					
	Pré	13/23 (56.52)	11/21 (52.38)	7/26 (26.92)	0.077 [#]
	Post	9/23 (39.13)	4/21 (19.05)	7/26 (26.92)	0.329 [#]
		0.289 [*]	0.065 [*]	1.00 [*]	
Stroma					
Number of vessels enhanced	Pre	12/23(52.17)	7/21(33.33)	14/26 (56.85)	Pre p = 3.27
Normal n (%)	Post	8/23(34.48)	5/21 (23.81)	11/26(42.31)	Post p=3.88
	Pre	10/23 (43.48)	13/21 (61.9)	12/26(45.15)	
Reduced n (%)	Post	14/23 (60.87)	16/21(76.19)	15/26 (57.69)	
	Pre	1/23 (4.35)	1(4.76)	0 (0)	
Comparison and post)	Post	1/23 (4.35)	0 (0)	0 (0)	
		0.234 [§]	0.824 [§]	0.514 [§]	

Disclosure(s):

Angela Flavia L. Waitzberg, n/a, N/A: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-07-35

Changes in Left Ventricular Global Longitudinal Strain in breast cancer patients receiving anti-HER2 and/or Adriamycin therapy and outcomes with early implementation of cardio-protective measures

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Background : The treatment of Human Epidermal Growth Factor -2 (HER2) positive breast cancer has advanced since Trastuzumab and subsequently Pertuzumab were introduced and approved as antibody-targeted therapy. With the incorporation of anti-HER2 therapy, cardiotoxicity poses a significant risk and is a well know side effect. This toxicity can increase with concomitant use of Anthracyclines. Left Ventricular Global Longitudinal Strain is assessed using speckle tracking analysis on 2D echocardiogram and a relative reduction in LV global longitudinal strain (GLS) of 10-15% from baseline appears to have specificity to predict downstream reduction in Left Ventricular Ejection Fraction (LVEF). There is growing use for identification of GLS changes in these patients and its incorporation into medical decision making that impacts oncological and cardiac care. **Methods :** We conducted an analysis of 200 patients receiving anti-HER2 therapy at Henry Ford Cancer institute from Jan 1, 2016 to June 1, 2022 to determine if there was a 10-15% reduction in GLS detected prior to a decrease in ejection fraction and if and how these detections resulted in the implementation of cardio protective measures and downstream effects on cancer therapy. **Results :** There were 198 patients with GLS and LVEF data. 175 patients (88.3%) completed one year of cancer therapy 107/198 patients (54%) had no change in GLS or LVEF. 91/198 patients (45%) had changes in GLS and or LVEF. 41/91 (45%) patients with LVEF decline did not have cardioprotective intervention implemented. Despite this, 34 (83%) of these patients completed cancer treatment. 50/91 (55%) patients did have cardioprotective interventions with 40 (78%) patients from this subgroup completing cancer treatment. 81% of patients with EF decline were able to complete treatment. 50% of patients with EF decline had EF recovery within 6 months of completion of cancer therapy. The odds of LVEF decline were 9.8 times higher for those with GLS decline (OR=9.0, p< 0.001). Patients with LVEF decline were more likely to have cardio preventive intervention (OR=18.8, p< 0.001). Multivariate analysis did not find an association between

cardiac risk factors such as hypertension, diabetes mellitus, smoking, obesity and hyperlipidemia with GLS decline. There was no disparity by race. Conclusion : Our study revealed that early changes in GLS and LVEF did not impact the completion of cancer treatment irrespective of implementation of cardioprotective measures.

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Hussna E. Abunafeesa, MD: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

P4-07-36

Chest-Wall and Nodal Irradiation in Non-Metastatic, Node Positive Breast Cancer Patients with Pathologic Complete Response After Neoadjuvant Chemotherapy and Surgery, in A Retrospective Cohort of Women Aged 45 Years and Younger.

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Purpose/Objective(s): Several randomized clinical trials and non-randomized studies have consistently shown that achievement of pathologic complete response (pCR) in the breast with negative axillary nodes is associated with excellent long-term outcomes. NSABP B-511 is a phase III trial aimed to determine if chest wall and regional nodal irradiation (CWRNI) post-op reduces invasive breast cancer recurrence-free interval in patients (pts) with positive axillary lymph nodes (LN) who achieve pCR after neoadjuvant chemotherapy (NAC). However, physicians might be biased towards avoiding enrollment of young patients (≤ 45 years) in this trial. Which in turn, could give way to this population becoming under-represented at the time of

determining the standard of care. Our primary objective is to determine if the omission of CWRNI is associated with an increased risk of recurrence in a young patient population. Materials/Methods: Data were obtained from two institutions in South Florida. Patients aged \leq 45 years, with non-metastatic invasive breast cancer, and positive clinical (LN) involvement, diagnosed between 2010 to 2017 and treated with NAC were identified through retrospective chart review. Disease recurrence including local and distant recurrence data were collected. The Kaplan-Meier survival function was used for plotting patients treated with CWRNI vs no CWRNI and the log-rank test was used to evaluate the recurrence-free survival according to groups. We reported recurrence probabilities at 5 years. Additionally, we also estimated hazard ratios (HRs) of patients treated with CWRNI vs no CWRNI using Cox proportional hazards regression analysis. Results: A total of 154 patients were identified. Median age was 39 years (24-45). Patients were 57% ER+, 33% HER2+, 29% triple negative and 59.1% were stage 3, with only 1 male patient in the cohort. pCR was achieved in 22.1% (34/154) of pts, and CWRNI frequency in these patients was 81.3%. Overall, 79.9% of pts received post-op CWRNI. Recurrence frequency in patients with a pCR who received CWRNI was 4/26 vs 2/6 in pts that did not receive CWRNI. The Kaplan-Meier survival curves indicated an overall probability of recurrence at 5 years of 31.9% (95%CI 3.8% – 51.8%) in patients that did not receive CWRNI vs 27.49% (95%CI 18.42% – 35.56%) in patients that received CWRNI (log rank $p=0.55$) however, statistical significance was not met. Cox regression indicated that omission of CWRNI was not associated with an increased risk of recurrence (HR 1.3, 95%CI 0.54 – 3.11, $p=0.55$). In patients that had a pCR after NAC, omission of CWRNI was not associated with an increased risk of recurrence (HR 2.004, 95%CI 0.36 – 10.9, $p=0.42$). However, the sample size for these analyses was too small to achieve significance. Conclusion: This data highlights the tendency of giving CWRNI to younger patients with clinically node-positive disease at diagnosis regardless of response to NAC. Overall, absolute recurrence in this cohort was very low. Although an absolute number of recurrences favored CWRNI in the setting of pCR, this was not statically significant given the small sample size.

Disclosure(s):

Danielle cerbon, MD: No financial relationships to disclose
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7:00 AM - 8:15 AM

P4-07-37

A UK study exploring the attitudes and experience of patients living with metastatic breast cancer with regard to clinical research: A patient advocate-academic collaborative study

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Background: Clinical trials are key to improving outcomes in metastatic breast cancer (MBC). However, participation is low. Little data exists regarding the attitudes and experiences of patients in relation to clinical research. This study co-developed by a patient living with MBC and researchers aims to explore the experiences and issues related to accessing and participating in clinical research. Material and Method: A mixed methods study consisting of an online survey and qualitative interviews. Participants responded to an online questionnaire which contained closed and open questions, this was live between 17th May 2021 and 30th November 2021. Qualitative interviews from a sample of patients who gave their consent were carried out between 15th August 2021 and 22nd November 2021. Descriptive statistical analysis of the quantitative results from the closed questions and thematic analysis of the qualitative data generated by the open-ended questions and interviews were utilised. Data were extracted on 1st December 2021. Results: 768 eligible responses were received (765 female, 2 male, 1 unknown gender). The greatest proportion of responders were aged 51-60 years (37%), 92% were white (n=708) and 45% employed (n=345). 31% (n=235) were diagnosed with MBC within the last year with 14% (n=107) >5 years ago. 86% (n=660) knew what a clinical trial was. With 23% (n=173) reported an oncologist raising trial participation while 32% (n=243) of

patients raising participation with their oncologist. Responses to such inquiries varied from positive and supportive to 'vague and dismissive'. Accessing new treatments (96%, n=737) and playing a more active role in own health (81%, n=619) would encourage trial participation while being unsure of potential benefits (43%, n=333) was the commonest reason for possible non-participation. Preferred sources of information on trials were a consultant (80%, n=612), nurse (61%, n=467) or trial database (29%, n=220). 36% (n=276) were willing to travel for a study increasing to 56% (n=430) if travel costs were covered, and 43% (n=306) would travel worldwide for a study. £0 to over £100 per month for travel was reported to be affordable. Of the 14% (107 of 768) who had taken part in clinical trials; 72% (n=77) found it a positive experience. Free text responses indicated this was related to additional/longer monitoring. The lack of information relating to trials was a recurring theme. 21 participants were interviewed for the qualitative sub study, with three complementary themes emerging from these namely (1) information about clinical trials/research, (2) barriers to participation and (3) research priorities. Conclusion: This large UK study provides insights into the experiences and attitudes of patients with MBC in relation to clinical research. It demonstrates that patients are keen to be involved in research but face barriers to inclusions. Key messages include the need to develop patient facing trial databases, the importance of clinical staff in the provision of study information and a willingness to travel for a trial but the need for financial support. Addressing the issues identified in this survey are key to ensuring MBC patients not only have opportunities to participate in clinical research but also the ability to take these opportunities up.

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Lesley Stephen, n/a: No financial relationships to disclose

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Carlo Palmieri, BSc MB BS PhD FRCP: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Research funding (Ongoing); Ellipses Pharma: Consulting Fees (e.g., advisory boards) (Ongoing); Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing), Research funding (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), onference fee and travel to conferences (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Terminated, January 3, 2022); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Research funding (Ongoing); Roche: Conference fee and travel to conferences (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing), Research funding (Ongoing)

12/8/2022

7:00 AM - 8:15 AM

P4-07-38

Real-world data of Advanced Breast Cancer (ABC) patients with HER2-positivity before the second-line therapy: data from the observational study GEICAM/2014-03 (RegistEM)

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Background: Over the last years, the treatment of HER2-positive (HER2+) breast cancer (BC) patients (pts) has been changing because of the development of new anti-HER2 agents. In the current analysis, we describe the features, treatment patterns, progression-free survival (PFS) and overall survival (OS) outcomes of BC pts with HER2 + (immunohistochemistry [IHC] 3+ or IHC 2+ and in situ hybridization [ISH]+), following ASCO/CAP 2018 guidelines in the most recent tumor lesion before the 2nd-line.

Methods: The RegistEM study is an ongoing BC registry study that is providing prospective data from around 1900 pts diagnosed with advanced BC (ABC) between 01/Jan/2016 and 31/Dec/2019, in 38 Spanish institutions from GEICAM network. In this analysis, 296 HER2+ BC pts have been included, representing the 18% of pts available in the database at the cut-off date (08/Apr/2022), with ABC diagnosis before 2019 (n=1559).

Results: At first ABC diagnosis, 58% (n=173) pts had recurrent disease (>36 months [mo] from initial BC diagnosis in 62%), 41% (n=120) de novo metastatic BC and 1% (n=3) unresectable locally ABC (ULABC); the median age was 58 years, 68% were postmenopausal and there was only 1 male pt. From total 296 pts, 66% had hormone receptor expression [HR+]; the BC subtype was assessed in tumor tissue from the breast (58%) or a metastatic lesion (34%), and in 8% pts, HER2 positivity was observed after the 1st-line. Family history of BC and/or ovarian cancer was reported in 28% pts, and a hereditary-risk genetic test was performed in 26% pts (n=74/282). Germline BRCA1/2 and TP53 genetic testing were reported in 14 and 26 pts

respectively, being mutated in 3/14 (21%) and 5/26 (19%) pts. Bone (50%), lymph nodes (49%), liver (35%), lung (31%), soft tissue (8%) and central nervous system (CNS), mostly in brain (8%), were the main metastatic sites. One hundred pts were diagnosed with CNS metastases: 24 at baseline, 48 during the 1st-line and 28 in subsequent lines. Additional data according to HR status and type of ABC are detailed in the table below, showing a worse prognosis in absence of HR expression. In HR- pts, bone metastases were less frequent and lymph nodes metastases more frequent compared to HR+ pts. Visceral disease was present in 69% (66% in HR+ and 74% in HR-; non-statistically significant) pts and ≈80% had ≤3 (54%, ≤2) locations involved. The most common therapies by line were: 1) 1st-line: Chemotherapy (CT) + biological therapy (BT) (38%), CT + BT+ endocrine therapy (ET) (35%), and ET + BT [11%]; 2) 2nd-line: BT (55%), CT + BT (20%) and ET + BT (15%); 3) 3rd-line: CT + BT (49%) and BT (31%). The median (95% confidence interval [CI]) progression-free survival (PFS) on 1st, 2nd and 3rd line was 18 (15-22), 8 (7-9) and 6 (5-8) mo, respectively. The median (95% CI) overall survival (OS) from ABC diagnosis was 43 (40-49) mo. These survival outcomes were higher in HR+ pts, however, the differences were only statistically significant in OS (p=0.006; log-rank). At database cut-off date, death was reported in 47% pts.

Conclusions: In spite of the anti-HER2 therapies administered in the advanced setting, the HR expression is a relevant prognostic factor, with a clinically and statistically significant impact in OS, improving the outcomes of HR+ pts.

	HR+ (n=191, 65%) Prior EBC 116 (60%) de novo MBC 75 (39%) ULABC 3 (1%)			HR- (n=104, 35%) Prior EBC 57 (56%) de novo MBC 45 (44%)			Prior EBC (n=173, 56%)			ULABC or de novo M1 (n=123, 42%)		
Time to recurrence in pts with prior EBC, n (%)												
≤ 12 mo	5 (4)			8 (14)			13 (7)					
> 12 to ≤ 24 mo	10 (9)			17 (30)			27 (16)					
< 24 to ≤ 36 mo	18 (15)			8 (14)			26 (15)					
> 36 to ≤ 60 mo	23 (20)			11 (19)			34 (20)					
> 60 mo	60 (52)			13 (23)			73 (42)			NA		
Visceral involvement, n (%)												
Yes	128 (66)			75 (73)			117 (57)			86 (70)		
No	64 (33)			27 (27)			55 (32)			36 (29)		
Unknown	2 (1)			0 (0)			1 (<1)			1 (<1)		
Number of metastatic locations, n (%)												
1	66 (34)			23 (23)			86 (50)			3 (2)		
2	41 (21)			29 (28)			43 (25)			27 (22)		
3	47 (24)			30 (29)			30 (17)			47 (38)		
≥ 4	40 (21)			20 (20)			14 (8)			46 (38)		
Location of metastatic sites, n (%)⁽¹⁾												
Bone	113 (58)			35 (34)			81 (47)			67 (54)		
Liver	67 (34)			35 (34)			53 (31)			49 (40)		
Lung	56 (29)			37 (36)			54 (31)			39 (32)		
Lymph nodes	83 (43)			81 (80)			55 (32)			89 (72)		
Soft tissue	14 (7)			11 (11)			29 (17)			5 (4)		
Central nervous system	12 (6)			12 (12)			19 (11)			5 (4)		
Line	1	2	3	1	2	3	1	2	3	1	2	3
n	193	122	77	100	62	42	170	115	77	123	69	42
Pts reaching the next line, n (%)	122 (63)	77 (63)	54 (70)	62 (62)	42 (68)	21 (50)	115 (68)	77 (67)	49 (60)	69 (56)	42 (61)	29 (69)
Deaths, n (%)	21 (11)	13 (11)	12 (16)	14 (14)	15 (24)	10 (24)	21 (12)	20 (17)	16 (21)	14 (11)	8 (12)	6 (14)
Therapies by line, n (%)												
ET*†	36 (16)	25 (20)	7 (9)	3 (3)	3 (5)	-	22 (13)	15 (13)	6 (8)	11 (9)	13 (19)	1 (2)
ET	17 (8)	4 (3)	2 (2)	0 (0)	-	-	16 (9)	2 (2)	1 (1)	1 (<1)	2 (3)	1 (2)
CT‡/B‡/ET	97 (50)	5 (4)	2 (2)	4 (4)	-	-	51 (30)	4 (3)	-	50 (40)	1 (1)	2 (5)
CT‡/B‡	36 (19)	21 (17)	36 (47)	76 (76)	15 (24)	22 (52)	55 (32)	29 (25)	30 (39)	57 (46)	7 (10)	28 (67)
CT	5 (2)	7 (6)	10 (13)	2 (2)	3 (5)	3 (7)	5 (3)	9 (8)	12 (15)	2 (2)	1 (1)	1 (2)
BT	8 (4)	60 (50)	20 (26)	15 (15)	41 (66)	17 (4)	21 (12)	56 (49)	28 (38)	2 (2)	45 (65)	9 (21)
The most frequent therapies, n (%)												
Taxane followed by AI + T2M + P2M	56 (29)	1 (<1)	-	3 (3)	-	-	32 (19)	1 (<1)	-	30 (24)	-	-
Taxane followed by other ET + T2M + P2M	28 (14)	-	-	-	-	-	16 (9)	-	-	12 (10)	-	-
CT followed by ET (AI or TMX) + T2M	5 (3)	1 (<1)	1 (1)	-	-	-	2 (1)	-	-	3 (2)	1 (1)	1 (2)
CT + T2M + P2M	28 (14)	9 (7)	5 (6)	62 (62)	5 (8)	2 (5)	36 (21)	11 (10)	3 (4)	54 (44)	4 (6)	3 (7)
CT + T2M	5 (3)	2 (2)	8 (10)	7 (7)	3 (5)	14 (33)	11 (6)	3 (3)	12 (16)	1 (<1)	1 (1)	10 (24)
CT + Lapatinib	-	8 (7)	19 (25)	2 (2)	5 (8)	6 (14)	2 (1)	11 (10)	12 (16)	-	2 (3)	13 (30)
CT + B2M	2 (1)	1 (<1)	1 (1)	2 (2)	-	-	2 (1)	1 (<1)	1 (1)	2 (2)	-	-
CT (single agent or in combination)†	5 (3)	7 (6)	10 (13)	2 (2)	3 (5)	3 (7)	5 (3)	9 (8)	12 (16)	2 (2)	1 (1)	1 (2)
ET* (mostly as single agent)	17 (9)	4 (3)	2 (3)	-	-	-	16 (9)	2 (2)	1 (1)	1 (<1)	2 (3)	1 (2)
ET (AI, TMX or Fulvestrant) + T2M	13 (7)	5 (4)	2 (3)	2 (2)	1 (2)	-	8 (5)	3 (3)	2 (3)	7 (6)	3 (4)	-
ET + T2M + P2M	-	7 (6)	-	-	2 (3)	-	-	4 (3)	-	-	5 (7)	-
ET + T-DM1	2 (1)	2 (2)	1 (1)	-	-	-	2 (1)	-	1 (1)	-	2 (3)	-
ET (AI or SERD) + CDK4/6i	12 (6)	2 (2)	4 (5)	1 (1)	-	-	11 (6)	1 (<1)	3 (4)	2 (2)	1 (1)	1 (2)
Anti-HER2 blockade** (single agent or in combination)‡	8 (4)	59 (48)	18 (23)	15 (15)	41 (66)	17 (40)	21 (12)	55 (48)	26 (34)	2 (2)	45 (65)	9 (21)
Median duration of treatment, mo	16	7	6	14	7	4	14	6	5	23	8	5
TTP (mo), median (range)	14 (0-64)	7 (0-58)	6 (0-18)	12 (1-63)	8 (0-27)	3 (2-12)	13 (0-63)	6 (0-58)	5 (0-17)	17 (1-64)	8 (0-36)	6 (1-18)
Median PFS mo (95% CI)	22 (16-25)	8 (7-11)	6 (6-9)	15 (12-18)	8 (5-9)	4 (3-6)	15 (13-17)	8 (6-9)	5 (4-7)	24 (18-32)	10 (8-14)	6 (4-9)
Median global OS mo (95% CI)	48 (42-52)			37 (31-42)			42 (37-49)			45 (40-51)		

HR: hormone receptor; EBC: early breast cancer; ULABC: unresectable locally advanced breast cancer; M1: metastatic; mo: month; ET: endocrine therapy; BT: biological therapy; CT: chemotherapy; T2M: trastuzumab; P2M: pertuzumab; AI: aromatase inhibitor; TMX: tamoxifen; B2M: bevacizumab; TTP: time to progression; PFS: progression-free survival. ⁽¹⁾ Percentages of the total of metastatic locations diagnosed. *ET includes aromatase inhibitors or selective estrogen receptor degraders. **This therapy is based on T-DM1 as a single agent in the majority of pts. †Predominantly as a single agent in 2nd line and only as a single agent in 3rd line. ‡T-DM1 in > 60% pts in 2nd line and ≥ 50% in 3rd line.

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P4-07-39

NEOADYUVANT TREATMENT IN THE COVID ERA

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Since Coronavirus Disease 2019 (COVID-19) was declared pandemic in March 2020, there have been 545.226.550 cases up to 4 July 2022 (1). Several studies concluded that patients (pts) with cancer are at increased risk of COVID-19 infection, morbidity and mortality. Those undergoing neoadjuvant treatment are at particularly risk of disease progression if chemotherapy or surgery are delayed. Also, is known that a higher NLR (neutrophil to lymphocyte ratio) is related to worse outcomes (3). Our hospital is located at the Northwest of Spain and in the last months we noticed a never seen number of infections in cancer population. The aim of this study is to evaluate the severity of COVID-19 and its impact on chemotherapy and surgery delay in pts undergoing neoadjuvant chemotherapy breast cancer.

METHODS:

We conducted a ambispective, unicenter, observational study of breast cancer pts, treated with neoadjuvant chemotherapy, between March 2020 and May 2022 at University Hospital A Coruña (Spain). We analyzed type of infection, need of hospitalization, chemotherapy and surgical delay, and its association with tumor type; BRCA germline mutation; clinical stage; treatment; vaccination status; and neutrophils, lymphocytes, and NLR before COVID-19 disease.

RESULTS:

During the study period, from 1 March 2020 to 31 May 2022, 183 pts underwent neoadjuvant chemotherapy. A total of 23 (12.5%) pts experienced COVID-19 infection, of which 21 were diagnosed between January and May 2022. The median age was 47,91 years [range 33 – 69 years]. Luminal B HER 2 negative comprised the most common molecular subtype (40.9%), followed by Triple Negative (36.4%), Luminal B HER 2 positive (13.6%), and HER 2 enriched (9.1%). Germline mutations in BRCA account for 13.6% pts. At diagnosis, 4.5%, 72.7%, and 22.7% had stages I, II, and III respectively. Chemotherapy treatments included: paclitaxel followed by Adryamicine-Cyclophosphamide (AC) (45.4%); carboplatin – paclitaxel – trastuzumab - pertuzumab (18,2%); carboplatin – paclitaxel followed by AC (18,2%); KEYNOTE-756: pembrolizumab/placebo - paclitaxel followed by AC (13.7%); and paclitaxel – trastuzumab – pertuzumab followed by myocet – cyclophosphamide – trastuzumab - pertuzumab (4.5%). The association of G-CSF occurred in 9 pts (40.9%). 22 pts were fully vaccinated, 8 pts (36.4%) with two doses and 13 pts (59.1%) with three doses. 77.3% pts experienced mild respiratory symptoms with 9.1% hospitalizations. The median duration of delays was 15 days for chemotherapy and 29,58 days for surgery.

NLR percentil 25 was associated with COVID-19 type of infection. For those pts with a lower rate, infection was asymptomatic and for those with a higher rate symptoms were moderate ($X^2= 5,119$, $p = 0,024$).

CONCLUSIONS:

COVID-19 disease become a high prevalent infection in pts undergoing neoadjuvant breast cancer chemotherapy. Most pts are fully vaccinated and experienced an indolent infection. NLR is an easily measurable and cost-effective parameter that could be useful as a prognostic marker of severity in COVID-19. We will continue to follow-up these pts to see the impact of chemotherapy or surgery delay in pathological complete response and disease-free survival until the congress in December 2022.

BIBLIOGRAPHY:

1. WHO Coronavirus (COVID-19) Dashboard [Internet]. world health organization. 2022 [3rd July 2022]. Disponible en: <https://covid19.who.int>.

2. Yekedüz E, Utkan G, ÜrÜN Y. A systematic review and meta-analysis: the effect of active cancer treatment on severity of COVID-19 [Internet]. European Journal of Cancer. 2020. [24th June 2022]. Disponible en:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7538140/pdf/main.pdf>

3. Jimeno S, Ventura PS, Castellano JM, García-Adasme SI, Miranda M, Touza P, et al. Prognostic implications of neutrophil-lymphocyte ratio in COVID-19 [Internet]. Eur J Clin Invest. 2021. [22th June 2022]. Disponible en: <https://onlinelibrary.wiley.com/doi/10.1111/eci.13404>.

TABLE 1: Clinical characteristics of patients

Characteristics	N=22 (%)
Age	
- Median (range)	47,91 (33-69 years)
Gender	
- Female	22 (100%)
- Male	0 (0%)
Molecular subtype	
- Luminal A	0 (0%)
- Luminal B HER2 Positive	3 (13,6%)
- Luminal B HER2 Negative	9 (40,9%)
- HER2 Positive	2 (9,1%)
- Triple Negative	8 (36,4%)
BRCAG mutations	
- BRCAG wild type	12 (54,5%)
- BRCAG mutation	3 (13,6%)
Type of chemotherapy	
- Paclitaxel weekly x12 --> AC x4	9 (40,9%)
- Paclitaxel weekly x12 --> AC x4 DD	1 (4,5%)
- Carboplatine d1 Paclitaxel d1, d8 Trastuzumab d1 Pertuzumab d1 x6	4 (18,2%)
- Carboplatine Paclitaxel x4 --> AC x4	4 (18,2%)
- CT keynote 756	3 (13,6%)
- CT Carabela	1 (4,5%)
- Paclitaxel weekly – trastuzumab – pertuzumab x4 - -> myocet – cyclophosphamide – trastuzumab - pertuzumab x4	0 (0%)
Clinical Stage	
- Stage I	1 (4,5%)
- Stage II	16 (72,7%)
- Stage III	5 (22,7%)
G-CSF (before or after COVID infection)	
- No	13 (59,1%)
- Yes	9 (40,9%)
Vaccination Status	
- Unvaccinated	1 (4,5%)
- One dose	8 (36,4%)
- Two doses	13 (59,1%)
- Three doses	13 (59,1%)
- Four doses	0 (0%)

TABLE 2: Blood cell count in percentils

	Blood Cell Count	N=22
25th percentil		
- Neutrophils (n/ml)	1765	4
- Lymphocytes (l/ml)	1252	5
- NLR	1,37	5
50th percentil		
- Neutrophils (n/ml)	2950	11
- Lymphocytes (l/ml)	1735	11
- NLR	1,70	11
75th percentil		
- Neutrophils (n/ml)	3650	17
- Lymphocytes (l/ml)	2155	17
- NLR	2,52	17

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7:00 AM - 8:15 AM

P4-07-40

Magnetic resonance imaging (MRI) and clinicopathological analysis of triple-negative breast cancer (TNBC) patients (pts) treated with primary anthracyclines(A)/taxanes(TX)-based chemotherapy.

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Background Radiological complete response (CR-MRI) to neoadjuvant chemotherapy (NAC) by MRI predicts pathologic complete response (pCR) rates in pts with TNBC treated preoperatively with A/TX-based regimens and in some studies, it correlates with disease-free survival (DFS). The main aim of this study was to assess the relevance of the MRI response to primary chemotherapy associated with clinical stage and HER2 expression (Zero vs Low), in a cohort of 143 TNBC pts treated with A and TX +/- carboplatin (CP) in the NAC setting. Methods Retrospective study of pts treated with NAC for TNBC between January 2002 and June 2021, who underwent MRI to assess tumour response before NAC, after 4 cycles of anthracycline and cyclophosphamide (AC) and after TX. Survival analysis was based on the Kaplan-Meier and survival curves were compared using the log-rank test. A p value of less than 0.05 was considered as statistically significant. Results A total of 143 TNBC pts with a median age of 52 years; 7, 63 and 73 pts had stage I, II and III disease, respectively. The NAC regimen consisted in 117 pts 4 cycles of AC followed by TX and in 24 pts the same adding CP (in 21 pts with non-CR-MRI, 2 with CR-MRI and 1 without MRI after AC). PCR was observed in 41%. Of 30 pts with CR-MRI after AC, 83% obtain a pCR ($p < 0.001$), and of 52 pts with CR-MRI at the end of NAC, 70.7% obtain a pCR ($p < 0,001$) of which 90% had a CR-MRI after AC. Adding CP

increased pCR by 6% ($p=0.564$). According HER2-zero vs low expression, the pCR was 38% and 47% respectively, with no significant differences. With a median follow-up of 60 months, 34% recurred and 16% died of TNBC. In pts with pCR, the DFS at 5 years (y) was 96% and 47% for pts without pCR ($p < 0.001$), with a DFS of 91% if CR-MRI at the end of NAC and 48% if non-CR-MRI ($p < 0.001$). In HER2-Zero tumours the DFS at 5 y was 64% vs 66% in HER-2 low. Interestingly, overall survival (OS) at 5 y was 72% in HER2-Zero and 84% in HER2-low ($p=0.080$). Conclusions Performing serial MRI in the course of NAC in TNBC may be a reliable indicator of pCR, adding platinum to TX in pts with CR-MRI may increase pCR rate. HER2-Zero expression in TNBC, seems to confer worse OS rates.

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7:00 AM - 8:15 AM

P4-07-41

Is axillary evaluation still necessary in DCIS?

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Background Ductal carcinoma-in-situ (DCIS) is a growing health problem in the world. Before the advent of screening mammography, the incidence of DCIS was low, and patients presented with DCIS that had become clinically symptomatic. Upon this evidence, a strategy of aggressive surgical therapy like the approach with invasive cancer was adopted. The status of the regional lymph nodes is the most important prognostic factor and predictor of survival in breast cancer, but as DCIS is a malignant proliferation of the epithelial inside the breast duct and, therefore, does not have the capacity to generate metastasis. However, an upstaging after surgery is possible. The need for sentinel node biopsy (SNB) in patients with a preoperative biopsy diagnosis of DCIS is still controversial but is done in selected cases. Objectives Our main objective in this study was to evaluate the surgical approach in the axilla (SNB or axillary dissection – AD) of patients diagnosed with DCIS in a single institution and describe the surgical treatment (mastectomy or breast conservative surgery – BCS). In addition, we aimed to find the reasons that led our surgeons to choose one or the other treatment. Methods A retrospective analysis was made using the Pérola Byington Hospital's database, from January 2011 to December 2019. During this period, 11,373 cases of breast cancer were treated in the institution and 812 (7.4%) were DCIS. Data was available and we could analyze 494 patients who underwent core biopsy or vacuum-guided biopsy guided by mammography or ultrasound and were diagnosed with DCIS and underwent surgical treatment at the Hospital. We grouped the patients into 3 age groups: under 40, 40-49, and 50 and over. In all groups, we had patients who underwent SNB using the patent blue technique or axillary dissection (AD) and were evaluated using the H&E method. We had also evaluated the type of surgery (BCS or

mastectomy) in each age group. Results DCIS was diagnosed through mammographic alterations in 62% of all cases and nuclear grade 2 was the most common, with 47%, followed by grade 3 and 1, 46% and 4%, respectively. In 2% of cases the data was missing. Comedonecrosis was present in 78% of our specimens. The type of surgery (radical or BCS) was evaluated and BCS was made in 360 patients (72,87% of the cases), with the axillary approach being performed in 125 patients of these patients (50,20% of cases that went to axillary approach including 9 patients that were submitted to AD). In 27,1% the surgical approach was a radical surgery (total mastectomy or skin sparing mastectomy) and in this group 92,5% were submitted to axillary approach. There was a strong correlation in the type of surgery and axillary approach (p-value 0,000) In the group of patients younger than 40 years, 74% of patients (17 out of 23 in total) underwent an axillary approach regardless of the type of surgery (p-value 0.036) When evaluating the predetermined age groups, we saw that most of our patients were 50 years or more (69%), followed by patients between 40-49 years (26%) and 5% in patients under 40 years. In only 3% of cases (16 in 494) we reclassified the lesion as invasive carcinoma after the surgery. None of them had a lymph node involved by malignant cells after surgery and that's include the cases reclassified as invasive carcinoma. Conclusion The results obtained in this analysis showing no axillary involvement will make us rethink the indications for the concomitant surgical approach of the breast and the axilla in cases with a diagnosis of DCIS to reduce the axillary surgical overtreatment. It was not our goal to compare the costs, mobility, and complications of the surgical treatment as the survival in these patients that can be addressed in another studies.

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P4-07-42

Intervention to Distant Metastatic Lesions in Patients with Breast Cancer

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INTRODUCTION

Approximately one-fourth of patients presenting with early-stage breast cancer develop distant metastatic disease, a prominent cause of mortality. The role of metastasis-directed intervention is still uncertain in this cohort. The aim of this study is to evaluate whether intervention to metastatic lesions impacts overall survival (OS) and post-distant recurrence survival (PDRS), defined as survival after first occurrence of metastatic disease.

METHODS

Our prospectively maintained international multi-center database of patients diagnosed with distant recurrence was retrospectively reviewed. Patients initially presenting with stage I-III breast cancer and diagnosed with metastatic disease to the bone, liver or lung from 2014-2020 were divided into cohorts receiving intervention to their metastases (IM, n=180) versus no interventions to their metastases (NI, n=120). The characteristics of the patients were compared with X2 test. OS curves were calculated by Kaplan-Meier method and multivariable analysis by Cox regression. Statistical significance was set at $p < 0.05$.

RESULTS

No significant differences in OS and PDRS were noted between the two groups when comparing age at diagnosis, menopausal status, tumor histopathology, pathological stage, axillary lymph node involvement, and hormone receptor and HER2 status. However, median OS and PDRS were significantly longer for patients who received IM compared to those who did not. The hazard of death was 59% lower with IM than with NI for both OS (HR 0.59: 95% CI 0.42 – 0.83; p=0.002) and for PDRS (HR 0.59: 95% CI 0.42 – 0.84). On multivariable analysis, OS was improved among patients with IM, and among those with lung metastases, compared to liver and bone metastases.

CONCLUSIONS

Metastatic site intervention had both an OS and PDRS benefit in this cohort. In order to explore the potential for interventions to their metastases, patients who develop limited metastatic disease following initial breast surgery should be discussed at a multidisciplinary tumor board.

Post-Distant Recurrence Survival in Patients with Breast Cancer Receiving Intervention to Metastatic Lesions (IM) Versus No Intervention (NI)

	N	Death	Median (months)	HR (95%CI)	P
IM	180	75	47	0.59 (0.42-0.84)	0.003
NI	120	59	24	Ref	-

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Effect of acupuncture and exercise therapy in rehabilitation of physical dysfunctions in breast cancer survivors: randomized clinical trial

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Introduction: The treatment of breast cancer can trigger physical dysfunctions and psychological difficulties such as pain, depression, limitation of upper limb function and shoulder range of motion (ROM) deficits. Exercise therapy is a treatment well established in the literature for these disorders and another form of treatment is acupuncture. However, most studies using acupuncture only assess pain. Objective: To compare three distinct rehabilitation treatments (exercise therapy, acupuncture and Stiper®) in women undergoing breast cancer surgery, assessing pain, depression, upper limb function and range of motion parameters (ROM). Methods: Seventy-nine women with pain above 3 on the visual analogue pain scale (VAS) and with more than 90 days of surgery were included. They were divided into three groups that received weekly treatment for 10 weeks: group I (G1) treated with standard, pre-defined exercise therapy, based on stretching of the cervical muscles, shoulder girdle and shoulder ROM exercises with a duration of 30 minutes, group II (G2) treated with 30 minutes of acupuncture using predefined points and group III (G3) treated with the same acupuncture points as group II, however, using the Stiper® (silicon oxide micronized quartz pellet) in place of needles. Results: Sixty-seven patients completed the treatment, being 26 from G1, 23 from G2 and 18 from G3. There was an improvement of pain over time in all groups (first session compared with the fifth ($p < 0.001$) and with the tenth ($p < 0.001$), but not between groups. There was a statistically significant difference in depressive symptoms using the Beck questionnaire over time in the three groups (between the first and tenth sessions ($p = 0.001$), between the first and fifth sessions ($p = 0.052$), but not between groups. Regarding the DASH questionnaire for shoulder function, there were significant differences overtime at all evaluated moments ($p < 0.001$), but not between groups. There was a statistically significant difference in ROM over time in the three groups, but not between groups. Conclusion: The rehabilitation of physical dysfunctions in women who survived breast cancer through exercise therapy, acupuncture and Stiper® in pain, depression, upper limb function and ROM, proved to be

effective, without statistically difference between the groups, which in leads to the conclusion that acupuncture don't showed the superiority of results when compared with exercise therapy, thus being an effective approach in the rehabilitation of these women.

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Association between tissue mobilization with physical exercise and physical exercise alone in patients with axillary web syndrome who underwent breast cancer surgery

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Abstract Introduction: Axillary web syndrome (AWS) is a complication in women with breast cancer and occurs immediately after axillary surgery. It is characterized by pain, limited shoulder range of motion (ROM), and presence of cords. Objectives: This study aimed to evaluate the impact of physical therapy interventions, such as physical exercise with tissue mobilization and exercise alone. Methods: A randomized clinical trial was conducted at the Division of Breast Cancer disease of the Universidade Federal de São Paulo. Seventy-three women with AWS were randomized into the mobilization (ME) group (N=37) and exercise (E) group (N=36) and followed up for 3 months after breast cancer surgery. Both groups were provided with specific guidelines for performing regular shoulder exercise at home, while tissue mobilization was performed in a specific group with a maximum of six sessions, according to the patient's need. ROM, pain, and presence of cords were evaluated in each postoperative period (PO). Results: In both treatment groups, at the end of 90 days, improvement in flexion was observed as well as less pain and number of cords. In terms of abduction, the E group was better than the ME group. Conclusions: Physical exercise after breast cancer surgery is extremely important for functional recovery, resumption of activities of daily living, improvement of pain, and reduction in the number of cords. Tissue mobilization appears as an adjunct for causing a more immediate improvement in ROM, pain, and presence of cords, but at times not sustaining the gains for the following PO. Keywords: breast neoplasms, axillary web syndrome, physical exercise, articular range of motion, pain

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Treatment strategies for advanced triple negative breast cancer patients as per routine clinical practice: analysis from the observational study GEICAM/2014-03 (RegistEM)

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Background: Triple negative breast cancer (TNBC) is well known for its more aggressive course and poorer prognosis compared to other BC subtypes. RegistEM study provides real world data to understand the distribution of BC subtypes in the advanced setting, being its primary objective. Biological samples collection is part of its procedures. This is a non-interventional cohort study and 1,907 patients (pts) have been enrolled up to now (females and males) with advanced BC (ABC), diagnosed from Jan-2016 to Dec-2019, either after recurrence or as first BC diagnosis, in 38 Spanish sites. These pts will be followed for at least 5 years.

Methods: In the current analysis (cut-off date 08/April/2022, database ongoing), we describe characteristics, treatment patterns and outcomes, including comparison between recurrent and de novo disease, of 157 pts with advanced TNBC included in the RegistEM study. Those pts represent the 10% of pts available in the database at the cut-off date and with ABC diagnosis up to December 2018 (n=1559). The BC clinical subtypes were histologically confirmed on the most recent tumor lesion (metastatic [M] or primary BC) before starting with the 1st-line therapy.

Results: At first ABC diagnosis, 73% pts had recurrent early BC (EBC), 26% de novo MBC and 1% unresectable locally ABC (ULABC). Median age was 57 years (range 30-88), all pts were women, 98% Caucasian and 65% postmenopausal. Family history of BC and/or ovarian cancer was reported in 37% pts, and a hereditary-risk genetic test was performed in 59 of 147 pts. Germline BRCA1/2 and TP53 were the most frequently mutated genes, 21% (6/28) and 47%

(8/17) pts, respectively. Visceral involvement was present in 69% pts (similar between recurrent EBC and de novo ABC, although brain metastases were only present in the recurrent EBC group), and ≤ 2 metastatic locations in 59%. In 61% (70/115) pts with recurrent EBC, the subtype was assessed in metastatic lesions, and 39 pts of them also had TN subtype in primary BC. In terms of the most frequent therapies by line: 1) 1st-line: chemotherapy (CT) (60%) and CT/biological therapy (BT) (39%). Of the 87 pts with CT alone, monotherapy was the preferred option in 57% pts (capecitabine 25%, taxanes 16%, and eribulin or vinorelbine, 5% each). Bevacizumab was the most frequent BT (79%) combined with CT (single agent in 56% pts, mostly taxanes and capecitabine). Progressive disease (PD) was reported in 85% pts (similar in pts with both recurrent and de novo MBC or ULABC); 2) 2nd-line: CT (79%) (monotherapy capecitabine, eribulin, taxanes) and CT/BT (17%) (CT-containing bevacizumab 82%). Progression was reported in 92% pts; 3) 3rd-line: CT (90%) (eribulin 33%, platinum-based 25%) and CT/BT (9%) (CT-containing bevacizumab 67%). Progression was reported in 88% pts. At database cut-off date, death was reported in 133 (85%) pts, mainly because of PD. Overall survival (OS) was similar between both groups, recurrent and de novo MBC. Conclusion: In this population of Spanish TNBC pts with ABC, three quarters had recurrent disease. De novo ABC pts had a higher proportion of non-visceral metastases, with absence of brain involvement at the first diagnosis. Single-agent CT and CT plus bevacizumab were the most frequent therapies, and OS was similar between recurrent and de novo MBC pts, although numerically higher in the later group.

	Recurrent EBC n=115 (72%)			ULABC, n=1 (1%) de novo MBC, n=81 (26%)		
TNM stage at EBC diagnosis, n (%)				NA		
I	19 (17)					
II	37 (30)					
III	29 (25)					
IV	5 (4)					
Time to recurrence, n (%)				NA		
0-12 mo	10 (9)					
13-24 mo	45 (39)					
25-36 mo	15 (13)					
> 36 mo	45 (39)					
Median time to ABC (interquartile range), mo	21 (14-32)			NA		
Location of metastatic sites, n (%)						
Brain	37 (33)			12 (28)		
Bone	25 (22)			12 (28)		
Liver	40 (35)			21 (50)		
Lung	49 (43)			30 (68)		
Lymph nodes	16 (14)			3 (7)		
Soft tissues	18 (16)			0		
Brain	18 (16)			0		
Line	1	2	3	1	2	3
n	108	73	52	40	28	16
Pts who reach next line, n (%)	73 (69)	52 (71)	35 (60)	28 (70)	16 (57)	7 (44)
Deaths, n	24	20	21	7	9	9
Therapies by line, n						
CT	1 (oncologic)	-	-	-	-	-
CT/BT	42	11	4	15	6	2
CT/BT	42	59	47	15	21	14
BT	1 (single-agent)	3	1	-	-	-
The most frequent therapies, n						
Capecitabine	21	16	3	1	4	3
Platinum-based CT	14	14	6	5	3	5
Taxane	10	3	1	4	4	1
Capecitabine + Bevacizumab	10	4	0	0	2	0
Taxane + Bevacizumab	9	2	3	5	1	0
Taxane + immunosuppressant inhibitor	7	0	0	0	0	0
Eribulin	4	14	10	0	1	2
Vinorelbine	4	3	6	0	1	0
Sequential anthracycline + taxane	0	0	0	6	0	0
Median treatment duration, mo	4	3	3	5	3	3
TTP (mo), median (range)	5	3	3	8	3	4
Median PFS, mo (95% CI)	(0-47)	(0-37)	(0-35)	(1-31)	(0-22)	(0-10)
Median Follow Up, mo (range)	(4-7)	(1-4)	(2-4)	(7-9)	(2-5)	(1-8)
Median OS, mo (95% CI)	21 (14-32)	21 (14-32)	21 (14-32)	28 (15-36)	28 (15-36)	28 (15-36)

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7:00 AM - 8:15 AM

P4-07-46

The Out-of-Pocket Cost of Breast Cancer Care in Nigeria: A Prospective Analysis

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Introduction A major barrier to timely breast cancer diagnosis and care in Nigeria is attributable to the out-of-pocket cost of accessing healthcare services, despite the presence of a National Health Insurance Scheme (NHIS). Excessive out-of-pocket payments are often associated with a catastrophic health care expenditure (CHE). Despite the rising incidence of breast cancer in Nigeria, there is a paucity of economic data on the cost of care and the impact healthcare expenditure may have on a household. This study provides a comprehensive, prospective analysis of out-of-pocket spending for breast cancer care at a single tertiary care institution in South West Nigeria. **Methods** Consecutive patients undergoing curative intent surgery for a new diagnosis of breast cancer at Obafemi Awolowo University Teaching Hospital (OAUTH) between August 2019-April 2022 were approached for enrolment. A novel, context specific questionnaire was developed for this study and administered by trained personnel. The questionnaire was delivered to patients and caregivers during hospital admission and again during six-month follow-up. Participants were asked to estimate monthly household income and expenditures. Out-of-pocket direct and indirect expenses for breast cancer diagnosis and care were elicited. Where feasible, hospital accounting records and individual receipts were used to minimize recall bias. Sequelae of the out-of-pocket costs were also elicited, such as the use of debt financing and important forgone expenditures, such as childhood education. Capacity-to-pay was calculated for each household from the provided data as the sum of annual non-food expenditures. A CHE was defined as an aggregate healthcare expenditure that exceeded 40% of a household's capacity-to-pay. All monetary figures were collected in the local currency (Naira) and converted to USD using the Nigerian Central Bank conversion rate of 415.83N to 1USD. Research ethics board approval was obtained for this study from OAUTH. **Results** Data were collected from 57 eligible patients with a mean age of 49.8 years (SD 12). The median household size was five (range 1-10) and the majority (75.4%) had completed at least secondary education. Seventy four percent (73.6%) of patients had \geq Stage III disease at presentation and 89.5% received systemic chemotherapy. Only seven percent (4/received

adjuvant radiotherapy. The mean annual capacity-to-pay for the cohort was \$2,840.8 (\$2,913.6). The mean cost of care, including direct and indirect expenditure was \$3,379.7 (SD \$3032.2). Excluding indirect costs, such as the cost of travel and self-reported lost income, the mean cost of direct expenditures associated with diagnosis and treatment was \$1,705.3 (SD \$1,236.6). Out of the 57 patients enrolled in the study 52 (91.2%) experienced a CHE as a result of their breast cancer treatment. As a result, 56% of households had to borrow money and seven percent withdrew children from school. Sixty-three percent of patients had no form of health insurance. Conclusions Over 90% of breast cancer patients at a tertiary care facility in Nigeria experience a CHE as a result of out-of-pocket costs associated with accessing care. This limits access to costly evidence-based adjuncts (i.e. radiotherapy) and has a negative impact on the wellbeing of the broader household. There is a need for national and global initiatives to ensure financial protection from the cost of breast cancer care.

Disclosure(s):

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P4-07-47

Real-world practice patterns in the management of metastatic breast cancer in Washington State

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Background:

Evidence-based recommendations for the management of metastatic breast cancer (MBC) endorse confirmation of recurrence with biopsy and reassessment of biomarker status. National guidelines support numerous treatment options and do not capture the nuances of real-world practice. Real world data may demonstrate disparities in adherence to guidelines.

Methods:

We collaborated with Hutchinson Institute for Cancer Outcomes Research (HICOR) to link enrollment and insurance claims records with Washington State cancer registries from 2008-2017. Our cohort comprised of women > 18 years old with MBC who met enrollment criteria in one of four payors (Premara, Regence, Medicare, or Medicaid). We identified receipt of biopsy and biomarker re-assessment at time of recurrence, receipt of first line treatment, categorized as CDK4/6 inhibitors (CDKi), chemotherapy (CT), or hormone therapy (HT) and examined factors influencing these practice patterns.

Results:

We identified 1,101 patients with MBC (recurrent MBC, N = 715; de novo MBC, N = 386) with a median age of 66 (range 54 – 74). Of the patients with MBC, there were a total of 677 patients with ER+/HER2- MBC. Table 1 shows demographic data. Most of the cohort were White (89%). Approximately 15% of patients lived in areas of high deprivation (area of deprivation index, ADI,

8-10). Patients had either Commercial (47%), Medicaid (4%), Medicare (35%) or multiple (13%) insurance. Of the patients with recurrent MBC, 49.5% received a biopsy to confirm metastatic diagnosis. Similarly, 48.7% of recurrent MBC patients underwent biomarker reassessment. Patients with highest co-morbidity index (2) were more likely to undergo biopsy confirmation (20.3% vs 13.0%, $p = 0.02$). Biopsy was more often performed at recurrence in patients receiving care at a high-volume center (74.3% vs 67.6%, $p = 0.03$) compared to low volume center (18.6% vs 26.6%, $p = 0.03$). First line treatment selection was directly associated with receipt of biopsy and biomarker testing. Hormone therapy only was more common in patients who did not undergo biopsy (62.3% vs 37.7%, $p < 0.001$) or biomarker reassessment (62.7% vs 37.3%, $p < 0.001$). Of the patients with ER+/HER2- MBC, the majority of patients received ET alone (69%), followed by chemotherapy (22%), and CDK4/6i + ET (9%). Dual agent CT was the more commonly prescribed compared to single agent in those who received CT (56% vs 44%). The majority of patients who received CDKi + ET were < 65 years old (65.2%, $p < 0.02$). Insurance influenced first line therapy selection and patients with commercial insurance were more likely to receive CDK4/6i + ET compared to those with Medicare/Medicaid. (60.9% vs 26.1%, $p = 0.10$). Patients with de novo MBC were more likely to receive CT (43.1% vs 13.4%, $p < 0.001$) and less likely to receive ET alone (47.9% vs 78.0%, $p < 0.001$). Almost all patients treated with CDK4/6i + ET received care a high-volume center (91.3%, $p = 0.11$).

Conclusion:

Our findings highlight key gaps for future investigations in the management of MBC and serve as a launching point for new patient-centered and quality-promoting research initiatives.

Table 1: Baseline Demographics

	Newly Diagnosed MBC (N = 386)	Recurrent MBC (N = 715)	Total (N = 1101)	p-value
Age at diagnosis, median (range)	68 (58-76)	63 (52, 72)	66 (54,74)	<0.001
Race, n (%)				0.356
Non-White	36 (9.3%)	81 (11.3%)	117 (10.6%)	
White	350	634 (88.7%)	984 (89.4%)	
Co-Morbidity Category				1.000
0	256 (67.0%)	489 (67.1%)	736 (67.1%)	
1	62 (16.2%)	116 (16.2%)	178 (16.2%)	
2	64 (16.8%)	119 (16.6%)	183 (16.7%)	
ADI, Area of Deprivation				0.001
1-4	188 (49.%)	433 (60.8%)	621 (56.7%)	
5-7	125 (32.6%)	184 (25.8%)	309 (28.2%)	
8-10	71 (18.5%)	95 (13.3%)	166 (15.1%)	
Insurance				<0.001
Commercial	137 (35.5%)	380 (53.1%)	517 (47.0%)	
Medicaid	16 (4.1%)	30 (4.2%)	46 (4.2%)	
Medicare	177 (45.9%)	212 (29.7%)	389 (35.3%)	
Multiple	56 (14.5%)	93 (13.0%)	149 (13.5%)	
Institution of Care [†]				<0.001
High	311 (80.6%)	507 (70.9%)	818 (74.3%)	
Low	45 (11.7%)	162 (22.7%)	207 (18.8%)	
Medium	30 (7.8%)	46 (6.4%)	76 (6.9%)	

1# of patients treated annually, high = >100, medium 25-100, low <25.

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Preliminary results of the FIRST (Freezing bReaST cancer in Brazil) trial: a before-after study

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Background: Image-guided tumor ablation is a non-surgical minimally invasive therapy available for the local treatment of carcinomas as an alternative to surgical treatment. However, studies evaluating this therapy in early breast cancer present variable success rates, raising the question of whether omitting surgery is permissible. Ongoing studies such as the Frost and Ice3 Trial may change the context of cryoablation in the treatment of early breast cancer. Objective: The main objective of this study is to assess the effectiveness of cryoablation in the local treatment of early breast cancer. The secondary objectives are to analyze the negative predictive value of magnetic resonance imaging (MRI) in predicting response to therapy and to assess ice ball size in relation to the largest tumor size. Methods: Non-randomized, single-arm, multicenter clinical study conducted in Brazil. The inclusion criteria will be patients with unifocal invasive breast carcinoma, tumors smaller than or equal to 2.5 cm, lesion visualized on ultrasound, and surgery indicated as the first treatment option. The exclusion criteria will be in situ ductal carcinoma, multifocal or multicentric tumors, clinical axillary involvement, lesion-to-skin distance of less than 5 mm, presence of distant metastasis, and neoadjuvant treatment. All patients will undergo local cryoablation treatment, which will be followed by conventional surgical treatment after an interval of 14 to 28 days. Imaging tests (mammography, ultrasound, and breast MRI) will be performed before and after cryoablation. Cryoablation effectiveness will be assessed through its success rate, defined as the absence of invasive or in situ malignant neoplastic cells in the surgical specimen. If the expected cryoablation success rate corroborates the 92% rate presented in the ACOSOG Z1072 study for patients without multifocal disease, this study will need at least 32 patients to verify if the technique is satisfactory (success rate > 70%) considering power of 95% and an alpha of 5%. The study was approved by the local ethics committee and registered in the Clinical Trials. Recruiting has started in 2020 and is expected to end in 2024. Results: Until now, eight patients have been included, all of them with invasive breast carcinoma of no special type, RH positive and HER 2 negative, histological grade 1 or 2. The mean age of the patients is 57 years, and the mean tumor size is 1.1 cm (0.5–1.8 cm). All patients underwent two cycles of 6-minute freezing and 4-minute thawing with only one cryoprobe coupled to the Argon and Helium gas system. The

complete ablation rate was 87.5% (7 of 8 cases) and the ablation rate considering only absence of invasive lesion was 100%. In our study, only one patient had in situ focal ductal carcinoma in one margin. The mean ice ball size on ultrasound was 3.8 x the size of the breast lesion. The negative predictive value of breast MRI was 100%. Conclusions Cryoablation is a promising therapy and may be an alternative to surgical treatment in patients with early breast cancer. This study confirms that this ablative technique is feasible. However, the results of other ongoing studies need to confirm the role of cryoablation in breast cancer treatment. ClinicalTrials.gov Identifier: NCT05398497

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P4-07-49

Neoadjuvant therapy in Asian breast cancer patients with early & locally advanced breast cancers – A contemporary experience from a large tertiary hospital in Singapore

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Background: Non-metastatic breast cancers (BC) are increasing treated with neoadjuvant therapy (NAT). Complete pathological response (pCR) is associated with improved survival. Early identification of care needs during NAT is crucial. We report our institution's experience with NAT. Methods: A prospectively recruited cohort diagnosed with BC, referred to NAT program at SingHealth acute hospitals between June 2020 and June 2021. Demographics, clinical data, pCR (absence of invasive carcinoma in breast and axilla), and Functional Assessment of Cancer Therapy Breast (FACT-B) as quality of life (QOL) measure were collected. Definition of young BC (YBC) were ≤ 40 years, older adults (OA) ≥ 65 years. Results: Among 119 eligible patients, 7 (6%) were clinically stage 1, 71 (60%) stage 2, and 41 (35%) stage 3. Twenty-eight (24%) were triple negative (TNBC; defined as HER2- hormonal receptor 0-10% [HR-]), 26 (22%) HER2+ HR-, 45 (38%) HER2+ HR+, 20 (17%) HER2- HR+. Among 71 HER2+ BC, two-thirds received anthracycline (A) based chemotherapy, a quarter A-sparing and remaining 9% taxane only. Majority (89%) received dual HER2 blockade. Among TNBC, 28 (71%) received additional platinum and 2 (7%) immunotherapy. Majority (77%; n=92) completed NAT. Toxicity was main reason for incompleteness. Three patients did not undergo surgery: 1 defaulted, 1 demised and the last patient's surgery was not due at analysis. Of the 116 who underwent surgery, 23 (20%) had breast conservation and 93 (80%) mastectomy.

Forty-nine (42%) achieved pCR - 12 (43%) TNBC, 17 (65%) HER2+ HR-, 20 (44%) HER2+ HR+ and 0 in HER2- HR+ ($p < 0.001$). The pCR rates were also lower by increasing age (Multivariable OR 0.93; 95% CI, 0.90-0.97). Baseline median FACT-B scores was 117 (IQR 102-126) for the cohort: 108 for YBC, 116 for OA and 120 for the rest ($p=0.200$). At baseline, median score was 28, 24, 18, 22 and 27 in physical, social, emotional, functional wellbeing and BC subscale, respectively, and YBC and OA patients had lower social wellbeing scores than the remaining cohort (22 vs 24, $p=0.011$). Conclusion: Highest pCR were observed with HER2+ followed by TNBC. Pre-operatively, FACT-B scores were comparable by demographics, staging and tumor subtypes. However, care must be paid to social wellbeing for women in age extremes undergoing NAT.

Disclosure(s):

Zewen Zhang, BEng (Hons), MD, MRCP (UK), MMed (Int Med): No financial relationships to disclose

Jun Ma, MBBS (Hons), MRCP (UK): No financial relationships to disclose

Jasmine Yun Ting Tan, n/a: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

P4-07-50

mRNA expression and delivery efficacy of lipid nanoparticles in the cells breast tumor microenvironment: in vitro and in vivo evaluation

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During the COVID-19 pandemics we have all witnessed the clinical importance of mRNA as current vaccines and future therapeutics. mRNA therapies have a potential to revolutionize cancer treatment. Delivery of mRNA requires lipid nanoparticles (LNP) to protect the cargo from degradation. mRNA has a negative charge and depends on positively charged lipids to be encapsulated in LNP. These lipids can be either ionizable at certain pH or constantly cationic. Even though previous studies had evaluated the formulation properties of ionizable and cationic LNP systems, there is the need to understand their specificity in terms of mRNA delivery and protein expression in breast cancer tumor microenvironment. The objective of this work was to assess the kinetics of LNP cellular uptake and mRNA expression in breast cancer (BC) cells and fibroblasts, the most frequent cell type in the tumor microenvironment cells, while studying the mechanisms involved in differential behaviors of LNP formulated with cationic and ionizable lipids. To achieve this goal mRNA-LNP containing ionizable lipids (LNP-A) and cationic lipids (LNP-B) were designed and formulated using Nanoassembler® Benchtop microfluidics mixer (Precision NanoSystems). mRNA-LNP were characterized for size, zeta potential using dynamic light scattering (DLS) and mRNA encapsulation efficiency using RiboGreen assay. LNP were tagged with rhodamine lipid to investigate the uptake kinetic and a reporter GFP mRNA to evaluate mRNA expression in murine 4T1 and human MCF7, MDA-231, SUM-159 and T-47D breast cancer cells and BJ fibroblasts. Live fluorescence microscopy imaging, IncuCyte S3®, was used to determine the LNP uptake and GFP mRNA expression. In vitro biocompatibility was assessed with WST-1 assay. Additionally, expression of mRNA delivered from LNP in tumor microenvironment was evaluated in vivo in a syngeneic 4T1 breast cancer model using mRNA luciferase and IVIS imaging. mRNA-LNPs possessed an average diameter of 77 - 107 nm, narrow size distribution, neutral zeta potential and high mRNA encapsulation efficiency (>94%). Our results demonstrated that mRNA expression was higher in breast cancer cells when delivered from LNP-A formulation and in BJ fibroblasts when delivered from LNP-B. LNP-A, the ionizable LNP, was tested in the breast cancer cells to confirm the efficacy of the delivery. The highest transfection efficacy, from high to low, T-47D, MCF7, SUM-159, 4T1 and MDA-231. We have further investigated the cellular uptake mechanisms of LNP using uptake pathway inhibitors for caveolae endocytosis, clathrin endocytosis, and phagocytosis. Our data

confirm that there are differences in mechanisms that govern the uptake of mRNA LNP in breast cancer cells and fibroblasts. Clathrin-mediated endocytosis was active in 4T1 breast cancer cells for ionizable and cationic LNP. Interestingly, despite in vitro differences in uptake and mRNA expression, in vivo results show that both formulations efficiently delivered luciferase-mRNA in the tumor microenvironment. Histology results demonstrated similar luciferase expression for both LNP in tumors. Additionally, we were able to confirm the prominent presence of fibroblast and similar distribution in the 4T1 subcutaneous model which could explain the similar efficacy of cationic and ionizable LNP. Understanding uptake and mRNA expression of different LNP formulations in the tumor microenvironment can help in achieving the necessary protein expression for breast cancer therapies. Furthermore, determining the most efficient carrier in early stages may reduce the time required for clinical translation. Acknowledgement: This research was supported in part by CPRIT Core for RNA Therapeutics and Research.

Disclosure(s):

Karem A. Court, Ph.D.: No financial relationships to disclose

Anjana Tiwari, Ph.D.: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-07-51

Impact of the Theralink CLIA protein/phosphoprotein assay on treatment selection in routine clinical practice: a prospective observational study in advanced breast cancer.

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Background: The Theralink Reverse Phase Protein Array-based (RPPA) CLIA assay is a novel molecular assay developed to assist physicians in therapy selection for patients diagnosed with advanced/recurrent breast cancer. The assay was specifically designed to quantitatively measure protein activation/phosphorylation of 32 FDA-approved and Phase III drug targets and pathway-linked downstream substrates, providing functional information on actionable oncogenic drivers in individual tumors. Given the recent commercialization of the Theralink assay (TLA), knowledge gaps exist regarding its use in routine clinical practice and the impact of the test on clinical decision-making in real world practice. The primary objective of this analysis was to assess how the TLA has been integrated in therapy selection for breast cancer patients with a focus on understanding its target population, the rationale for patient selection by the treating physician, and the utilization of the molecule information generated by the assay as part of the therapeutic decision-making process. Findings from this study will help optimize patient selection and maximize the clinical impact of the test as a tool for advancing precision oncology. Methods: We prospectively collected data from 124 women with advanced breast cancer whose tumors were profiled using the Breast Cancer TLA from February, 2021 to May, 2022. All patients were confirmed as actively managed for advanced/recurrent breast cancer. Eight μm FFPE sections (n=5) from a recently collected tissue biopsy were used to isolate tumor epithelia via Laser Capture Microdissection and to generate RPPA-based molecular profiles. Clinical management and therapy selection information for 68 patients was gathered via surveys completed by treating physicians. Results: Median age of the 124 participants was 53 years (range 26-82) and 111 (89.5%) patients had stage IV disease. The cohort included 66 hormone receptors positive (of which 5 were HER2+), 51 triple negative, and 7 HR-/HER2+ breast cancers. The TLA yielded molecular information for all specimens and profiles were generated on average in 11 days. One or more targets were highly activated (highly actionable)

in 91 patients (73.4%) and moderately activated (partially actionable) in 29 patients; only 4 patients had no actionable target (3.2%). Previous treatment information was available for 118 (95.2%) patients. The TLA was requested to assist with the selection of first-line treatment in 36 patients (of which 24 had previously received neoadjuvant treatment), second-line treatment in 35 patients and third- or subsequent-lines of treatment in 47 patients. Clinicians provided feedback on the use of the assay for 68 patients included in the study. The survey revealed that the TLA impacted treatment selection in 50 (73.5%) cases and was used to either expand options beyond standard of care (30 cases), refine/re-prioritize available treatments (11 cases), narrow treatment from a plethora of options (2 cases) or a combination of the three (7 cases). When TLA data were used for treatment selection, physicians defined the assay highly and moderately beneficial for patient management in 15 and 27 cases, respectively. Conclusion: Our study suggests the TLA yields useful information for selecting treatment for breast cancer patients with advanced/recurrent disease. In this prospective analysis, the assay identified actionable targets in more than 90% of patients, which is significantly higher than what has previously been reported for genomic profiling alone. Overall, physicians found the information yielded by the assay useful for selecting treatment. The inclusion of the TLA in oncology may offer important insights for advancing precision medicine for breast cancer patients.

Disclosure(s):

Kris Weinberg, MS: Theralink technologies inc: Employee and Leadership (Ongoing), Salary (Ongoing)

Mariaelena Pierobon, MD, MPH: Theralink technologies inc: Consulting Fees (e.g., advisory boards) (Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Royalty (Ongoing)

Edik Blais, PhD: Perthera Inc: Employee and Leadership (Ongoing), Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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12/8/2022

7:00 AM - 8:15 AM

P4-07-52

Caloric Restriction for Oncology Research (CaReFOR): Assessing dietary adherence and outcomes in African American patients during breast cancer treatment.

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Purpose: Epidemiologic and clinical evidence have shown an association between obesity and increased risk for breast cancer (BC) incidence and mortality. Data from human and animal studies support a potential role for weight loss in counteracting tumor-promoting properties of obesity in BC. However, dietary intervention clinical trials often show low patient adherence, especially among African American (AA) women compared to Caucasian (CC) women. They also show that AA women are disproportionately obese and lose less weight during behavior lifestyle interventions compared to CC with similar risk factors. We evaluated the efficacy and feasibility of a 10-week caloric restricted diet in patients undergoing radiation and have performed analysis to determine if adherence to dietary alterations is feasible in underrepresented patients. Methods: In an IRB approved clinical trial, we determined the feasibility and toxicity of dietary intervention during radiation in breast cancer patients 18 years and older who were undergoing breast conservation therapy with T1-2N0 cancers. The dietary intervention consisted of caloric intake reduction of 25% from baseline for a total of 10 weeks during their six-week radiation treatment which was administered to the whole breast to a dose of 50Gy with a 10Gy boost to the tumor bed. To optimize adherence to caloric restriction (CR), patients received personalized counseling, maintained food diaries, and were educated on behavioral modifications at weekly visits. To characterize the effects of CR, baseline physiologic and blood parameters were collected and compared with post intervention measurements and samples. Biometric and biological data collected during the study comparing compliant participants before and after the CaReFOR intervention was stratified by race and analyzed via two-sample paired t-test. The difference between AA and CC study participants was determined to be significant if the calculated p-value was less than < 0.05 (CI 95%). Results: A total of 32 female patients were enrolled in the CaReFOR trial, 16 were AA and 16 were CC. Participant demographics were similar across age, primary tumor size (pT), nuclear grade, and hormone receptor status. Evaluation of patients' baseline diet demonstrated similar macronutrients across races, with AA showing less fruit/vegetable and grains. AA patients were more overweight compared to their CC counterparts. They also showed a more inflamed state compared to CC patients. The baseline inflammatory biomarker levels for ESR

and cholesterol were significantly higher while adiponectin was significantly lower in AA than that of CC patients. The trends for insulin, HbA1c, and leptin were also higher for AA compared to CC. Following the 10-week diet, AA patients (87.3%) were more compliant than CC's (81.3%). Both AA and CC patients lost weight during the trial, with AA having a significant loss in body fat and gain in muscle mass compared to CC. Similarly, after completing the CR diet, biological inflammatory markers improved in AA and CC patients. Particularly, in AA, there was a significant decrease in cholesterol levels, while insulin, leptin, and ESR serum levels trended downwards, suggesting a decreased inflammatory state. Conclusions: Contrary to published studies, we found AA patients are successful in adhering to dietary alterations and have a benefit with respect to physiologic and biologic parameters. Our dietary intervention was able to positively affect our AA patients adverse baseline factors such as obesity and inflammation. Future studies should consider dietary alterations as a possible means to decrease AA patient disparate outcomes in breast cancer.

Disclosure(s):

Siani Harding, n/a: No financial relationships to disclose

Adeseye Adekeye, MD: No financial relationships to disclose

Edith P. Mitchell, MD, MACP, MD, MACP, FCPP, FRCP (London): Astellas: Consulting Fees (e.g., advisory boards) (Ongoing); Genentech: Consulting Fees (e.g., advisory boards) (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing)

Nicole Simone, MD: No financial relationships to disclose

12/8/2022

7:00 AM - 8:15 AM

P4-07-53

Adverse events (AEs) in phase III clinical trials of patients with human epidermal growth factor receptor-2 positive (HER2+) breast cancer (BC): a meta-analysis

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Background. In the last five years, several new drugs have been approved for BC in the United States, many of which target HER2, including neratinib, margetuximab, tucatinib, and trastuzumab deruxtecan. These approvals depend on a drug's benefits outweighing its risks in clinical trials (CTs). However, limited information on safety is available from single CTs. The objective of this study is to identify recently published phase III CTs that report AEs in patients (pts) with HER2+ BC and perform a meta-analysis to estimate the frequency of the most common AEs reported in ≥ 2 CTs. Methods. A literature search was conducted (Ovid, ClinicalTrials.gov) to identify phase III CTs published from 2017-2021. Search terms included BC, HER2+, phase III, CT, and others. Articles were independently screened by two researchers in two levels (title/abstract; full text) and were included if they reported AEs in pts with HER2+ BC. Meta-analysis was performed in Comprehensive Meta Analysis v3 to estimate frequency of AEs using random effects models. Results. Of 519 articles identified, 33 were included for analysis (455 excluded in level 1 screening; 31 excluded in level 2 screening). Most excluded articles were not phase III or did not include only pts with HER2+ BC. BC treatments most commonly included chemotherapy and HER2-targeted agents (e.g., trastuzumab), including antibody-drug conjugates (ADCs; e.g., trastuzumab emtansine). Most trials (N=27) included ≥ 1 treatment arm with pts who received chemotherapy in combination with a HER2-targeted agent. Fewer trials (N=10) included ≥ 1 treatment arm with pts who received only a HER2-targeted agent. Across all 33 trials, 181 unique AEs were reported. Specific chemotherapy agents used were not always reported, but included taxanes, anthracyclines, cyclophosphamide, 5-fluorouracil, capecitabine, and carboplatin. In chemotherapy treated pts (with or without reported concomitant HER2-targeted agent), the most frequent any grade AEs were hand-foot syndrome (63.8%, N=1814), alopecia (56.6%, N=9677), and diarrhea (39.9%, N=12628); the most frequent grade ≥ 3 AEs were neutropenia (21.7%, N=14349), hand-foot syndrome (12.2%, N=2252), and leukopenia (8.4%, N=3852). HER2-targeted agents included trastuzumab emtansine, trastuzumab, pertuzumab, lapatinib, and neratinib. In pts treated with any HER2-targeted agent (without reported concomitant chemotherapy), the most frequent any grade AEs were diarrhea (31.7%, N=5518), nausea (30.8%, N=5518), and epistaxis (24.9%, N=3622); the most frequent grade ≥ 3 AEs were thrombocytopenia (4.8%, N=3980), anemia

(4.2%, N=3845), and aspartate aminotransferase increase (3.3%, N=3975). In the subgroup of pts treated with an ADC (trastuzumab emtansine), the most frequent any grade AEs were nausea (41.4%, N=3622), fatigue (31.6%, N=2895), and headache (28.0%, N=3622); the most frequent grade ≥ 3 AEs were similar to those in pts treated with any HER2-targeted agent. Significant heterogeneity was detected among trials for the outcomes reported here (Q statistic ranged from 12-2176, $p < 0.05$). No analysis was conducted in pts who received hormone therapy due to limited available information about this group in the included trials. Conclusion. When evaluating pooled data, the most commonly reported AEs in CTs of patients with HER2+ BC varied by drug classes included in treatment regimens. This meta-analysis provides a more comprehensive understanding of the most frequent AEs in this population by pooling patient data from several CTs and will contribute to better contextualize the safety of products used in this population. Future research including real-world studies can be used to better understand the safety profile of these medications.

Disclosure(s):

Mackenzie Henderson, PharmD: Daiichi Sankyo, Inc.: Salary (Ongoing)

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7:00 AM - 8:15 AM

P4-07-54

Health related quality of life of patients treated with bevacizumab and paclitaxel as first-line treatment for HER2 negative metastatic breast cancer: impact of clinical factors

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Background: Advances in screening and treatment have led to increase in breast cancer (BC) survival in recent years but prognoses for metastatic BC remain poor with poorer outcomes as health-related quality of life (HRQOL). Treatment as bevacizumab and paclitaxel for metastatic BC, although that can increase time to progression of disease, often carry toxicity and is not curative but rather palliative in intent with the goal to improve or maintain HRQOL. The aim of this work was to assess impact of clinical factors such as disease progression, toxicity on HRQOL. Methods: COMET study is a multicenter prospective single-arm cohort study in France whose main objective was to identify biological factor that could predict the clinical benefit of bevacizumab-paclitaxel combination therapy as first treatment in HER2 negative metastatic BC. HRQOL was assessed at baseline, at every cycle (every for 4 weeks) until progression and then every 3 months up to death using the EORTC QLQ-C30 questionnaire and its BC specific module, the EORTC QLQ-BR23. In this ancillary study, we targeted 5 dimensions HRQOL for the primary analyses: Global health status (GHS), physical functioning (PF), Emotional functioning (EF), fatigue (FA) and pain (PA). The primary endpoint was time until definitive deterioration (TUDD) in HRQOL scales that defined as time between inclusion and the first decrease HRQOL score ≥ 5 points compared to baseline score, with no further improvement of at least 5 points. Multivariable Cox model with time dependent covariate was performed to

assess clinical factors associated with TUDD for each of the 5 target dimensions HRQOL. We performed 3 models for each dimension: model 1 including all covariate with $p < 0.10$ in univariable; model 2 including model 1 and adjusted on cancer subtype and model 3 included model 1 stratified by cancer subtype. P value < 0.01 were considered statistically significant. Results: Out of 510 patients included in COMET study, 432 patients with available HRQOL data were analyzed in this study. Median age at inclusion was 58 years (range: 29-83), and 24.4% of patients had triple negative tumor subtype. About 79 % of cancers were invasive ductal carcinoma and 43 % patients had least 3 metastasis sites at baseline. At baseline, patients reported a mean score for GHS of 57.6 (SD=22.7), for PF of 75.8 (23.2), for EF of 62.2 (25.8), for FA of 42.2 (29.60) and for PA of 38.1 (31.5). The Median TUDDs for the 5 targeted dimensions was 10.1 months [7.5-16.9] for GHS, 6.1 months [4.1-8.9] for PF, 21.6 [18.7-31.2] for EF, 10.8 [6.2-16.6] for FA and 13.6[10.1-22.5] months for PA. In multivariable analyses, Disease Progression was associated with TUDD of GHS (HR [99%CI] =2.4 [1.2-4.9] and TUDD of PF (2.1 [1.1-3.7]). After adjusted on cancer subtype, association persisted with TUDD of GHS ($p=0.009$). Performance Status was associated with TUDD of PF (1.6 [1.2-2.3]), and TUDD of Pain (1.6 [1.1-2.3]). Performance Status association with TUDD of PF continued after adjustment on cancer subtype ($p=0.0003$). Prior endocrine therapy was associated with TUDD of pain in patients with tumor with positive hormone receptor (HR+) (2.4 [1.2-4.7]). There was no factor associated with TUDD of EF and TUDD of FA. Conclusion: Results of this study have shown that among the 5 targeted dimensions HRQOL, Physical Functioning was deteriorated in the shortest time. Disease progression, base line performance status and prior endocrine therapy for HR+ subtype, are clinical factors that could influence HRQOL in HER2 negative metastatic BC treated with first line chemotherapy.

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7:00 AM - 8:15 AM

P4-07-55

Neoadjuvant trastuzumab and pertuzumab in combination with anthracyclines in HER2-positive early breast cancer: real-world data on effect of body mass index in cardiac safety

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BACKGROUND: Neoadjuvant therapy with trastuzumab and pertuzumab (HP) combined with chemotherapy (ChT) is the standard of care in \geq cT2cN0 or N+ HER2-positive early breast cancer (EBC). Although cardiotoxicity is a known adverse effect of anti HER2-therapy and

anthracyclines, recently BERENICE final analysis showed cardiac safety of HP in combination with standard or dose-dense anthracycline-based ChT. However, real-world data is lacking, specifically in patients (pts) with identified cardiovascular (cv) risk factors. Our study aimed to evaluate cardiac safety of HP and anthracyclines in HER2+ EBC and explore potential impact of body mass index (BMI). METHODS: This retrospective analysis included HER2+ EBC pts receiving neoadjuvant HP and anthracycline- and taxane- based ChT, at our institution, between 2016 and 2021. Baseline clinical, demographic, histopathological and immunohistochemical features were reported. Pts were categorized as underweight (< 18.5kg/m²), normal (≥18.5;< 25kg/m²), overweight (≥25;< 30kg/m²) and obese (≥30kg/m²), according to basal BMI WHO categories. The primary objective was to evaluate cardiac safety, assessed by incidence of left ventricular ejection fraction (LVEF) declines (≥10% from baseline and to a value < 50%) and NYHA class III/IV heart failure. Univariate and multivariate logistic regression analysis were performed using BMI as a categorical variable. Safety data were compared in subgroup analyses for underweight/normal and overweight/obese pts. Statistics were performed with IBM™ SPSS software, version 23. RESULTS: Our analysis enrolled 112 female pts, with a median age of 54 years (30-78), including 22pts (19.6%) with ≥65years and 55 (49.1%) postmenopausal women. Most pts (n=89; 79.5%) had HR-positive disease. 44pts (39.3%) had stage II and 68pts (60.7%) had stage III disease. According to BMI, pts were classified as underweight (n=3; 2.7%), normal (n=40; 35.7%), overweight (n=47; 42%) and obese (n=22; 19.6%). No association was found between BMI and tumor stage (p=0.829), grade (p=0.753) and HR status (p=0.212). Other baseline cv risk factors were identified: former/active smoker (n=34;30.4%), diabetes (n=10;8.9%), hypertension (n=30;26.8%), and dyslipidemia (n=32;28.6%). Most pts had ≥2 cv risk factors (n=66;58.9%). Two different regimes were used FEC100-D+HP (2016-2019, n=84) and ddAC-wkPaclitaxel+HP (2020-2021, n=28). Overall, pCR was achieved in 62 pts (55.4%). Regarding cardiac safety evaluation, 4 pts (3.6%) experienced at least one LVEF decline ≥10% from baseline and to a value < 50%, including 3 pts that were overweight/obese. Declines were reversible in all pts, with recovery by next assessment. Two pts (1.8%) experienced one NYHA class III heart failure event. Both pts were overweight/obese and had another concomitant risk factor for cardiovascular disease. Both pts discontinued treatment. No statistically significant association was found between overweight/obesity and cardiac events (OR 1.26, 95%CI 0.22-7.20; p=0.792). Median follow-up duration was 39 months. No new safety signals were identified. CONCLUSION: Cardiac safety of neoadjuvant HP in combination with anthracyclines in HER2-positive EBC in our real-world data is consistent with previous studies. Despite most cardiac events occurred in overweight/obese pts, no statistically significant effect was found. Further studies are needed to evaluate cardiotoxicity in pts with cv risk factors and evaluate impact of therapeutic interventions.

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Diana Simão, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-07-56

Mayo Clinic Enterprise patterns of growth-factor utilization for sacituzumab govitecan (SG)-induced neutropenia among patients with metastatic triple negative breast cancer

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Background:

SG was approved in 2020 for the treatment of metastatic triple negative breast cancer (TNBC). The most common grade 3/4 adverse event in the ASCENT trial was neutropenia (51.2%) with a 6% incidence of febrile neutropenia. 1 Package insert recommendations do not endorse primary prophylactic growth factor support, rather only initiating if severe neutropenia occurs on treatment.²

Objective:

This study retrospectively reviewed the utilization of growth factor support in patients (pts) with metastatic TNBC initiated on SG at each Mayo Clinic Enterprise site.

Methods:

We performed a multi-center, retrospective review of all pts with TNBC who received SG from January 2021 to December 2021 at Mayo Clinic sites in Minnesota, Florida, Arizona, and its community-based health system network. Data collected included history of neutropenia with previous cycles of SG resulting in a treatment delay, number of cycles, grade of neutropenia and cycle/day of treatment plan when growth factor added. Pts who received only one dose of SG were excluded. The Fisher's exact test was utilized to compare the difference in the use of primary prophylaxis between sites.

Results:

67 pts received at least two doses of SG. Within this cohort, 42 pts (63%) received growth factor support during treatment with SG. Growth factor support was most often added during the first two cycles (59.5%). A total of 12 patients initiated growth factor with no history of delays related to neutropenia and without neutropenia at the time of administration. Eleven of these pts had growth factor support added on Cycle 1 as primary prophylaxis. Primary prophylaxis was most common at Mayo Clinic – Rochester compared to the other sites (Table 1), however there was not a statistically significant difference ($p=0.27$). There were 26 pts (39%) with a treatment delay due to neutropenia while receiving SG, of which 21 (81%) were managed with the addition of growth factor (13 pegfilgrastim, 8 filgrastim). The median number of cycles for all pts was 5 (range: 1-25). Pts who received growth factor were treated with a median of 5 cycles (range: 1-25) and pts who did not receive growth factor were treated with a median of 4 cycles (range: 1-19) ($p=0.10$).

Conclusions:

We observed wide variability in the use of prophylactic growth factor between Mayo Clinic sites with SG. The optimal practice of growth factor use with SG warrants further exploration.

References:

1. Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. *N Engl J Med*. 2021;384(16):1529-1541
2. Immunomedics, Inc. Trodelvy (sacituzumab govitecan-hziy) [package insert]. Foster City, CA: Gilead Sciences; 2020.

Grade of neutropenia for patients receiving SG when growth factor initiated

Grade of Neutropenia	Total (n=42) ¹	Arizona (n=7) ¹	Florida (n=9) ¹	Health System (n=5) ¹	Rochester (n=21) ¹
no neutropenia	12 (29)	1 (14)	1 (11)	1 (20)	9 (43)
1	1 (2)	0 (0)	1 (11)	0 (0)	0 (0)
2	5 (12)	0 (0)	1 (11)	0 (0)	4 (19)
3	14 (33)	2 (29)	3 (33)	1 (20)	8 (38)
4	10 (24)	4 (57)	3 (33)	3 (60)	0 (0)

¹n (%)

Disclosure(s):

Kaylee Clark, Pharm.D.: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

P4-07-57

Outcomes of Triple-Negative Breast Cancer In Older Versus Younger Women

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Background: Triple-negative breast cancer (TNBC) is an aggressive disease characterized by lack of targeted therapy; main-stay of treatment being limited to surgery and chemotherapy. Older patients with TNBC are often underrepresented in the clinical trials, due to competing mortality risks. This study aims to assess the treatment and outcomes of triple negative breast cancer (TNBC) in older women relative to younger women. Methods: This was a retrospective cohort study of patients who presented with primary TNBC, age 34-94 years; stage I-III from Jan 1, 2013 to Dec 31, 2015. Patients' demographics, clinical characteristics, treatment and outcomes were retrieved from the CANISC Register and individual patient (N=88). Breast cancer-specific survival (BCSS) was estimated by using Kaplan--Meier method, and adjusted for age, tumor size, tumor grade, nodal status and chemotherapy, using SPSS-19. Results: Fifty-one patients were less than 70 years old (57.9%) and 37 were 70 years and older (42.1%). There was no difference in the stage at presentation (stage I: 43% vs. 35%; stage 2: 49% vs. 49%; stage 3: 8% vs. 11%; P=.061). Older patients were less often treated with adjuvant chemotherapy (75% vs. 24%; P< 0.001). Mean follow-up was 48 months. Five-year BCSS was significantly poor for older patients (54% vs. 75%, P=.032). 5-year overall survival was also significantly worse for patients who did not receive adjuvant chemotherapy (50% vs. 88% P =0< 021). Conclusions: Overall survival in triple negative breast cancer is much worse in older women as compared to younger women and there is a significant benefit with adjuvant chemotherapy.

Disclosure(s):

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P4-07-58

Adjuvant Endocrine Therapy adherence in Breast Cancer patients and the Brazilian National Health System

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Introduction: Breast Cancer is one of the most prevalent malignant disease in women and its first line neo- and/or adjuvant treatment on hormone positive (HR+) subtypes is the endocrine therapy. Even though Adjuvant Endocrine Therapy (AET) had significantly increased overall survival in the long-run, some studies have reported suboptimal treatment adherence rates, varying from 40-95.7%. One possible cause for this great variability on AET adherence is the patients' expenses on treatment. Recent studies have demonstrated that as the cost of treatment increases the treatment adherence decreases. Nonetheless, as far as the authors have searched, no studies have tried to understand such relationship in Brazil, where medications can be taken without any out-of-pocket expenses through the Sistema Único de Saúde (SUS), or through Health insurance companies; and through direct out-of-pocket expenses. Methods: This was an observational cross-sectional pilot study, carried out with an online questionnaire applied to patients from the Centro de Tratamento Oncológico Pro Onco [Pro Onco Oncological Treatment Center] and Centro de Apoio ao Paciente com Câncer de Londrina [Londrina Cancer Support Center] (State of Paraná, Brazil). The questionnaire applied

in this study included objective questions that aimed to understand the systemic endocrine therapy adherence among Breast Cancer patients. In order to do that, the Morisky-Green (MG) test was used. A linear regression model was built using the MG test as dependent variable, and how the patients obtained the drugs as independent variable, controlled by other sociodemographic and clinical covariates. Results: Between December 2021 and March 2022, 95 patients were included in this study. Mean age was 50.71 (SD = 10.00) and mean age at diagnosis was 45.86 (SD = 8.66). Patients obtained the drugs mainly via Health Insurance (45 patients or 47.37%), followed by the SUS (44 patients or 46.32%) and private health expenses (6 patients or 6.32%). It was found that how the patient obtained the medication was statistically significant in predicting adherence. Patients that obtained the medication via the SUS had poorer adherence compared to those that obtained the medication via Health Insurance (coeff.=-0.38 [-0.68;-0.09]; p-value = 0.010) and via Private Health Expenses (coeff.=-0.81 [-1.42;-0.21]; p-value = 0.008). It was also found that considering all three main options available to obtain the medication, 30 patients (68.18%) that obtained the medication via the SUS had already forgotten to take the medication once; whereas only 18 patients (40%) that obtained the medication via Health Insurance had done (Chi-Square = 7.1116; p-value = 0.008). Besides that, it was found that only 22 patients (50%) that obtained the medication via the SUS knew the type of cancer they had. Considering only patients that obtained the medication via Health Insurance, 35 patients (77.78%) knew the type of cancer they had (Chi-Square = 7.4546; p-value = 0.006). Conclusion: The results of this study do not match the literature on the topic, and it could be explained by a poorer doctor-patient relationship at SUS as non-clarification on the importance of adjuvant treatment can be related to a poorer adherence.

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7:00 AM - 8:15 AM

P4-07-59

Management of Isolated Contralateral Axillary Lymph Node Metastasis in Breast Cancer: A Single Institution Experience

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Background: Contralateral axillary lymph node metastasis (CAM) in breast cancer (BC) is uncommon with an incidence of 1.9-6%. It is considered as stage IV disease based on the TNM classification in the 8th edition of the American Joint Committee on Cancer (AJCC) staging manual. However, in the absence of other distant metastases, patients with CAM have been found to have better outcomes compared to those with stage IV disease. Recent studies suggest that CAM may represent locoregional spread of tumor through lymphatics rather than hematogenous spread and patients should be classified as N3 rather than M1. There are no clear guidelines on the optimal management of these patients and it is unclear if patients with isolated CAM should be treated as curative intent or as metastatic disease with palliative treatment. The goal of this study was to describe the management and outcomes of patients with BC and isolated CAM seen at our institution.

Methods: We performed a retrospective chart review on all patients with BC and isolated CAM but no other distant metastases who were seen at our institution between 2000-2021. We collected information on demographics, tumor characteristics, intent of therapy (curative versus palliative), types of treatment (systemic treatments including chemotherapy (CT), hormone therapy, targeted therapy; radiation therapy; surgery), and response to frontline treatment.

Results: We identified a total of ten eligible patients who were diagnosed between 2011-2020. The median age of diagnosis was 57 years and 70% had de novo cancers while the remainder had recurrent disease. The table below describes each patient's cancer, treatment, and response. Patients are listed in chronological order, with those at the top diagnosed in 2011 and bottom in 2020. Four patients had hormone receptor (HR)-positive and HER2-negative BC, 3 patients had triple negative BC, 2 had HER2-positive BC and 1 had HR-positive and HER2-positive BC. Regarding treatment, 50% of patients were treated with curative intent, of whom 3 have no evidence of recurrence at a follow up of 23-137 months. Of the other two patients, one had response to systemic treatment but remains surgically unresectable and the other patient developed recurrent disease. In the 5 patients treated with palliative systemic therapy as Stage IV disease, 3 patients had clinical response to first line treatment with control of disease. One patient who passed away had triple negative disease. The last patient developed progression of disease and is on second line systemic treatment.

Conclusions: At our institution, among patients treated with palliative intent systemic therapy, most (60%) had a response to first line treatment. In the 5 patients treated with curative intent, 3 patients remain without evidence of recurrence of whom 2 have had 9 years of follow up. The current study illustrates the heterogeneity in management for patients with CAM. Our findings highlight the need for larger studies focusing on BC patients with CAM to optimize their treatment and outcomes. Limitations of our study include its retrospective nature and small sample size given rarity of CAM.

Table 1. Treatment and Outcomes of Patients with CAM

Table 1. Treatment and Outcomes of Patients with CAM

Disease Status	Receptor Status	Intent of Treatment	Initial Treatment	Follow Up (mos)	Outcome
De novo	HER2+	Curative	Neoadjuvant CT, surgery, RT	137	No evidence of recurrence
De novo	Triple negative	Curative	Neoadjuvant CT, surgery	132	No evidence of recurrence
Recurrent	ER+/PR+	Palliative	Hormone therapy, CDK 4/6i	49	Clinical response; remains on 1st line tx
Recurrent	Triple negative	Curative	Neoadjuvant CT, surgery, adjuvant CT	39	Recurrent disease 3 months after completing adjuvant tx
De novo	HER2+	Palliative	HER2-targeted therapy	33	Clinical response; remains on 1st line tx
Recurrent	Triple negative	Palliative	CT, immunotherapy	33	Progression of disease, death
De novo	ER+/PR+	Curative	Neoadjuvant CT, surgery, adjuvant RT, hormone therapy	23	No evidence of recurrence
De novo	ER+/PR+	Curative	Neoadjuvant CT followed by hormone therapy, CDK 4/6i	18	Clinical response but remains surgically unresectable
De novo	ER+/PR+	Palliative	Hormone therapy, CDK 4/6i	16	Clinical response; remains on 1st line tx
De novo	Triple positive	Palliative	CT, HER2-targeted antibodies	16	Progression of disease; on 2nd line tx

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P4-07-60

Identification of Optimal Carboplatin Containing Regimen for Triple Negative Breast Cancer

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Background: Current management for triple negative breast cancer (TNBC) involves chemotherapy and immunotherapy systemic treatments. TNBC treatment remains a challenge, with up to 40% of those treated using standard methods for stage I to III TNBC experiencing recurrence. Currently, the optimal carboplatin regimen for TNBC is yet to be defined. In our previous study, we identified an optimal carboplatin containing chemotherapy regimen that improved patient outcomes. In this study, we expanded the cohort as an extension of the previous prospective study to further verify these promising results.

Patients and Methods: We performed a retrospective review of 37 TNBC patients who had < 10% estrogen and progesterone receptor positivity and were human epidermal growth factor receptor-2 (HER2) negative. This study was originally done in an adjuvant setting, but patients with locally advanced tumors received neoadjuvant chemotherapy. Patients received dose-dense Adriamycin, cyclophosphamide, and paclitaxel every two weeks for sixteen weeks. Adriamycin (60 mg/m²) and cyclophosphamide (600 mg/m²) were given intravenously every two weeks for four cycles, followed by paclitaxel (175 mg/m²) every two weeks for four cycles. Carboplatin with an area under the curve of 6 was added to cycles two and four of paclitaxel. Last, we changed the parameters of continuing chemotherapy to allow platelet counts > 70,000

x 10⁹. Only paclitaxel could be modified for neuropathy.

Results: Of 37 patients enrolled in this trial, 35 patients survived without recurrence, one required a dose reduction in paclitaxel, and one has incomplete staging as grade is still pending. The two patients that did experience recurrence died. Of these two patients, the first had American Joint Committee on Cancer (AJCC) 7 stage IIIC cancer, and the second had two separate TNBCs at presentation – AJCC-7 IIB cancer of the right breast and AJCC-7 IIA cancer of the left breast. Under the AJCC-8 system, the first patient had AJCC-8 IIIB cancer, while the second patient had AJCC-8 IIIB cancer of the right and left breasts. These data suggest a completion rate of 97%, overall survival (OS) rates of 95% (AJCC-7 & 8), and progression free survival (PFS) rates of 95% and 94% (AJCC-7 & 8, respectively; Table 1). Additional stage-specific survival metrics and patient staging information are available in Table 1. Median follow-up in this study was 3.14 years. This is consistent with data from our previous study with significant PFS benefit over historic chemotherapy. All patients completed this regimen with no dose reductions of carboplatin and a 32% dose reduction in paclitaxel due to neuropathy. Toxicity was established in our previous study. The favourable toxicity profiling of the regimen allowed maximal tolerance for patients.

Conclusion: Although administration of carboplatin with chemotherapy for TNBC is known to be beneficial, the ideal carboplatin containing regimen has not been identified because of concerns regarding toxicity and low completion rates. Here, an optimal carboplatin-containing regimen identified in our previous clinical trial led to 95% overall survival rates (AJCC-7 & 8), 95% and 94% progression free survival rates (AJCC-7 & 8, respectively), and a 97% completion rate for 37 TNBC patients. A limitation is that this is a small single center trial, and plans are underway to test this regimen with immunotherapy in a larger randomized control trial.

Table 1: Patient Staging and Survival Metrics.

Metric of Interest		AJCC-7	AJCC-8
Patients per Stage	Stage 1	2	5
	Stage 2	27	21
	Stage 3	8	10
	Stage 4	0	0
Survival	Overall PFS	95%	94%
	Overall Survival	95%	95%
	Stage 2 PFS	96%	100%
	Stage 2 OS	96%	100%
	Stage 3 PFS	88%	80%
	Stage 3 OS	88%	80%

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Lymphedema, shoulder range of motion, pain, and presence of cords in patients undergoing breast cancer treatment with axillary web syndrome: Late follow-up.

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Introduction: Axillary web syndrome (AWS) is a common complication in the immediate postoperative period in women after breast cancer surgery. The symptoms are defined as the presence of cords, pain, and limited shoulder range of motion (ROM). Pathophysiology has been described as lymphatic thrombosis, which could be a risk factor for the development of lymphedema. Considered by some to be self-limiting, it has been described as a chronic complication, persisting for years after initial onset. Objective: To determine the prevalence of AWS in a longitudinal cohort of women in a late follow-up after breast cancer surgery and to assess shoulder ROM, presence of pain, permanence of cords and correlation with lymphedema. Methods: A longitudinal cohort study was carried out at the Division of Breast Cancer Disease of the Universidade Federal de São Paulo. Twenty-five women were followed up and reassessed regarding the permanence of cords, pain, ROM, and presence of lymphedema. Results: Of the 25 patients analyzed, 64% (16 patients) showed prevalence of AWS. On recall, all cords were palpable and 87.5% were in the axilla. There was no correlation between AWS and lymphedema. Conclusions: AWS is an important complication in the immediate postoperative period, that persists for several years, without restrictions on function, pain or shoulder ROM limitations. We must therefore consider it as a complication that becomes chronic but has no impact on quality of life. The correlation with lymphedema was not significant in our study. Key words: breast neoplasms, axillary web syndrome, physical exercise, articular range of motion, pain, lymphedema.

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Real-World, Single-Center Experience on the Outcomes of Neoadjuvant Chemotherapy and Trastuzumab alone or in Combination with Pertuzumab in Human Epidermal Growth Factor Receptor 2 Breast Cancer Patients

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Background: Neoadjuvant chemotherapy is the standard of care for early stage breast cancer. Human epidermal growth factor receptor 2 (HER2) positive disease constitutes a large proportion of breast cancer patients, and HER2 overexpression is associated with poor prognosis. The induction of HER2+ targeted therapies, such as trastuzumab and pertuzumab, has resulted in improved outcomes in HER2+ breast cancers. Neoadjuvant chemotherapy in combination with HER2 targeted therapies aims at achieving pathological complete response (pCR) and an improved survival.

Methods: We performed a retrospective review of HER2+ breast cancer patients who were treated at Medanta – The Medicity Hospital, Gurugram, Haryana, India, between 2011 and 2021. A total of 108 HER2+ breast cancer patients who received neoadjuvant chemotherapy with platinum, anthracycline or taxane-based regimens, along with trastuzumab alone or in combination with pertuzumab, were included.

Results: Of 108 enrolled patients, 66 and 42 patients received single-blockade (trastuzumab) and dual-blockade (trastuzumab and pertuzumab) neoadjuvant anti-HER2 therapy, respectively. The majority of patients were aged < 60 years. The patient populations were comparable in terms of clinical stage, hormone receptor status, histopathology category (IDC being most common) and Ki67 status for single- and dual-blockade groups. All patients had IHC3+/FISH+ HER2 expression. No significant (p=0.896) difference was observed for breast conserving surgery between the groups. A higher pCR rate after surgery was reported in the dual-blockade group versus single-blockade group (50% vs. 39.2%; p=0.271). The median follow-up duration was 21.9 and 15.2 months in the single-blockade and dual-blockade groups, respectively. For dual- vs. single- blockade groups, the 1-year OS rates were 100% vs. 100%, and 3-year OS rates were 100% vs. 98.48%. For dual- vs. single- blockade groups, the 1-year DFS rates were 100% vs. 95.45%, and 3-year DFS rates were 92.85% vs. 80.3%.

Conclusion: Neoadjuvant chemotherapy with dual HER2-blockade had higher pCR and survival rates compared with the single HER2-blockade strategy in HER2 positive breast cancer.

Table. Patient characteristics

Parameter	All patients (N=108)	Chemotherapy + trastuzumab (n=66)	Chemotherapy + trastuzumab + pertuzumab (n=42)	P-value
Age (n, %)				
<60 years	80 (74.1)	54 (81.8)	26 (61.9)	0.0213
≥60 years	28 (25.9)	12 (18.2)	16 (38.1)	
Cancer stage, n (%)				
II	47 (43.52)	28 (42.42)	19 (45.23)	0.7737
III	61 (56.48)	38 (57.57)	23 (54.76)	
Hormone receptor status (n, %)				
HR positive	57 (52.78)	37 (56.06)	20 (47.61)	0.3916
HR negative	51 (47.22)	29 (43.94)	22 (52.39)	
Pathology (n, %)				
IDC	104 (96.3)	63 (95.5)	41 (97.6)	0.456
ILC	2 (1.9)	2 (3.0)	0	
Others	2 (1.9)	1 (1.5)0	1 (2.4)	
Ki67 Status, n (%)				
<60%	19 (90.48)	8 (88.89)	11 (91.67)	0.8301
≥60	2 (9.52)	1 (11.11)	1 (8.33)	
BCS, n (%)	29 (26.9)	18 (27.3)	11 (26.2)	0.896

BCS, breast conserving surgery; ER, estrogen receptor; PR, progesterone receptor; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

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Local delivery of immunotherapeutics as an in situ vaccine in triple negative breast cancer

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Introduction. Breast cancer (BC) is among the most common types of cancer among women, with an estimated 287,850 new cases and 43,250 deaths in 2022 [1]. Triple negative breast cancer (TNBC), characterized by lack of ER/PR/HER2 receptors, constitutes 10-15% of diagnosed BC and correlates with the worst prognosis and most aggressive form of the disease [2]. Additionally, compared to the other BC subtypes, TNBC have higher rates of recurrence and highest therapy resistance [2]. Because TNBC lacks a clearly defined target, in situ vaccination may pose a viable therapy option, to locally stimulate an immune response and thereby reduce the tumor burden and prevent recurrence and metastasis. To this end, we developed an injectable delivery medium to effectively localize immune agonists at the site of the tumor. **Materials and methods.** Hydrogel delivery medium: Low-viscosity, high-deacetylated chitosan was crosslinked with 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride and N-hydroxysuccinimide at room temperature overnight. The mixture was dialyzed and freeze-dried. A hydrogel was formed by dissolving the chitosan in deionized water at concentrations from 25-50 mg/mL. **In vivo tumor treatment:** 1e5 E0771 breast cancer cells were implanted subcutaneously in the right flank of C57BL/6 mice. When tumors were 50-100mm³, mice were treated intratumorally with 50ug Poly(I:C) + 50ug CpG in 30 mg/mL chitosan gel, with 50ug Poly(I:C) + 50ug CpG in saline, or with gel alone. In the second experiment, to enhance the anti-tumor effect of the immunotherapeutic, 2ug of the cytokine interleukin-12 in the chitosan gel will be delivered intratumorally. All experiments involving laboratory animals were approved by the Institutional Animal Care and Use Committee at North Carolina State University. **Results and Discussion.** The gel was effectively localized within the tumor environment upon injection. The localized Poly(I:C) + CpG in the gel demonstrated an enhanced anti-tumor effect, compared to gel alone. Ongoing work will determine the efficacy of administering the cytokine IL-12. **Acknowledgements.** This work is supported by an NSF Graduate Research Fellowship. **References.** [1] Siegel R, et al. *CA A Cancer J Clin* (2022) 72(1):7-33. [2] Retecki K, et al. *Cancers* (2021) 13(23):6012

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Impact of baseline ECOG, comorbidities, and surgery treatment election on overall survival

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Background: Breast cancer is the most common type of neoplasm in women. According to statistics from Globocan 2020, the incidence of breast cancer in Ecuador, as well as worldwide is 47.8 per 100,000 people/year, with a mortality rate of 13.6 per 100,000 people/year. Our health system provides coverage to approximately 60% of the population by the Ministry of Public Health (MSP), 30% by The Ecuadorian social security Institute (IESS) , 5% by other entities (ISSFA, ISSPOL, MUNICIPIOS), and < 3% of the population have private medical coverage. Medical care attentions for breast cancer, covered by the MSP was 7,134 consults in 2013, with an increase to 8,767 in 2018. SOLCA Guayaquil, as a national reference Center, provides 24.425 oncologic consults per year, with 38% corresponding to breast cancer. The presentation of breast cancer, at diagnosis, corresponds approximately to 63% in localized stage, 29% as locally advanced, 6% as metastatic disease, with a 5-year overall survival of 99%, 85% and 29% respectively. The proportion of clinical stage IV breast cancer diagnoses varies from 5-10%, with an average of 6% in urban areas, reaching up to 50% in rural areas, so metastatic breast cancer is a public health challenge, especially for countries with emerging economies like ours. Methods: An observational, retrospective, descriptive, single-center study was carried out. All patients with metastatic breast cancer who had been treated at the National Oncology Institute SOLCA Guayaquil, in the period from 2016 to 2020 were included in the analysis. The clinical and pathological characteristics were recorded and their impact on overall survival was calculated by the Kaplan-Meier method and compared by the long-rank test, multivariable adjusted hazard ratios (HR) were estimated by Cox regression models. Results: 3700 patients were identified between January 2016-December 2020. A total of 2587 patients were excluded. Of a total of 1113 remaining patients, 84 debuted as metastatic disease. No male patients were reported with metastatic breast cancer in the past 5 years. Median age at diagnosis was 53,31 years (28-88 years). The most frequent metastatic sites, were: bone 63.86% (N:53), lungs 50.6% (N:42), liver 30,12% (N:25), soft tissue 22.89% (N:19), CNS 16.87% (N:14); A multivariable analysis was performed, all metastatic sites have a higher risk of mortality vs not having any metastasis, but the only significant one is CNS metastases RR 1.31 (1.08-1.61), $p < 0.005$. A total of 28 patients (33.73%) had 2 metastatic sites at presentation; 21 patients (25.30%) had 3 or more metastatic sites at presentation with a RR 1,22 (0.95-1,57) $p:0,011$, with overall survival -OS- (36 months vs 15 months) (long Rank 0,001). ECOG 1 was reported in 59 patients (71.08%), ECOG 2 in 18 (21.69%) and ECOG 3 in 5 (6,02%). A multivariable analysis was performed with ECOG 2-3, RR 1.03 (0,43-2-44), $p:0,94$. Principal reported comorbidities where: hypertension in 28 patients (33,73%), dyslipidemia in 16 (19,28%), obesity 14 (16,87%), Diabetes 8 (9,64%). By grouping 2 or more comorbidities, the RR 1,04 (0,83-1.30), $p:0,71$. Surgery was classified as done or not, where 33 patients (39,77%) underwent rescue mastectomy. Multivariable analysis shows Not Surgery with a RR 1,88 (1.07-3,3) $p:0.02$. Median OS was estimated for surgery 44,48 months $\pm 4,7SD$; Not surgery 20,72 months $\pm 2,8 SD$. Conclusions: In our population, metastatic breast cancer occurs in 7.6% (84 patients out of 1113 total), similar to that reported worldwide. Being a neoplasm with multiple immunophenotypes, and therefore, different treatment options, OS depends on multiple clinicopathological variables. This study showed that CNS metastases

have a negative impact on OS, it is an independent variable for RR of mortality. ECOG and comorbidities did not show an impact on OS. Ultimately, mastectomy was offered to patients with good clinical response to systemic chemotherapy, and shows positive impact in OS.

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Effect of sacituzumab govitecan vs chemotherapy in HR+/HER2- metastatic breast cancer: patient-reported outcomes from the TROPiCS-02 trial

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Background: For HR+/HER2- metastatic breast cancer (MBC) patients, after resistance to endocrine therapy (ET), treatment options are mostly limited to traditional chemotherapies (CT) that offer poor survival and quality of life (QoL), creating an area of unmet need. The antibody-drug conjugate sacituzumab govitecan (SG) comprises an anti-Trop-2 antibody coupled to SN-38 via a hydrolyzable linker. In the phase 3 TROPiCS-02 trial, heavily pretreated patients with relapsed/refractory HR+/HER2- MBC received SG vs single-agent chemotherapy treatment of physician's choice (TPC). The study met its primary endpoint of improved progression-free survival with SG vs TPC. Here, we report the effect of SG vs TPC on patient-reported outcomes (PROs) from TROPiCS-02.

Patients and Methods: Patients who had received ≥ 1 CDK 4/6 inhibitor, ≥ 1 ET, and 2-4 prior lines of CT were randomized to receive SG (10 mg/kg intravenous on days 1 and 8 of a 21-day treatment cycle) or TPC (capecitabine, eribulin, gemcitabine, or vinorelbine). In the PRO-evaluable population (all randomized patients with an evaluable assessment at baseline (BL) and ≥ 1 post-BL visit) SG and TPC were compared regarding time to first clinically meaningful worsening (TTD) or death from BL on the EORTC QLQ-C30 domains (≥ 10 points), EQ-5D-5L health utility index (≥ 0.08 points), and EQ-VAS (≥ 7 points). For the EORTC QLQ-C30 function and global health status/QoL domains, patients with a BL score ≥ 10 and for symptom scales, patients with a BL score ≤ 90 were included. In the safety population (all randomized patients who received ≥ 1 dose of study drug), SG and TPC were compared regarding worst level of toxicities during treatment for the PRO-CTCAE items. For TTD, a stratified Cox proportional hazards regression analysis was conducted and the PRO-CTCAE items were summarized descriptively (numbers and percentages).

Results: Of 543 randomized patients, 446 (82%), 445 (82%), and 517 (95%) were included in the PRO-evaluable population (EORTC QLQ-C30: SG vs TPC n=236 vs 210 and EQ-5D-5L: n=238 vs 207) and in the safety population for PRO-CTCAE (SG vs TPC n=268 vs 249), respectively. TTD of EORTC QLQ-C30 global health status/QoL, physical functioning, emotional functioning, fatigue, dyspnea, insomnia, and financial difficulties and EQ-VAS were significantly longer in the SG vs the TPC arm (Table). TTD of EORTC QLQ-C30 diarrhea was significantly shorter for SG vs TPC. For PRO-CTCAE items, decreased appetite, nausea, vomiting, constipation, abdominal pain, shortness of breath, and fatigue were similar between SG and TPC arms, whereas frequency of diarrhea and amount of hair loss were higher in the SG vs TPC arm.

Conclusions: In this trial, SG significantly delayed worsening of overall QoL, physical and emotional functioning, and symptoms like fatigue, dyspnea, and insomnia. Overall, our findings suggest that SG has more favorable effects on PROs compared with TPC in pts with HR+/HER2- MBC.

Table: Time to First Clinically Meaningful Deterioration of PRO Scores

Domain	Median time to first clinically meaningful deterioration (TTD) (months)		Hazard ratio	95% confidence interval
	SG	TPC		
EORTC QLQ-C30 (N=446)				
Global health status/QoL	4.0	2.9	0.736	0.593-0.913**
Physical functioning	5.0	3.7	0.771	0.622-0.956*
Role functioning	2.6	2.8	0.924	0.750-1.139
Emotional functioning	7.4	5.0	0.672	0.537-0.842**
Cognitive functioning	4.6	4.6	0.889	0.715-1.104
Social functioning	2.9	3.6	0.889	0.718-1.101
Fatigue	2.1	1.4	0.756	0.616-0.927**
Nausea and vomiting	2.2	4.6	1.129	0.914-1.394
Pain	3.7	3.4	0.921	0.744-1.138
Dyspnea	5.7	4.4	0.753	0.605-0.937*
Insomnia	6.2	4.4	0.772	0.616-0.969*
Appetite loss	3.6	4.5	0.977	0.784-1.217
Constipation	3.8	4.9	1.066	0.857-1.325
Diarrhea	2.2	5.8	1.541	1.241-1.913**
Financial difficulties	9.2	6.8	0.786	0.621-0.994*
Summary score	5.0	5.3	0.922	0.742-1.146
EQ-5D-5L (N=445)				
Health utility index	5.3	5.1	0.937	0.752-1.168
EQ-VAS	4.4	3.5	0.790	0.637-0.979*

* P<0.05; ** P<0.01

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Targeting CDK7 enhances the antitumor efficacy of enzalutamide in androgen receptor-positive triple-negative breast cancer

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Background: Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer. Among TNBC subtypes, the luminal androgen receptor (LAR) subtype expresses high levels of androgen receptor (AR), tends to be less proliferative, and generally responds poorly to neoadjuvant therapy. Previous studies have shown that AR inhibition suppressed proliferation of AR+ or LAR subtype TNBC cells and tumor growth in xenograft models. Thus, AR is a

promising therapeutic target for this TNBC subtype. Here, we identified kinase targets for enhancing the antitumor efficacy of the AR inhibitor enzalutamide in preclinical models and investigated the underlying molecular mechanisms. Methods: We performed a nonbiased high-throughput kinome siRNA screening (targeting 709 genes) to identify a synergistic partner for enhancing the antitumor efficacy of the AR inhibitor enzalutamide in AR+ LAR TNBC. The growth inhibitory effects of enzalutamide alone or combined with kinase inhibitors were determined using the sulforhodamine B staining assay and clonogenic assay. The effect of treatments on the expression of target proteins of interest was examined by Western blot analysis. Results: Enzalutamide was not effective as a single agent to inhibit the proliferation of AR+ TNBC cells (IC50 >15 μ M in MDA-MB-453, CAL-51, CAL-148, MFM223, HCC2185, SUM149, SUM159, and SUM185 cells). Nonbiased high-throughput kinome siRNA screening identified PI3K/AKT/mTOR, cell cycle, and JNK pathways as potential canonical targets for combination with enzalutamide to enhance its antitumor efficacy in AR+ LAR TNBC. Among these pathways, inhibition of cell cycle progression using the CDK7 inhibitor UD-017 showed the most synergistic anti-proliferation effect with enzalutamide in AR+ LAR MDA-MB-453 (50.61% reduction in proliferation compared with enzalutamide alone, $P < 0.001$; and 48.98% reduction in proliferation compared with UD-017 alone, $P < 0.001$) and SUM185 (40.41% reduction in proliferation compared with enzalutamide alone, $P < 0.05$; and 42.76% reduction in proliferation compared with UD-017 alone, $P < 0.05$) TNBC cells. Furthermore, CDK7 knockdown using siRNA significantly enhanced the sensitivity of MDA-MB-453 (60.98%, $P < 0.01$) and SUM185 (30.99%, $P < 0.01$) cells to enzalutamide, and AR knockdown significantly enhanced the sensitivity of MDA-MB-453 (32.64%, $P < 0.01$) and SUM185 (43.62%, $P < 0.01$) cells to UD-017, in both cases with a sensitivity similar to that of enzalutamide plus UD-017. This result suggests that the synergy of enzalutamide and UD-017 results from specific targeting of AR and CDK7. Downstream target analysis revealed that the combination of enzalutamide and UD-017 dramatically reduced the expression of c-MYC. c-MYC knockdown using siRNA dramatically suppressed colony formation in both MDA-MB-453 and SUM185 cells at a degree similar to that of enzalutamide plus UD-017, whereas c-MYC overexpression reversed the synergistic effect of the combination treatment. This result suggests that UD-017 synergizes with enzalutamide through inhibition of c-MYC-mediated tumorigenesis. Conclusion: Our results suggest that enzalutamide synergizes with UD-017 by inhibiting c-MYC-mediated oncogenic activity. These in vitro data warrant future in vivo studies of the antitumor synergy of enzalutamide plus UD-017 in AR+ LAR TNBC models.

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P4-08-02

LOXO-783: A potent, highly mutant selective and brain-penetrant allosteric PI3K α H1047R inhibitor in combination with standard of care (SOC) treatments in preclinical PI3K α H1047R-mutant breast cancer models

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Background Phosphoinositide 3-kinase alpha (PI3K α) H1047R mutations are activating oncogenic events that occur in ~15% of breast cancers (BC). Early generation PI3K α inhibitors target both wild-type (WT) and mutant PI3K α and, as a result, their efficacy may be limited by on-target WT PI3K α -mediated toxicities, including hyperglycemia, skin rash, and diarrhea. LOXO-783 is an oral, potent and highly mutant-selective, brain-penetrant allosteric PI3K α H1047R inhibitor that is currently in phase 1 testing. Preclinically, LOXO-783 as a single agent is highly selective for PI3K α H1047R over WT PI3K α and other PI3K isoforms, and induces single-agent tumor regressions in ER+, HER2- PI3K α H1047R-mutant breast cancer models without causing hyperglycemia or increases in plasma insulin / C-peptide. LOXO-783 also demonstrates brain penetration in vivo with dose-dependent tumor growth inhibition in brain metastasis models. Here we report the efficacy of LOXO-783 with SOC treatments in preclinical breast cancer models. Methods Cell proliferation assays and in vivo studies to evaluate combination effects were performed in various PI3K α H1047R mutant HR+, HER2- and triple negative breast cancer models. For each combination in vitro, a combination index (CI) based on the Loewe Additivity Method was calculated ($CI > 2$ antagonism, $0.5 < CI < 2$ additivity, $CI < 0.5$ synergy). For the in vivo studies, the Bliss Independence Method was used to evaluate the statistical significance of the combination effects. Results Combining LOXO-783 with either fulvestrant (FUL; CI at 50% inhibition = 0.28) or imlunestrant (CI at 50% inhibition = 0.43) showed increased efficacy in cell proliferation assays using the HR+, HER2-, PI3K α H1047R-mutant T47D model. LOXO-783 also demonstrated an additive effect in combination with these endocrine therapies in vivo. Similar results were observed in a T47D model engineered to express ESR1 D538G, as well as in an HR+, HER2- PI3K α double in-cis mutant model (H1047R/D350G) also harboring ESR1 D538G and derived from a patient who had progressed on prior letrozole plus taselisib. Moreover, LOXO-783 plus abemaciclib demonstrated an additive effect in vitro (CI at 50% inhibition = 0.61), and in T47D xenograft and PDX models in vivo. Combinations of LOXO-783 with abemaciclib plus imlunestrant resulted in a mean tumor regression of -48.1%; LOXO-783 with abemaciclib plus FUL showed mean tumor regression of -43.9% in T47D xenografts. Similar efficacy was not observed in the absence of LOXO-783 (mean tumor regression was -7.3% with abemaciclib plus imlunestrant, and 3.2% with abemaciclib plus FUL). We observed comparable results in PDX models. These data collectively demonstrate the additive effect of LOXO-783 with SOC treatments. Extending these studies to additional treatment settings, LOXO-783 was similarly efficacious as a single agent in abemaciclib-resistant and abemaciclib/FUL double-resistant models, and was additive in combination with paclitaxel in a triple negative breast cancer model in vitro and in vivo. Conclusions LOXO-783 shows additive effects when combined with SOC in breast cancers harboring the PI3K α H1047R-mutation (as single or double in-cis mutations) in both HR+ and triple negative settings. LOXO-783 is also efficacious in ESR1 mutant as well as in abemaciclib and abemaciclib/FUL double-resistant models. A phase 1 trial of LOXO-783 alone or in combination with anticancer therapies is ongoing (PIKASSO-01; NCT05307705).

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Operation of eIF4A1-PD-L1 axis in therapy-naïve and drug-resistant TNBC

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Operation of eIF4A1-PD-L1 axis in therapy-naïve and drug-resistant TNBC Background and Premise: Triple-negative breast cancer (TNBC) is an aggressive, metastatic disease with high mortality. The standard-of-care neoadjuvant chemotherapy (NACT) in TNBC shows an initial response but followed by an increase in tumor relapse and distant metastases. Furthermore, metastatic TNBC (mTNBC) patients often develop resistance to NACT and targeted therapies. Immunotherapy with therapeutic antibodies such as anti-programmed death ligand-1 (PD-L1) has shown efficacy in treating a subset of TNBC patients, but currently only 20% of patients qualify for that treatment. Hence, there is an unmet need for developing a precision approach against novel actionable targets along with immunotherapy to treat mTNBC. Eukaryotic initiation factor 4A1 (eIF4A1) is an integral part of the translational machinery for many oncogenic mRNAs including survivin, c-MYC, Rho kinase1, and Cyclins D1 and D3, which all require the helicase activity of eIF4A1 for their translation. Our lab previously established that the eIF4A1 is a vulnerable target in breast cancer stem-like cells (BCSCs) and bulk tumor cells. We further demonstrated a key role for eIF4A1 in cancer stemness and drug resistance. Interestingly, we also observed a reduction in levels of PD-L1 when eIF4A1 is pharmacologically inhibited or genetically ablated. Many downstream effectors of eIF4A1 such as c-MYC, STAT1 and ARF6 (involved in recycling of PD-L1 back to the plasma membrane) are indeed upstream regulators of PD-L1 gene expression and cell surface expression of PD-L1. In this study, we examine human TNBC biospecimens for total eIF4A1 level, levels of STAT1, c-MYC, ARF6 and PD-L1. This will help establish the differential operation of the eIF4A1-PD-L1 axis in therapy-naïve and drug-resistant primary and mTNBC. Approach: Human biospecimens were obtained from CHTN NIH repositories and now we have a collection of more than 100 TNBC tumor samples as well as some lymph node, lung and brain metastases and one sample of male breast primary tumor. These specimens are analyzed for role of eIF4A1 in translation of oncogenic mRNAs that contribute to the gene expression of immune checkpoint PD-L1 and other emerging immune checkpoint markers such as VISTA, TIGIT, and LAG3. To mimic the inclusion criteria for current PD-L1 monoclonal antibody treatment, TNBC tumors are examined for PD-L1 expression via immunohistochemistry after subjecting the samples to deglycosylation for effective detection and also by immunoblotting. Results: The levels of total eIF4A1 from 16 matched, therapy naive TNBC tissue were compared to adjacent normal breast tissue from the same patient via immunoblotting. Total eIF4A1 levels were found

to be significantly elevated in TNBC compared to adjacent normal tissue. The downstream effectors of eIF4A1 such as STAT1 and ARF6 were also significantly elevated indicating a robust helicase activity of eIF4A1 in tumor samples. Importantly, PD-L1 levels was found to be elevated. Additionally, the total eIF4A1 level from tumor lysates from TNBC patients that had received a variety of NACT (i.e., patients with demonstrated drug resistance) were compared against normal untreated breast tissue from volunteers who underwent reduction mammoplasty by immunoblotting. The total eIF4A1 was found to be elevated in drug-resistant TNBC specimens compared to control, therapy-naïve TNBC samples. Conclusion: The eIF4A1-STAT1-PD-L1 axis is highly active in TNBC especially in drug-resistant situations. Currently, we are evaluating emerging immune checkpoints such as VISTA, TIGIT, and LAG3.

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NOS inhibition reverses epithelial-to-mesenchymal transition and synergizes with alpelisib in metaplastic breast cancer.

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Background: Metaplastic breast cancer (MpBC) is a rare, lethal, and highly chemoresistant breast cancer subtype, with no FDA-approved therapeutic options. Most MpBCs are triple-negative, yet have a worse prognosis than non-metaplastic triple-negative breast cancer (non-MpTNBC). MpBC tumors are enriched for markers of epithelial-to-mesenchymal transition (EMT)/cancer stem cells (CSC), produce high nitric oxide (NO) levels, and have a hyperactive phosphoinositide 3-kinase (PI3K) signaling pathway. Increased PI3K and inducible nitric oxide synthase (iNOS) activity are poor prognostic indicators in MpBC. NO can activate multiple oncogenic pathways spatially and temporally, such as PI3K and transforming growth factor beta (TGF β), a critical regulator of EMT. Therefore, our study evaluates whether pan-NOS inhibitor NG-monomethyl-L-arginine (L-NMMA) augments the efficacy of alpha isoform-specific PI3K inhibitor alpelisib in MpBC in vitro and in vivo models. Methods: MpBC cell lines (SUM159, BT549, Hs578T, HCC1806) and Patient-Derived Xenograft (PDX) models were used in our studies. Droplet digital polymerase chain reaction (ddPCR) was conducted to evaluate the iNOS-associated mutation (RPL39 A14V) and PIK3CA hotspot mutation rates in PDX models. Cell viability (SRB/Cell Titer-Glo), combination index (CI), immunoblotting, and immunofluorescence of treated MpBC cell lines and tumor tissues were evaluated. Results: Immunostaining analysis revealed that MpBC PDX tumors had elevated co-expression of iNOS and pAkt (60% vs 23%, $p=0.0495$) relative to non-MpTNBC PDX tumors. MpBC PDX tumors had higher RPL39 A14V (66% vs 4.7%, $p<0.0006$) and PIK3CA hotspot mutation rates (50% vs 19.1%, $p=0.1247$) than non-MpTNBC PDX tumors. Combining L-NMMA with alpelisib was synergistic in MpBC cell lines harboring PIK3CA/PIK3R1 mutations ($CI<1$) and antagonistic in PIK3CA-wild type and PTEN-deleted models ($CI>1$). In vivo evaluation using MpBC PDX tumors found that L-NMMA significantly augmented the efficacy of alpelisib in reducing tumor volume in PIK3CA-mutated MpBC PDX models. Transcriptomic analysis found gene sets associated with EMT reversal, such as the formation of cornified envelope ($P_{adj}=0.0254$) and keratinization pathway ($P_{adj}=0.048$) were enriched pathways in MpBC PDX tumors that responded to combination therapy. Pharmacological and genomic inhibition of iNOS reversed EMT in MpBC cells, as shown by decreased expression of Zeb1, TGF β , Snail, Vimentin, and increased expression of E-cadherin and ZO-1 in immunoblotting analysis. MpBC cells with NOS2 knockout acquired an epithelial-like cellular morphology and this reversal of EMT rendered MpBC cells more sensitive to alpelisib and taxane-chemotherapy. MpBC PDX tumors that responded to combination therapy also exhibited a reversal in EMT, with an associated decrease in aldehyde dehydrogenase (ALDH1), a CSC marker. L-NMMA and alpelisib therapy also resulted in the loss of tumor-initiating ability, enhanced chemosensitivity, and improved overall survival in MpBC PDX models. These studies paralleled results from a phase 1b/2 clinical trial with L-NMMA combined with taxane chemotherapy in a cohort of anthracycline-refractory MpBC patients ($n=15$, NCT02834403). The clinical benefit rate was 40% (6/15), the overall response rate was 20% (3/15), and one patient achieved a pathologic complete response. Relative to baseline tumors, the responder end-of-treatment tumors had undergone reversal of EMT, with enhanced expression of E-cadherin, and decreased expression of iNOS, Zeb1, and ALDH1. Conclusion: Our findings suggest that combining L-NMMA and alpelisib is a novel therapeutic strategy to treat MpBC by reversing EMT and decreasing CSCs, rendering MpBC tumors more chemosensitive. This combination therapy is being tested in a first multicenter phase 2 study targeting this orphan disease.

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12/8/2022

7:00 AM - 8:15 AM

P4-08-06

Clock Genes in Breast Cancer

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Background: Disruption of circadian processes has been linked to cancer initiation, progression, metastasis, resistance, and mortality. Clock proteins are an emerging target for therapy in breast cancer. Circadian rhythms are controlled by a network of transcription/translation feedback loops primarily driven by BMAL and CLOCK and the transcriptional repressors period (PER1-3) and cryptochrome (CRY1-2). We investigated the molecular and clinical associations of clock genes in breast cancer. Methods: A total of 9563 breast tumors underwent molecular profiling (Caris Life Sciences). Analyses included next-generation sequencing of DNA (592 genes-NextSeq, WES-NovaSeq) and RNA (NovaSeq). Clock gene Score (CS) was determined using expression of clock pathway gene Z scores (positives of BMAL, CLOCK and negatives of PER1/2 and CRY1/2) and then stratified into quartiles. xCell was used to quantify immune cell infiltration in the tumor microenvironment (TME). ER/PR was tested by IHC and HER2 was tested by either IHC or CISH. Significance was determined as P values adjusted for multiple comparison (Q) of < 0.05. Real-world survival information was obtained from insurance claims data and was calculated from either tissue collection to last contact or time on treatment (TOT); comparison was done by Kaplan-Meier test. Results: TNBC had the highest median CS score, while HR+/HER2- had the lowest CS (0.96 vs 0.26 $q < .001$). In TNBC, PDL1 was significantly associated with higher CS (56% Q4 vs 28% Q1, $q < .05$). TP53 mutation was associated with higher CS (88% Q4 vs 75% Q1), while CDH1 and STK11 mutations were associated with lower CS (3.4% Q4 vs 8.7% Q1 and 0.1% Q4 vs 2.2% Q1). For the TME (xCell) in TNBC, CD8+ T cells, B cells, monocytes and NK cells were positively associated with CS, whereas CD4+ central and effector memory T cells, eosinophils, and endothelial cells were associated with lower CS (Q1 vs Q4 all $q < .05$). In HR+/HER2- tumors, PDL1 was also associated with higher CS (24% Q4 vs 14% Q1, $q < .05$). TP53 mutations (39% Q4 vs 23% Q1), HMGA2 (2% Q4 vs 0.4% Q1) and LGR5 amplifications (3% Q4 vs 0.4% Q1), and LOH (WES) (35% Q4 vs 21% Q1) were associated with higher CS. CDH1 (12% Q4 vs 23% Q1), KMT2C (6% Q4 vs 10% Q1) and PIK3CA mutations (37% Q4 vs 45% Q1) were associated with lower CS (all $q < .05$). In HR+/HER2- tumors there was a decrease in CD4+ central memory cells, common myeloid progenitor cells, endothelial cells, and eosinophils in high CS tumors. Activated myeloid dendritic cells, B cells, CD4+ memory T cells, CD8+ naïve T cells, M1 macrophages, and Tregs all had higher abundance in high CS tumors. In HR+/HER2+ tumors, PDL1 trended positively with CS but did not reach significance likely due to sample size. For all tumors, PDL1 expression positively correlated with CS (17% Q1 vs 37% Q4) while ER (75% Q1 vs 55% Q4) and PR (49% Q1 vs 38% Q4, all $q < .05$) were negatively associated; no association was seen with HER2. Expression of TIMELESS (HR:0.7, CI: 0.65-0.77) and CLOCK (HR: 0.8, CI: 0.72-0.86) below median were associated with longer OS, while expression of CRY2 (HR: 1.4, CI: 1.3-1.6); PER2/3 (HR: 1.1, CI:1.0-1.2; HR:1.3, CI:1.2-1.4) above median was associated with longer OS. In TNBC, TOT IO therapy was prolonged with higher expression of CLOCK (HR: 0.5, CI: 0.41-0.72), TIMELESS (HR: 0.7 CI: 0.53-0.91), ARNTL (HR: 0.7 CI:0.54-0.92) and CRY1/2 (HR: 0.6, CI: 0.46-0.80; HR: 0.75 CI: 0.57-0.98). Conclusions: Dysregulation of clock

genes is strongly associated with breast cancer subtype and survival. Higher CS is associated with TNBC and PDL1 expression and supports the use of checkpoint inhibitors. Prognosis is better with low expression of TIMELESS and CLOCK and high expression of CRY2 and PER2/3, suggesting a role in tumor development and maintenance. HR+/HER2- tumors have lowest CS, fitting with less aggressive phenotype and better prognosis. Clock genes are novel predictive and prognostic molecular markers and emerging targets for the development of new treatments in breast cancer.

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-08-07

Inhibition of the NUDT5 phosphatase suppresses the growth of triple-negative breast cancers

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Inhibition of the NUDT5 Phosphatase Suppresses the Growth of Triple-negative Breast Cancers Jing Qian¹, Yanxia Ma¹, Abhijit Mazumdar¹, Cassandra Moyer¹, Brent D. G. Page³, William Tahaney², Jamal Hill¹, Darian Coleman¹, Powel. H. Brown¹, 2 1 Department of Clinical Cancer Prevention, UT MD Anderson Cancer Center, Houston, TX 2 Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, TX 3 Faculty of Pharmaceutical Sciences, University of British Columbia, Canada, Vancouver BC Background: 281,550 new cases of invasive breast cancer will be diagnosed in US this year. 15% of these patients will be diagnosed with triple-negative breast cancers (TNBCs), which is the most aggressive subtype of breast cancer. Non-specific chemotherapy remains the current standard of care for TNBCs, due to the lack of targeted therapy. We have previously conducted a whole phosphatase RNA microarray analysis of TNBCs compared to estrogen receptor (ER)-positive breast cancers. These studies identified phosphatases that were either over-expressed or under-expressed in TNBCs as compared to ER-positive breast cancers. In this study, we investigated one of the highly expressed phosphatases NUDT5, which hydrolyzes 8-oxo-dGDP and ADP-ribose, as a potential new target for the treatment of TNBCs. Hypothesis: NUDT5 is a critical phosphatase that is necessary for the growth of triple-negative breast cancers. Methods: We obtained NUDT5 mRNA expression levels from publicly-available TCGA, METABRIC, and the CCLE datasets, and compared NUDT5 mRNA level in TNBCs versus ER-positive breast cancers. To demonstrate the effect of NUDT5 inhibition on cell growth, we used siRNA, shRNA, sgRNA, and the small molecule inhibitor TH5427 on various ER-positive cell lines and TNBC cell lines. Cell number was counted on Day 1, 3, 5 and 7. We then investigated the biological mechanisms of growth inhibition by Annexin V-PI, DRAQ7, and BrdU proliferation assays. We studied the effect of NUDT5 loss on oxidative stress and DNA damage pathways by measuring 8-oxoG level and γ H2AX positivity in the nucleus. Using nude mouse xenograft models, we also investigated the effect of TH5427 on TNBC growth in vivo. Results: NUDT5 mRNA was highly overexpressed in TNBCs as compared to ER-positive breast cancers in several publically-available datasets. NUDT5 loss significantly inhibited the growth of the TNBC cell lines MDAMB231 and MDAMB436, but not the ER-positive cell lines MCF7 and MDAMB361. NUDT5 inhibition via siRNA or TH5427 did not induce apoptosis or cell death, but did suppress growth as assessed by BrdU incorporation.. In the nucleus, loss of NUDT5 induces the accumulation of the oxidative DNA marker, 8-oxoG, and the DNA damage marker, γ H2AX, in TNBCs cells, indicating that loss of NUDT5 induces oxidative DNA damage response. In the MDAMB231 xenograft models, the inhibitor of NUDT5 suppressed TNBC tumor growth in mice. Conclusions: Our results showed NUDT5 is highly expressed in TNBCs as compared to ER-positive tumors. inhibition of NUDT5 suppresses the growth of TNBC but not of ER-positive breast cancer cells. NUDT5 loss also induces oxidative DNA damage, with increased 8-oxoG

and γ H2AX positivity. These results demonstrate that NUDT5 is essential for the growth of TNBC cells and suggest that NUDT5 is a promising new target for the treatment of these aggressive breast cancers. This work was supported by Charles Cain Endowment (PB).

Disclosure(s):

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P4-08-09

Deoxycytidine kinase (dCK) inhibition is synthetic lethal with BRCA2-deficiency

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BRCA2 is a well-established cancer driver in several human malignancies. While the remarkable success of PARP inhibitors proved the clinical potential of targeting BRCA deficiencies, the emergence of resistance mechanisms underscores the importance of seeking novel Synthetic Lethal (SL) targets for future drug development efforts. In this work, we performed a BRCA2-centric SL screen with a collection of plant-derived compounds from South America. We identified the steroidal alkaloid Solanocapsine as a selective SL inducer, and we were able to substantially increase its potency by deriving multiple analogs. The use of two complementary chemoproteomic approaches led to the identification of the nucleotide salvage pathway enzyme deoxycytidine kinase (dCK) as Solanocapsine's target responsible for its BRCA2-liked SL induction. Additional confirmatory evidence was obtained by using a highly specific dCK inhibitor (DI-87), which induces SL in multiple BRCA2-deficient and KO contexts. Interestingly, dCK-induced SL is mechanistically different from the one induced by PARP inhibitors. dCK inhibition generates substantially lower levels of DNA damage, and cytotoxic phenotypes are associated exclusively with mitosis, thus suggesting that the fine-tuning of nucleotide supply in mitosis is critical for the survival of BRCA2-deficient cells. Moreover, by using a xenograft model of contralateral tumors, we show that dCK impairment suffices to trigger SL in-vivo. Taken together, our findings unveil dCK as a promising new target for BRCA2-deficient cancers, which provides future therapeutic alternatives to PARP inhibitors.

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7:00 AM - 8:15 AM

P4-08-10

Azeliragon (TTP488), an orally- available small molecule RAGE inhibitor, reduces metastasis in preclinical mouse models of breast cancer

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Background: Triple-negative breast cancer (TNBC) is a highly aggressive breast cancer subtype with a high metastatic rate. Despite significant advances in breast cancer therapeutics, due to the lack of specific therapeutic targets in TNBC, cytotoxic chemotherapy is still the mainstay of treatment for this BC subtype. Preclinical studies have shown that the Receptor for Advanced Glycation End-products (RAGE) drives the progression and metastasis of aggressive cancer subtypes, including TNBC. RAGE plays a multifaceted role in driving tumorigenesis and metastasis through tumor cell-intrinsic mechanisms, such as cancer cell invasion, migration and epithelial-mesenchymal transition, and tumor cell-extrinsic mechanisms. This multifaceted role in cancer progression and metastasis makes RAGE a promising therapeutic target in the prevention and treatment of breast cancer. Here we tested the preclinical anti-metastatic efficacy of two small molecule RAGE inhibitors; TTP48 (Azeliragon) and FPS-ZM1. Importantly, TTP488 displays a high safety profile in human trials and has previously undergone Phase 3 clinical trials for Alzheimer's disease. While FPS-ZM1 is a well-known RAGE inhibitor in preclinical cancer models, TTP488 has not been tested for its anti-cancer activity in breast cancer. Methods: We tested the in vitro anti-metastatic effect of TTP488 and FPS-ZM1 on cancer cell migration and invasion in Boyden chamber assays with TNBC cell lines (MDA-MB-231 and 4T-1). We used the 4175 highly metastatic MDA-MB-231 variant in xenograft studies in

NSG mice to test the efficacy of the RAGE inhibitors in vivo on tumor progression and metastasis. Experimental metastasis assays were performed with tail-vein injection of 4T-1 cells into BALBc mice. We performed bulk RNA sequencing on the MDA-MB-231/4175/NSG tumors to unveil and compare the mechanism of action of the two small molecule RAGE inhibitors. Results: Our results showed that TTP488 and FPS-ZM1 impaired mechanisms of metastasis in vitro with both MDA-MB231/4175 and 4T-1 cells. TTP488 and FPS-ZM1 significantly inhibited MDA-MB231/4175 cell metastasis from the orthotopic site in NSG mice without displaying any deleterious effects on mouse health. In the syngeneic 4T-1/BALBc model, both TTP488 and FPS-ZM1 impaired metastasis in tail-vein injected experimental metastasis assays. Transcriptomic analysis of primary xenograft tumors from NSG mice revealed that TTP488 and FPS-ZM1 displayed high concordance in gene expression changes. Pathway enrichment analysis showed that both RAGE inhibitors affected metastatic pathways, including focal adhesion, ECM-receptor interaction, cell cycle, and DNA replication. Conclusions: These results show that TTP488 impairs metastasis of multiple highly aggressive TNBC models for the first time. Importantly, as TTP488 displays a high safety profile in human trials, this study provides the rationale for evaluating TTP488 in clinical trials to treat or prevent metastatic breast cancer.

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P4-08-11

AKT and EZH2 inhibitors kill TNBCs by hijacking mechanisms of involution

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Triple negative breast cancer (TNBC) is the most aggressive breast cancer subtype and has the highest rate of recurrence. The predominant standard of care for advanced TNBC is systemic chemotherapy with or without immunotherapy, however responses are typically short-lived. Thus, there is an urgent need to develop more effective treatments. PI3K pathway components represent plausible therapeutic targets, as approximately 40% of TNBCs have PIK3CA/AKT1/PTEN alterations. However, unlike hormone receptor-positive tumors, it is still unclear if or how PI3K pathway inhibitors will be effective in triple-negative disease. Here we identify a promising AKT inhibitor-based therapeutic combination for TNBC. Specifically, we show that AKT inhibitors potently synergize with agents that suppress the histone methyltransferase, EZH2, and promote robust tumor regression in multiple TNBC models in vivo. AKT and EZH2 inhibitors exert these effects by first cooperatively driving basal-like TNBC cells into a more differentiated, luminal-like state, which cannot be effectively induced by either agent alone. More importantly, once differentiated, these agents kill TNBCs by hijacking signals that normally drive mammary gland involution. Together these findings identify a promising therapeutic strategy for this highly aggressive tumor type and illustrate how deregulated epigenetic enzymes can insulate tumors from oncogenic vulnerabilities. These studies also reveal how developmental tissue-specific cell death pathways may be co-opted for therapeutic benefit.

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Clinical and Genomic Landscape of Breast Cancers Carrying CCNE1 Amplification

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Background: Cyclin E1 (CCNE1) plays a critical role in cell cycle regulation. CCNE1 overexpression and/or gene amplification (amp) have been associated with poor outcome in several tumors, including breast cancer (BC). CCNE1 amp has recently been identified as a potential therapeutic target for novel synthetic lethality-based therapies. Here we sought to define the clinical and genomic features of BCs carrying CCNE1 amp. Methods: Genomic and clinical data from all consecutive BCs, which had been subjected to targeted sequencing using the FDA-authorized MSK-IMPACT assay from April 2014 to December 2021, were retrieved. Allele-specific copy number and fraction genome altered (FGA) were assessed using FACETS. Whole genome doubling (WGD) status was inferred from MSK-IMPACT sequencing data. Samples were categorized as CCNE1 amp or non-amp based on copy number profile assessed by FACETS. Mutual exclusivity and co-occurrence analyses between CCNE1 amp and other genetic alterations were performed using CoMEt. Multiple testing correction using the Benjamini–Hochberg procedure was applied to control for the false discovery rate. Progression-free survival (PFS) was assessed by Kaplan Meier method and Cox proportional-hazards models. Survival analyses were restricted to only patients with available pre-treatment samples.

Results: Of 3,753 BCs with full clinical and genomic data, 125 (3.3%) harbored CCNE1 amp. A significant difference in the proportion of CCNE1 amp between treatment-naïve and post-treatment/metastatic samples was observed (2.4% vs 4%, $p=0.007$). CCNE1 amp was significantly less frequently detected in hormone receptor (HR)+/HER2- BCs than in HR-/HER2+ and HR-/HER2- subtypes (2% vs 7.6% and 7.2%, respectively, $p < 0.001$), and was particularly rare in invasive lobular BCs (1/452 cases). BCs with CCNE1 amp displayed a higher frequency of WGD ($p < 0.001$) and higher median FGA ($p < 0.001$) than non-amp tumors, overall and in different subtypes, suggesting increased genomic instability. No difference in tumor mutational burden (TMB) between CCNE1 amp and non-amp was found. In primary BC ($n=1,385$), a higher proportion of TP53 alterations was found in cases with CCNE1 amp (odds ratio [OR] 6.0, 95% confidence interval [CI] 2.5-16.6, $q < 0.001$). Conversely, CCNE1 amp was mutually exclusive with CDH1 alterations ($q < 0.001$). Comparable results were found in the analysis of post-treatment/metastatic samples ($n=2,368$). A subset analysis on HR+/HER2- BCs confirmed that TP53 (OR 4.2, 95%CI 2.28-8.11, $q < 0.001$) and CDH1 (OR 0.09, 95%CI 0.002-0.57, $q < 0.1$) alterations co-occurred and were mutually exclusive, respectively, with CCNE1 amp. ARID2 alterations were also enriched in HR+/HER2- tumors harboring CCNE1 amp (OR 10.6, 95%CI 2.54-33.93, $q < 0.1$). CCNE1 amp was significantly associated with reduced median PFS (8.8 vs 15.2 months in CCNE1 amp [$n=9$] vs CCNE1 non-amp [$n=402$]; hazard ratio [HR] 2.82, 95% CI 1.38-5.75, $p=0.004$) on first line treatment with CDK4/6 inhibitor plus endocrine therapy (ET) in HR+/HER2- metastatic BCs, regardless of the ET partner, FGA and TMB. CCNE1 amp was also associated with numerically inferior median PFS (7.3 vs 20.8 months in CCNE1 amp [$n=5$] vs CCNE1 non-amp [$n=106$]; HR 3.1, 95% CI 1.24-7.87, $p=0.01$) on first line trastuzumab/pertuzumab/taxane treatment in HER2+ metastatic BCs, with a trend toward significance after adjusting for FGA and TMB ($p=0.09$). Conclusions: CCNE1 amp is associated with specific clinicopathological and genomic features in BCs and linked to an increased genomic instability. CCNE1 amp defines a subset of metastatic BCs with marked poor clinical response to available standard-of-care treatments. Further studies testing novel therapeutic approaches, including synthetic lethality-based strategies targeting CCNE1 amp and CDK2-selective inhibition, are warranted.

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7:00 AM - 8:15 AM

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The Use of Reverse Phase Protein Arrays (RPPA), Principal Component Analysis (PCA), and CScape Pathway Mapping to Identify New Tumor Vulnerability and Actionable Targets in Human Malignant Triple-Negative Breast cancer cell lines

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Breast cancer is the major leading cause of cancer-related fatalities nationally and globally. There will be 287,850 new breast cancer cases and 43,250 breast cancer related deaths in the United States in 2022. The relapsed, treatment-resistant, undruggable, and incurable breast cancers are often associated with EGFR/HER2/K-RAS/SIAH pathway activation. The EGFR/HER2/K-RAS/SIAH pathway is a major tumor-driver whose hyperactivation is associated malignant tumor growth, multidrug-resistant phenotypes, early tumor relapse, and systematic metastasis. Seven-In-Absentia (SINA) homologues (SIAH) are extraordinarily evolutionarily-conserved E3 ubiquitin ligases that play a critical gatekeeper role downstream of the EGFR/HER2/K-RAS pathway. SIAH is a major tumor vulnerability that is ideally positioned to become an attractive target for innovative targeted therapy development against metastatic breast cancer (MBC). Prior studies have shown that tumor growth was abolished in malignant

tumor cell lines such as MDA-MB-231, MDA-MB-468, MiaPaCa, A459, and HeLa following SIAH inhibition in xenograft models; however, the underpinning molecular mechanisms that give rise to this striking anti-EGFR/K-RAS and anticancer phenotype remain unclear. Specific objectives: to delineate the molecular mechanism(s) of why anti-SIAH2PD targeted therapy is so effective in impeding and eradicating the stage IV and aggressive tumors, we conducted reverse phase protein array (RPPA)-based kinomic analysis to delineate how major cancer signaling pathways and EGFR/HER2/K-RAS/SIAH-dependent signaling networks are rewired and remodeled in response to anti-SIAH2 targeted therapy. Brief statement of methods: About 300 proteins/phosphoproteins were quantitatively measured by the RPPA platform to identify new tumor vulnerabilities and actionable targets, compensatory signaling network activation/inhibition in response to anti-SIAH targeted therapies in five highly malignant cancer cell lines. Doxycycline (DOX)-inducible Tet-ON MDA-MB-231, MDA-MB-468, MiaPaCa, HeLa and A459 cell lines were amplified from single cell and DOX-induced SIAH2PD expression was confirmed. Each of the cell lines was then subjected to one of four experimental conditions: Tet-ON control cells without DOX induction (group A), Tet-ON control cells with DOX induction (group B), Tet-ON-SIAH2PD cancer cells without DOX-induction (no SIAH2PD inhibitor) (group C), Tet-ON-SIAH2PD cancer cells with DOX-induction (SIAH2PD inhibitor) (group D). Reverse Phase Protein Array (RPPA) in conjunction with Principal Component Analysis (PCA) was conducted to quantify fold-changes of proteins/phosphoproteins in response to SIAH inhibition. The ratios of D/C/B/A, D/C, D/B, C/A, and B/A were calculated using GAPDH normalized data. Summary of results: Supported by statistical analyses, we identified 6 unique phospho-proteins that were either up- or down-regulated in response to SIAH Loss-of-function. Many have known roles in controlling and regulating cell growth, cell death, NFκB signaling, stress response, DNA damage, and cell attachment pathways, supporting a tumor eradication phenotype in the absence of SIAH function in these cancer cell lines. Conclusion: Cancer landscape (CScape) functional protein pathway mapping has categorized the synergistic feedforward, feedback, and compensatory signaling pathway activation/inactivation in response to SIAH blockade in these EGFR/HER2/K-RAS-driven malignant human cell lines. Further validation analysis will be conducted to gain better insight into the global cancer pathway alterations to reveal the molecular mechanism(s) of why SIAH inhibition works so effectively to shut down malignant tumor growth in the preclinical models.

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Overcoming drug transport barriers in breast cancer liver metastasis by using macrophages as carriers: valuation in 2D and 3D models

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Breast cancer liver metastasis (BCLM) is encountered in >50% of breast cancer patients with advanced disease and is associated with the poorest disease prognosis. Unlike primary tumors and metastatic lesions in other organs, BCLM growth relies heavily on the liver vasculature, leading to lesions that are hypo-vascularized. Consequently, most BCLM clinically appear as hypoattenuating spots. This under-vascularization prevents systemically administered agents from reaching all of the cells in these lesions, causing physiological, transport-related resistance to therapy. The liver is an organ enriched in macrophages, which play important roles by affecting tumor growth, angiogenesis, metastasis and chemoresistance. These phagocytic cells remain in close proximity to BCLM and have been clinically utilized for imaging with nanomaterials. We have previously shown (T. Tanei et al, *Cancer Res.* 2016) that drug transport barriers can be overcome using macrophages as carriers for nanotherapeutics, leading to an efficient therapy for BCLM. The prerequisite for this therapy is the ability of BCLM to attract macrophages from surrounding liver tissue. The drug-carrying macrophages can escape host defense mechanisms, hence extending the therapeutic agent half-life and releasing it in close proximity of tumor cells under-exposed to vascular-borne drugs. In the present study, we aimed to evaluate the ability of different breast cancer cells to attract macrophages, further exploiting these cells as a viable candidate for targeted delivery of lipid nanoparticles. For this purpose, we evaluated the transport phenomena of macrophages in the presence of a variety of human breast cancer cells, including, MCF7 (ER+, PR+/-, HER2-), T-47D (ER+, PR+/-, HER2-), MDA-MB-231 (TNBC), SUM-159 (TNBC). The studies were conducted in tumor cell-macrophage co-cultures in 2-dimensional (2D) and 3-dimensional (3D, hypovascularized model) settings. Human macrophages were derived from buffy coats from healthy donors and prelabelled for the co-culture experiments. The majority of macrophages were M0 phenotype. The following parameters were assessed for macrophage infiltration: a)

static (confocal) and kinetic (Incucyte) microscopy imaging of cell transport, b) cell counts for migration assay, c) immunofluorescence, d) directionality/path length. The datapoint towards the variability in behaviors of macrophage transport towards the tumor cells in both 2D and 3D settings. MDA-MB-231 (triple negative breast cancer cell line) was more prominent in recruiting macrophages, which can be clinically correlated to higher tumor grade and reduced overall and relapse-free survival. These findings were further utilized to mathematically model and experimentally evaluate BCLM therapeutic response to nanocarriers loaded with high molecular weight (HMW) therapeutics. Longer term, this work provides a methodology for macrophage-mediated targeting of particular patient hypo-vascularized BCLM. Acknowledgement: This research is partial support by Department of Defense/U.S. Army Medical Research grant

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Identification of target kinases whose inhibition enhances antitumor efficacy of sacituzumab-govitecan in metastatic HER2-negative breast cancer

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BACKGROUND HER2-negative (HER2-) breast cancer (BC) subtypes, such as luminal A and triple-negative breast cancer (TNBC), express human trophoblast cell-surface antigen 2 (Trop-2). A high level of Trop-2 expression is associated with a poor prognosis in solid tumors. Sacituzumab-govitecan (SG), a Trop-2-directed antibody conjugated with SN-38 (topoisomerase I inhibitor) significantly improves survival in patients with metastatic TNBC. Also, the IMMU-132-01 phase I / II study revealed that SG has antitumor activity in previously treated hormone receptor (HR)+/HER2- metastatic BC. In a phase III trial (TROPICS-02), SG demonstrated statistically significant progression-free survival in patients with heavily pre-treated HR+/HER2- endocrine-resistant metastatic BC. To augment the efficacy of SG, we sought to identify potential kinase targets whose inhibition enhances the antitumor efficacy of SG to formulate an SG-based combination therapy. MATERIALS AND METHODS

Fluorescence-activated cell sorting analysis and Western blotting were used to evaluate the expression of Trop-2 in 24 TNBC and 8 HR+ BC cell lines. Non-biased high-throughput kinome-wide RNAi screening was performed with BT-20 (TNBC) and T47D tamoxifen/abemaciclib double-resistant (HR+) cell lines to identify target kinases whose inhibition produces synergistic antitumor efficacy of SG. To validate the combination antitumor effect of SG and selected kinase target inhibitors, sulforhodamine B staining proliferation assays, cell cycle analysis, and caspase 3/7 activity assays were performed in Trop-2+ TNBC and HR+ BC cell lines, including cell lines resistant to tamoxifen and double-resistant to tamoxifen and CDK4/6 inhibitor (palbociclib or abemaciclib). RESULTS In vitro proliferation assays revealed that the half-maximal inhibitory concentration (IC50) of SG in tested TNBC cell lines ranged from 10 nM to 84 nM, and that of HR+ cell lines ranged from 12.5 nM to >250 nM. We identified 69 kinase targets in TNBC cell line BT-20 and 44 kinase targets in HR+ BC cell line T47D (tamoxifen/abemaciclib double-resistant) by the sensitivity index analysis (>0.15) of RNAi screening results, and further pathway analysis revealed DNA damage response (DDR), (drug: BAY1895344), PI3k/Akt/mTOR (drug: copanlisib), and MAPK (drug: trametinib) as potential target canonical pathways whose targeting enhanced the cytotoxic effect of SG in both TNBC and HR+ BC. Among these strategies, inhibition of the DDR pathway with ATR inhibitor (BAY1895344) yielded a synergistic antiproliferative effect in combination with SG compared to SG or BAY1895344 alone in all tested TNBC and HR+ BC cell lines. Growth inhibition by SG combined with BAY1895344 averaged 97.1% in TNBC cell lines and ranged from 30.7% to 81.3% in HR+ BC cell lines, with $P < 0.001$. Other combinations with SG showed partially synergistic antiproliferative effects (copanlisib: effective in 3 of 5 cell lines, trametinib: effective in 2 of 5 cell lines). CONCLUSIONS RNAi screening uncovered DDR, PI3k/Akt/mTOR, and MAPK pathways as potential targets for combination with SG. Among inhibitors of these targets, DDR pathway inhibitor BAY1895344 had the most robust synergy with SG, compared to two other target inhibitors, against Trop-2+ TNBC and HR+ BC cell lines. These in vitro data warrant future in vivo validation studies of the synergistic antitumor effect of SG and BAY1895344 in metastatic HER2- breast cancer.

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7:00 AM - 8:15 AM

P4-08-16

Selective Androgen Receptor Modulators in combination with CDK4/6 inhibitors demonstrate anti-cancer activity in preclinical treatment resistant ER+AR+ breast cancer models.

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Background: The Androgen Receptor (AR) is expressed in up to 90% of all ER+ breast cancers and has been associated with better patient outcome. While androgens were used at a high dose as an anticancer therapy historically, this was discontinued with the advent of Tamoxifen due to virilising effects. Non-steroidal, tissue selective AR modulators (SARMs) represent an attractive alternative, offering a targeted approach to AR activation. Recent compelling pre-clinical data has established that the AR is a tumour suppressor in ER+ breast cancers and that AR activation with a natural androgen or a SARM suppressed ER-driven tumour growth, in preclinical models of endocrine-sensitive and -resistant ER+ breast cancer. Here, we evaluate the efficacy of a SARM (enobosarm) and a natural AR ligand (dihydrotestosterone, DHT) in the context of metastatic, CDK4/6 inhibitor (CDK4/6i) resistant breast cancer. Methods: Enobosarm

and palbociclib treatments were evaluated in vitro by colony forming assays using CDK4/6i resistant (MCF7 PalbR) and both endocrine and CDK4/6i resistant (MCF7 cTamPalbR) cell lines. Next, enobosarm or DHT and palbociclib treatment were evaluated in vivo using endocrine and CDK4/6i resistant ER+ patient derived xenograft models (PDX) and cell line xenograft models. IHC, RNA and ChIP sequencing (AR, ER, H3K27ac) were subsequently performed on the harvested tumours. Results: While in vitro and in vivo growth of CDK4/6i resistant preclinical models was inhibited by treatment with a SARM or DHT alone, growth inhibition was more potent and durable in combination with a CDK4/6i. Gene set enrichment analysis of RNA-seq data integrated with ChIP-seq data revealed upregulation of an AR gene signature associated with a better prognosis following treatment with SARM. Co-treatment with a SARM and a CDK4/6i also enhanced AR signalling compared to SARM alone indicating an interaction of the two signalling pathways. Conclusion: Our data indicates that combination treatment with an AR agonist and a CDK4/6i represents a novel therapeutic strategy for CDK4/6i resistant ER+AR+ breast cancers

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7:00 AM - 8:15 AM

P4-08-17

Repurposing proteasome inhibitors for improved treatment of triple-negative breast cancer

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Background: The de novo drug development process is expensive and challenging, with a high risk of failure. Drug repurposing can ideally identify novel therapeutic indications for FDA-approved drugs with pre-existing pre-clinical and clinical evidence. Both aspirin and tamoxifen drugs are good examples of successful drug repurposing in oncology. Although proteasome inhibitors such as bortezomib and carfilzomib are currently only used to treat multiple myeloma and basal cell lymphoma, we and others have shown that triple-negative breast cancer (TNBC) is particularly sensitive to proteasome inhibition. TNBC is an aggressive form of breast cancer with an urgent need for novel treatment options. Here, we evaluate the potency of proteasome inhibitors and other clinically relevant chemotherapeutic agents on TNBC cell lines. Methods: We performed a high-throughput drug sensitivity screen with eight cell lines representing the four TNBC subtypes (basal-like 1: HCC70 and MDA-MB-468; basal-like 2: HCC1806 and MDA-MB-436; mesenchymal-like: BT-549 and HCC38; luminal androgen receptor: CAL-148 and MDA-MB-435) and MCF-7 as control (estrogen and progesterone receptor-positive) exposed to 18 drugs (11 proteasome inhibitors, 2 mitosis inhibitors, 2 topoisomerase inhibitors, and 3 platinum agents) for 24 hours. Drug potency was determined using the IC50, GR50, GRmax

drug metrics. IDACombo was then used to predict efficacious drug combinations, followed by calculation of synergistic drug combinations with SynergyFinder. Results: TNBC cell lines were generally more sensitive to proteasome inhibitors with significantly reduced cell viability than clinically relevant drugs, e.g. paclitaxel. Although the potency of different proteasome inhibitors varied, the most potent proteasome inhibitors included bortezomib, carfilzomib, delanzomib, epoxomicin, and MLN-2238. According to the GR50 values, HCC38 (range, 8.2-382.7 nM) and MDA-MB-468 (range, 10.8-110.6 nM) were most sensitive to proteasome inhibition, whereas the least sensitive TNBC cell lines were HCC1806 (range, 289.9-Inf nM) and BT-549 (range, 101.0-Inf nM). Using the drug sensitivity screening results for single drugs, IDACombo predicted potent drug combinations for different combinations of bortezomib, carboplatin, carfilzomib, delanzomib, docetaxel, doxorubicin, epirubicin, epoxomicin, MLN-2238, MLN-9708, and nedaplatin. Conclusions: In summary, some proteasome inhibitors (e.g. bortezomib) had a substantial impact on TNBC cell survival. These findings indicate that proteasome inhibitors, together with other forms of chemotherapy, may be further explored as a novel complement treatment for TNBC.

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Engineered Toxin Bodies Specific for TROP2 Positive Cancers

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response and the capacity to restore a functional immune clearance program against the tumor. Three ETBs are in clinical development (MT-5111 targeting HER2, MT-0169 targeting CD38, and AST enabled MT-6402 targeting PD-L1). The novel mechanisms of action have potential benefit in different indications including in the relapsed setting, when disease has progressed after chemotherapies and other targeted therapies, and additionally may be able to combine with standard of care. ETBs are being developed that target other cell surface receptors expressed on solid tumors including tumor-associated calcium signal transducer 2 (TROP2). TROP2 is a clinically validated target in metastatic triple-negative breast cancer (mTNBC) and other cancers such as metastatic urothelial carcinoma (mUC) using antibody drug conjugate (ADC) therapies such as sacituzumab govitecan (Trodelvy®). In vitro, ETBs targeting TROP2 specifically and directly kill tumor cells expressing TROP2 with picomolar activity. ETBs can bind to TROP2 in the presence of the Trodelvy parent monoclonal antibody, sacituzumab, and ETBs retain potency on TROP2 positive cell lines in the presence of clinically relevant concentrations of sacituzumab. AST enabled Trop2 targeted ETBs retain direct cell killing activity and can deliver multiple viral antigens to induce cytokine secretion and T-cell mediated killing in a co-culture assay of TROP2 target cells with antigen matched HLA type and antigen specific T-cells. In vivo, TROP2 targeted ETBs demonstrate good tolerability in a murine HCC1806 triple-negative breast cancer xenograft model and significantly reduce tumor burden relative to vehicle control. These pre-clinical in vitro and in vivo data suggest AST enabled Trop2 targeted ETBs have the potential to deplete Trop2 positive malignancies through multiple unique mechanisms of action.

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Biomarker analysis: Multi-omics elucidation of Cohort 1 from a phase II study of a triple combination of Atezolizumab + cobimetinib + eribulin in patients with metastatic inflammatory breast cancer.

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Background: Inflammatory breast cancer (IBC) is a rare but aggressive tumor type accounting for up to 10% of breast cancer deaths. One-third of IBCs express high PD-L1 that can be targeted by atezolizumab (Az). MEK inhibitor cobimetinib (Co) not only inhibits the RAS-MAPK pathway but can further enhance immune-mediated killing. Thus, we hypothesize that Az+Co may enhance the efficacy of chemotherapy in metastatic IBC (mIBC). We opened a trial to test this hypothesis with a comprehensive multi-omics biomarker assessment. Patients and Methods: In a single-center, open-label phase II study, cohort 1 received one cycle of Az+ Co, followed by four cycles of Az+Co+eribulin (E) to induce a maximum clinical response, followed by Az+Co maintenance. Pre and Post one cycle of Az+Co tumors were collected for immunohistochemistry (IHC), multiplex immunofluorescence (mIF), whole-exome sequencing (WES), and RNA sequencing (RNAseq). Blood was collected for circulating tumor DNA (ctDNA). Results: Seventeen patients were enrolled in cohort 1. Seven had PR, and three had SD as the best responses. Fourteen had pre, and six had pre/post tumors. The levels of PD-L1 expression at pre/post were not associated with responses. WES revealed the median tumor mutation burden at pre- was 9mt/Mb. More than 50% had TP53 and PI3K pathway mutations at pre. RTK-RAS and Notch pathways were altered in 4/9 cases. PRDM9 and DPY19L2 single-gene mutations were commonly noted in pre. No cancer-associated gene aberration, including potential biomarkers of anti-PDL1 agent response was associated with clinical outcomes. Transcriptomic gene set enrichment analysis demonstrated a greater degree of TNF α and TGF β signaling, Oxphos, angiogenesis, and epithelial-to-mesenchymal transition (EMT) processes in tumors from patients with poor response. Immune profiling by RNAseq revealed two responders to have elevated effector memory T cells, NK T cells, myeloid dendritic cells, and M1 macrophage signatures in pre-samples, but post-samples were not available. mIF confirmed a higher frequency of NK-T cells. The ctDNA analysis from serially collected blood samples is ongoing. Discussion: In this comprehensive multi-omics analysis of pre-and-post-Az+Co, we observed several novel findings, while conventional biomarkers for Az and Co did not correlate with clinical responses. EMT, Oxphos, Notch, and chronic inflammation pathways, which are not previously well reported, were observed in this IBC cohort. These markers warrant further validation to see if they carry significance as therapeutic targets in IBC.

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P4-08-20

Inhibition of TACC3 blocks the growth of highly aggressive breast cancers with centrosome amplification

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Centrosome amplification (CA) is a hallmark of cancer that is strongly associated with highly aggressive disease and worse clinical outcome. Enhanced mitotic progression via clustering of extra centrosomes is a major coping mechanism utilized by cancer cells with CA that would otherwise undergo mitotic cell death due to formation of multipolar spindles. However, the underlying molecular mechanisms have largely been unexplored. Furthermore, mitosis-targeting inhibitors have mostly been unsuccessful in clinical settings with poor efficacy and severe side effects. Therefore, there is a dire need to uncover novel molecular mechanisms of CA-driven tumor growth and identify therapeutic targets playing key roles not only in mitosis, but also in interphase of cancer cells with CA to achieve durable anti-tumor effect with minimal toxicity. Here, we identified Transforming Acidic Coiled-Coil Containing Protein 3 (TACC3) as a novel CA-directed dependency, driving highly aggressive cell growth by forming distinct functional interactomes during cell cycle progression. We demonstrated, for the first time, that TACC3 interacts with the Kinesin Family Member C1 (KIFC1) via its TACC domain in mitotic cells with CA to promote centrosome clustering (CC) and facilitate mitotic progression. On the other hand, TACC3 interacts with the members of the nucleosome remodeling and deacetylase (NuRD) complex (HDAC2 and MBD2) in the nucleus of interphase cells with CA, thereby suppressing the transcription of key tumor suppressors to facilitate G1/S progression and cell survival. Inhibiting TACC3 in mitotic cells blocks the formation of TACC3/KIFC1 complex, leading to formation of multipolar spindles and activation of spindle assembly checkpoint (SAC)/CDK1/p-Bcl2 axis that ultimately results in mitotic cell death; whereas TACC3 inhibition in interphase cells blocks TACC3/HDAC2/MBD2 complex, leading to enhanced transcription of cyclin-dependent kinase inhibitors (e.g., p21 and p16) and apoptosis regulators (e.g., APAF1), ultimately causing p53-independent G1 arrest and strong apoptosis. Notably, inducing CA by chemical (cytochalasin D) or genomic (PLK4 overexpression or p53 loss) modulations renders cancer cells highly sensitive to TACC3 inhibition, showing the dependency of cells with CA to TACC3. Targeting TACC3 by small molecule inhibitors or CrispR-CAS9-mediated knock-out significantly reduces colony formation ability, inhibits the growth of organoids of patient-derived xenografts (PDXs) with CA, and strongly inhibits tumor growth in breast cancer cell line xenografts and PDXs with CA. Notably, we demonstrated that high CA tumors express much higher levels of TACC3, and high TACC3 expression, in association with its downstream effectors, KIFC1, HDAC2 and MBD2, leads to drastically worse clinical outcome in cancer

patients with CA. Altogether, our results show, for the first time, that TACC3 is a multifunctional driver of the growth of the highly aggressive breast tumors with CA and that targeting TACC3 is a promising approach to tackle this aggressive disease.

Disclosure(s):

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Development of novel inhibitors of the serum/glucocorticoid induced kinase (SGK) family to address limitations of AKT/PI3K/mTOR inhibitors in breast cancer

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Activation of the AKT/PI3K/mTOR signaling through genetic and epigenetic mechanisms is a frequent event in all subtypes of breast cancer, and it is associated with resistance to various therapies. Development of inhibitors targeting this pathway has been met with limited success so far, mainly due to various feedback and crosstalk mechanisms amongst different members of the pathway. Several therapies that target the PI3K pathway have also been associated with dose limiting toxicities such as hyperglycemia, hyperinsulinemia, skin rashes and infections, limiting their use. The SGK family of kinases has recently been implicated in the resistance to

AKT and PI3K inhibitors by promoting AKT-independent signaling to maintain the activation of the AKT/PI3K/mTOR pathway. The SGK and AKT families share similar domain structures as well as upstream activators such as PDK1 and mTORC2, and downstream effectors such as TSC2, FOXO3, and GSK3B, providing a strong rationale for the development of inhibitors targeting the SGK family. Here we present the development of novel small molecule ATP-competitive inhibitors of the SGK family. Several compounds displayed low nanomolar affinity towards SGK1 in whole cell assays, with IC50s ranging between 10-100 nM, which is 30-300 folds and 80-1000 folds higher than the previously characterized SGK1 inhibitors GSK650394 and EMD638683, respectively, as well as good selectivity against related AGC family kinases. Experiments in cells have shown a strong dose-dependent decrease in the phosphorylation of its downstream target NDRG1 at sub-micromolar concentrations, confirming selective targeting of SGK1 in whole cells. Single agent activity of SGK1 inhibition was modest in different cancer cell lines, with IC50 values for inhibition of their proliferation ranging from 1-10 μ M, in agreement with the role of the SGK family in regulation of stress-induced signaling and not normal cell proliferation. However, combinations of SGK with AKT inhibitors displayed strong synergies in different breast cancer cell lines, especially in cells with resistance to AKT/PI3K inhibitors. For example, strong Bliss synergy index scores > 18 were obtained with different SGK1 inhibitors when combined with either AKT inhibitors MK-2206, ipatasertib, or capivasertib, in the JIMT-1 breast cancer cell line, which is a model of resistance to AKT, PI3K, and HER2-directed therapies. These results suggest that the combination of SGK with AKT inhibitors could be an effective therapeutic strategy to alleviate toxicities associated with AKT/PI3K/mTOR inhibitors by lowering their required dose, while maintaining anti-tumor activity and delaying the development of resistance.

Disclosure(s):

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P4-08-22

Expression of Dual Specific Phosphatase-7 (DUSP7/PYST2) and it's Connection with Salt Inducible Kinases (SIKs) and Downstream MKKs in breast cancer

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Expression of Dual Specific Phosphatase-7 (DUSP7/PYST2) and it's Connection with Salt Inducible Kinases (SIKs) and Downstream MKKs in breast cancer Wenxiao Ji¹, Emily Ling Xin^{1,2}, Lin Ye¹, Eleri Davies³, Wen G. Jiang¹, Tracey A. Martin¹ ¹CCMRC, Cardiff University School of Medicine, Cardiff, Wales, UK ²Breast Centre, Peking University First Hospital, Xicheng District, Beijing, China ³Wales Breast Centre, University Llandough Hospital, Cardiff CF64 2XX, UK Introduction. DUSP7 is a member of the large Dual specific phosphatase family, able to regulate the phosphorylation of both tyrosine and serine/threonine protein kinases. The role of DUSP7 in cancer is not clear, however, it has been identified as a possible target for therapy in cancers including breast cancer. It has also been reported as having value in prognosis of certain cancers, such as haematological malignancies, breast cancer and certain types of gynaecological cancer. The signalling network for DUSP7 is not fully established but is known to connect to ERKs and MAP2Ks. DUSP7 also appears to be linked with salt inducible kinases (SIKs), a small family of kinases linked with progression and response to therapies in breast cancer. Thus, DUSP7 and salt inducible kinases may interact with each other and with the downstream kinases including MAP2Ks and STK11 to influence the clinical course of breast cancer. The present study explored if the pattern of DUSP7 together with salt inducible kinases and the downstream MKKs in breast cancer. Methods. The expression of DUSP7 was quantified in a cohort of breast cancer tissues (both normal mammary tissues and breast cancer tissues). The expression of the potential downstream kinases including MKK1, MKK2, MKK3, MKK4 and STK11 was also quantified. The expression profile of these molecule, together with the salt inducible kinases reported to be aberrant in our previous studies, were analysed against clinical and outcome information. Results. Breast cancer tissues expressed high levels of DUSP7 compared with normal mammary tissues, although not statistically

significant. When we explored the relationship between DUSP7 and other potential related molecules in the database of the cohort, we found a highly significant correlation between DUSP7 and SIK1 ($r=0.385$, $p < 0.001$), SIK2 ($r=0.590$, $p < 0.001$), but not SIK3 ($r=0.158$, $p > 0.05$). Together with SIK1 and SIK2 (known to link to drug sensitivity), DUSP7, MKK1 (MAP2K1) and MKK3 (MAP2K3) appear to form a gene signature that is of significant value in predicting the overall survival of the patients (ROC 0.723, $p=0.001$). This allowed us to significantly distinguish between those with good OS and poor OS ($p < 0.001$, Hazard Ratio (HR) =1.443 (95%CI 1.154-1.804)). Multivariate analysis has shown that this signature is independent in predicting overall survival ($p=0.013$, HR=1.432). The signature is more significant in predicting OS in ER(-) tumours ($p < 0.001$) than ER(+) tumours ($p=0.61$). The same is seen when predicting OS with triple negative breast cancers (TNBC) ($p < 0.001$) than non-TNBC tumours ($p=0.044$). The gene signature also predicted disease free outcome ($p=0.007$, HR=1.266 (95% CI 1.065-1.504)). Conclusion. The dual specific phosphatase DUSP7 together with potentially correlated salt inducible kinases (SIK-1 and SIK-2) and downstream MKKs (MKK-1 and MKK3) have important clinical value in breast cancer. This provides support that DUSP7 may be a valuable therapeutic target in breast cancer.

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ZHX2 promotes HIF1 α oncogenic signaling in triple-negative breast cancer

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Background: Triple-negative breast cancer (TNBC) is an aggressive and highly lethal disease in women, while the oncogenic mechanisms which contribute to TNBC development, progression,

and metastasis are poorly investigated and therefore warrant the critical need to identify novel oncogenic signalings and develop new therapeutic targets. Results: We show that Zinc Fingers and Homeoboxes 2 (ZHX2) is amplified or overexpressed in TNBC cell lines and patients. Functionally, depletion of ZHX2 inhibited TNBC cell growth and invasion in vitro, orthotopic tumor growth, and spontaneous lung metastasis in vivo. Mechanistically, ZHX2 bound with hypoxia-inducible factor (HIF) family members and positively regulated HIF1 α protein level and activity in TNBC. Integrated ChIP-seq and gene expression profiling demonstrated that ZHX2 co-occupied with HIF1 α on transcriptionally active promoters marked by H3K4me3 and H3K27ac, thereby promoting gene expression. Among the identified ZHX2 and HIF1 α coregulated genes, overexpression of AP2B1, COX20, KDM3A, or PTGES3L could partially rescue TNBC cell growth defect by ZHX2 depletion, suggesting that these downstream targets contribute to the oncogenic role of ZHX2 in an accumulative fashion. Furthermore, multiple residues (R491, R581, and R674) on ZHX2 are important in regulating its phenotype, which correspond with their roles in controlling ZHX2 transcriptional activity in TNBC cells. These studies establish that ZHX2 activates oncogenic HIF1 α signaling, therefore serving as a potential therapeutic target for TNBC. Conclusion: ZHX2 has been highlighted as one critical hypoxia-related factors regulator contributing to triple-negative breast cancer in this work, which has enriched the upstream regulatory network of HIF-1 α signaling. Moreover, identification of key residuals determining biological function of ZHX2 provides novel approaches for treating TNBC via targeting the hypoxia pathway.

Disclosure(s):

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P4-08-24

Palmitoylation of Flotillin-1 contributes to Breast Cancer Metastasis

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BACKGROUND Breast Cancer metastasis results in the majority of cancer-related mortality. Flotillin-1 is overexpressed in numerous solid tumors and has been demonstrated to contribute to invasion and metastasis in breast cancer. Though its expression alone has been associated with metastasis, there has yet to be any investigation as to how certain post-translational modifications can affect its metastatic capabilities. Flotillin-1 is modified through palmitoylation, a post-translational modification essential for protein stability, processing, and localization. By generating a palmitoylation defective mutant of flotillin-1, we have demonstrated that flotillin-1 palmitoylation contributes to its stability and metastatic capabilities in both 3D and in vivo models of invasion and metastasis. **MATERIALS AND METHODS** Flotillin-1 wild type or palmitoylation defective C-34-A mutants were expressed in stable flotillin-1 knockdown MDA-MB-231 and SUM-159 triple negative breast cancer cells. These cells were subjected to 2D invasion chambers and 3D collagen invasion assays. Further, both wild type and C34A expressing cells were used for experimental lung metastases in mice by tail vein injection. 2-bromopalmitate (50 μ M) was used as a chemical palmitoylation inhibitor and MG-132 (10 μ M) for proteasomal inhibition. **RESULTS** Invasion in stable knockdown cells was restored by re-expression of flotillin-1, but not by follitillin-1 C34A. We further observed a significant decrease in lung metastasis in flotillin-1 C34A cells compared to wild type flotillin-1. Flotillin-1 C34A expression led to a significant decrease in protein stability, which was restored by MG-132. **CONCLUSION** Flotillin-1 palmitoylation contributes to its stability and subsequent metastatic capabilities in breast cancer cells and experimental metastasis models. Thus, flotillin-1 palmitoylation could be a promising target for breast cancer metastasis.

Disclosure(s):

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P4-08-25

Unravelling the role of human endogenous retrovirus K (HERV-K) in inducible nitric oxide synthase (iNOS) mediated triple negative breast cancer progression

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Human endogenous retrovirus K (HERV-K) belongs to a family of endogenous retroviruses that are present in our genome with similarities to present day exogenous retroviruses. This virus can express several proteins but our knowledge of HERV-K expression in human cancers is mainly limited to the envelope (Env) protein. Elevated HERV-K env protein expression has been shown in breast cancer both in in vitro and in vivo studies. This project aimed to decipher mechanisms of HERV-K induction in triple negative breast cancer (TNBC), and the impact of HERV-K targeting shRNA mediated knockdown on TNBC characteristics including cell migration, invasion and proliferative capacity in 2D and 3D cell culture models. Our results show that a role for inducible nitric oxide synthase (iNOS) in the induction of HERV-K in TNBC cell lines. RNA seq and bioinformatics analysis was performed to identify key molecular processes regulated by HERV-K and nitric oxide (NO) in MDA-MB-231 TNBC cells. Reduced rates of migration, invasion and proliferation in HERV-K knockdowns points towards the essential role of HERV-K in tumorigenesis and metastasis. HERV-K knockdown also modulated key gene expression signatures traditionally associated with the basal and mesenchymal phenotypes in breast cancer, cellular senescence and MHC class gene regulation. The co-expression of iNOS and HERV-K was assessed in over 150 TNBC cases and the association with patient outcomes assessed. Taken together, our findings indicate that NO and HERV-K may be a useful molecular target for the treatment of TNBC.

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P4-09-02

A molecular classification system for basal-like breast cancer based on the tumor microenvironment is prognostic for survival

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Recent advancements in molecular profiling have revealed distinct breast cancer subtypes, but many clinical NGS assays rely on gene panels, such as PAM50, limiting their clinical utility. Basal-like breast cancer (BLBC), one of the most aggressive subtypes, has highly variable molecular and clinical characteristics. Now, the tumor microenvironment (TME) is recognized as a vital participant in tumor progression and therapeutic response. The development of more refined classifications based on the TME, capable of accounting for tissue heterogeneity, may improve NGS clinical utility for BLBC. Here, we apply our transcriptomic-based approach, recently described by Bagaev et. al., to classify the BLBC TME into discrete immune portraits, to potentially improve clinical outcomes and facilitate therapeutic decisions.

We collected a cohort of 1,708 BLBC samples based on the expression levels of 50 genes (PAM50) from 10 publicly available datasets, with clinical outcomes available (n = 819). Using methodology described by Bagaev et. al., 31 functional gene expression signatures (Fges)

were selected, and unsupervised dense Louvain clustering was performed to identify TME subtypes. A novel RNA-seq deconvolution algorithm was used to determine the cell types within the TME. Validation of the histological features, including stroma, tumor infiltrating lymphocytes (TILs), and tertiary lymphoid structures (TLS), relative to gene expression patterns in the TME subtypes was performed by automated and manual annotation of BLBC H&E slides (n = 146) from an independent TCGA cohort. Overall survival (OS) analysis was performed using Kaplan-Meier and Cox regression methods.

We revealed 5 BLBC subtypes with distinct expression patterns: immune-enriched, non-fibrotic (IE, 19%), B-cell-enriched, TLS-like (TLS, 25.5%), granulocyte-enriched (G, 12.8%), fibrotic (F, 28%), and immune desert (D, 17.7%) (Table). IE tumors featured an active immune TME, with high immune checkpoint expression and T cell activity. The TLS subtype also had an immune-rich TME, presenting high levels of B cells, T helper cells, and TLS ($p < 0.001$). The TLS subtype exhibited the highest number of stromal TILs on TCGA H&E slides. The G subtype was characterized by high expression of granulocytes and granulocyte traffic molecules. In accordance with our findings, deconvolution predicted the highest percent of neutrophils in the G subtype ($p < 0.001$). The F subtype demonstrated the highest levels of angiogenesis, stromal Fges, and VEGFR1-3, FGFR1, and EGFR expression. By histological evaluation, 84% of F subtype samples demonstrated a medium or high level of fibrosis. The D subtype showed a high proliferation rate and low stromal and immune Fges. Indicative of proliferation rate, CCNB1 and cyclin B1 were highest in G, D, and IE subtypes. OS analysis revealed a significant association between TME subtypes (TLS = baseline; log HR G = 0.87, $p < 0.05$; IE = 0.39, $p = 0.18$; F = 0.99, $p < 0.05$; D = 1.21, $p < 0.05$), and survival outcomes. The immune-enriched subtypes, IE and TLS, demonstrated good prognosis and higher expression of immune checkpoint genes, while immune desert D and granulocyte-enriched G subtypes exhibited the worst OS.

Using our transcriptomic-based approach, BLBC was classified into 5 distinct subtypes, each with unique therapeutic vulnerabilities. Further investigation of these TME subtypes may lead to potential clinical utility as a prognostic tool to improve clinical decision making.

Table. Characteristics of Basal-like breast cancer (BLBC) tumor microenvironment (TME) subtypes.

TME Subtypes	G	IE	TLS	F	D
<i>Fges, median z-score</i>					
Proliferation signature	0.33	0.56	-0.59	-0.52	0.57
T cells signature	-0.23	0.36	1	-0.29	-0.93
B cells signature	-0.24	0.1	1.36	-0.4	-0.53
TLS signature	-0.18	0.21	0.98	-0.25	-0.92
Granulocyte traffic signature	1.5	-0.11	-0.07	-0.12	-0.26
CAF signature	0	-0.67	0.02	0.84	-0.47
<i>Pathology analysis</i>					
Median lymphocyte immune infiltration area, mm²	6.24	5.32	7.06	2.37	2.32
Median TLS area, mm²	1.05	1.34	2.33	0.49	0.35
% of samples with high fibrosis, manual annotation	19%	20%	30%	42%	23%
<i>Samples with high RNA expression (high ≥ 0.83 quantile of the cohort)</i>					
CD274 expression	21%	28%	31%	4%	3%
CTLA4 expression	10%	21%	44%	4%	3%
PDGFRB expression	2%	0%	10%	49%	2%
VGFR2 expression	10%	6%	20%	30%	8%
<i>Overall survival (OS), 60 months</i>					
OS, %	71%	80%	85%	64%	60%
Log hazard ratio (p-value)	0.87 (<0.05)	0.39 (=0.18)	0	0.99 (<0.05)	1.21 (<0.05)

TLS - Tertiary lymphoid structures; CAF - cancer-associated fibroblasts

Disclosure(s):

Svetlana Khorkova, n/a: BostonGene: Salary (Ongoing)

Diana Shamsutdinova, n/a: BostonGene: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Salary (Ongoing)

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12/8/2022

7:00 AM - 8:15 AM

P4-09-03

Survival differences between HER2-zero and HER2-low-expressing breast cancer—A meta-analysis of early breast cancer patient data from 12 studies including 39831 patients

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Background:

HER2-low-expressing breast cancer takes up 40-50% in all breast cancer subtypes. Survival difference between HER2 low expression and HER2-zero breast cancer remains controversial. Therefore, the aim of this study was to compare the survival outcome of the two subtypes and to explore the impact of hormone receptor status.

Methods:

A comprehensive medical literature search was performed by PubMed, EMBASE, and the Cochrane Library through June 2022. We included observational studies reporting hazard ratios (HRs) with corresponding 95% confidence intervals (CIs). The results of individual studies were pooled by fixed-effects models. Twelve articles with a total of 39,831 breast cancer patients were included in the meta-analysis.

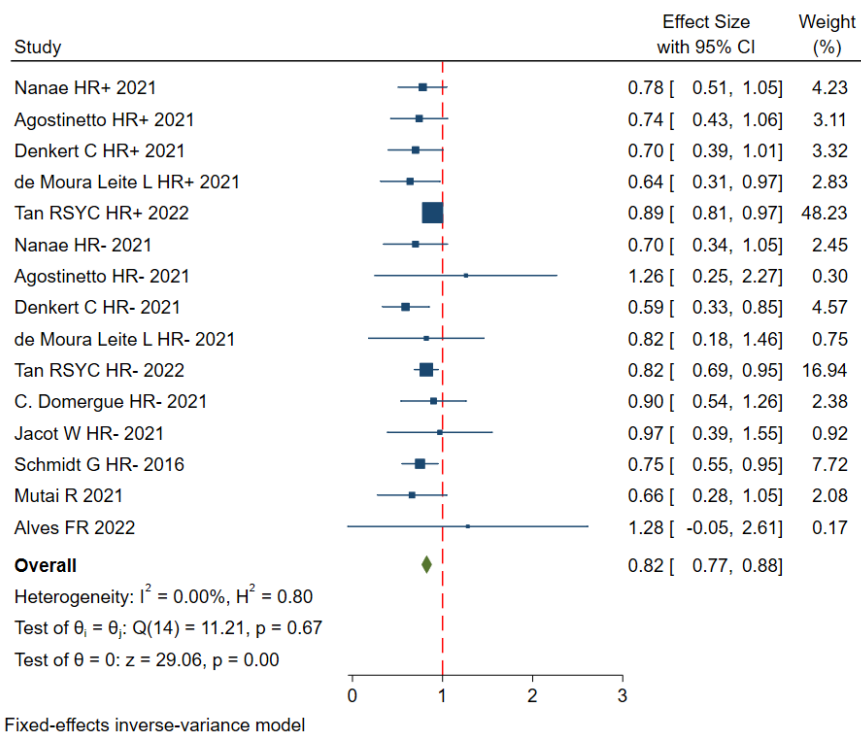
Results:

We observed a statistically significant association between low HER2 expression levels and better breast cancer survival outcomes (OS: HR: 0.82; 95% confidence interval: 0.77, 0.88; DFS/RFS: HR: 0.88; 95% confidence interval: 0.83, 0.93). In a subgroup analysis, we found that HER2-low patients had better survival outcomes among hormone receptor-positive breast cancer patients (OS: HR: 0.85; 95% confidence interval: 0.78, 0.92; DFS/RFS: HR: 0.90; 95% confidence interval: 0.84, 0.96). Similarly, in triple-negative breast cancer patients, we also observed a positive association between HER2 low expression and better survival (OS: HR: 0.78; 95% confidence interval: 0.69, 0.87; DFS/RFS: HR: 0.86; 95% confidence interval: 0.77, 0.94).

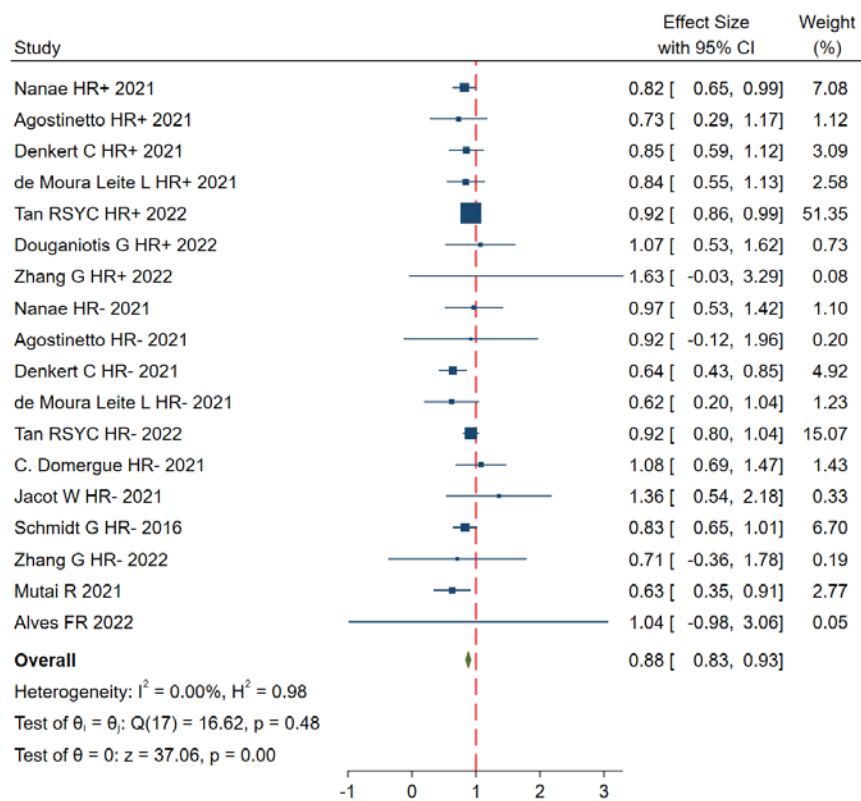
Conclusions:

Our study showed that HER2 low expressing breast cancer had better survival outcomes compared to HER2 negative breast cancer in patients with early stage breast cancer, regardless of hormone receptor status. The result has a positive effect on us to further explore the clinical features, molecular characteristics and better treatment strategies of HER2-low-expressing breast cancer.

Forest plot of HER2 low expression and overall survival in overall population



Forest plot of HER2 low expression and disease free survival or relapse free survival in overall population



Fixed-effects inverse-variance model

Disclosure(s):

Xiaoqi Zhang, n/a: No financial relationships to disclose

Ciqiu Yang, Attending doctor: No financial relationships to disclose

Kun Wang, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P4-09-04

Correlation between histology and molecular subtypes in triple negative breast cancer

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systems. Here, we describe the histopathologic features of TNBC according to four molecular subtypes: basal-like immune activated (BLIA), basal-like immune suppressed (BLIS), luminal androgen receptor (LAR) and mesenchymal (MES), classified using the NanoString BC360 gene expression assay. Methods Stage II and III invasive breast cancers were identified in the Kaiser Permanente (KP) clinical pathology archives (2005-2015) and triple negative status was determined from the KP Northern California Cancer Registry data on immunohistochemistry. Selected slides were reviewed by two pathologists who recorded key histopathologic features [histologic subtype, presence of apocrine, metaplastic or micropapillary features, nuclear grade, mitotic score, and Tumor Infiltrating Lymphocytes (TILs)] and marked the best tumor areas for molecular analysis. TILs were evaluated according to the guidelines of the International TILs Working Group. Cases were macrodissected and evaluated using the NanoString BC360 gene expression assay. Histologic features were then summarized according to molecular subtype. Results Of 72 TNBCs, 60 were classified as Basal-like (83.3%), 7 as HER2-enriched (9.7%) and 5 as Luminal A (6.9%). 41 cases were classified as BLIA (56.9%), 14 as BLIS (19.4%), 13 as LAR (18.0%) and 4 as MES (5.5%). Both BLIA and BLIS tumors showed uniformly high nuclear grade and high mitotic score but differed significantly in TILs (BLIA average 32% vs BLIS average 9%; p value< 0.001, t-test for mean difference in TILs). The majority of LAR cases (69%) showed apocrine differentiation, not present in any other molecular subtype (p value< 0.001, chi-square test for presence of apocrine differentiation). LAR cases showed high nuclear grade but a lower average mitotic score (average score of 2) compared with the basal-like subtypes. TILs in LAR tumors were intermediate (17%) between BLIA and BLIS tumors. Of the 4 MES cases, all showed high nuclear grade. TILs in the MES cases were also intermediate (14%) between BLIA and BLIS tumors. Other histologic features, including lobular subtype, metaplastic and micropapillary features were not associated with specific triple negative molecular subtypes. Conclusion TILs are high in the BLIA molecular subtype (average 32%), low in the BLIS subtype (average 9%) and intermediate in LAR (average 17%) and MES (average 14%) subtypes. Apocrine features, if present in a TNBC, are a strong predictor of LAR molecular subtype. The inclusion of TILs and apocrine features (both easily derived from H&E slides) in routine pathology reporting could improve the classification of TNBC and aid in the identification of patients more likely to respond to specific therapies for the BLIA, BLIS and LAR subtypes, especially in resource-limited settings.

Disclosure(s):

Tabata Alves Domingos, MD: No financial relationships to disclose

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Ashka Patel, BS: No financial relationships to disclose

Krishan Taneja, PhD: No financial relationships to disclose

Wendy Y. Chen, MD, MPH: No financial relationships to disclose

Elizabeth A. Mittendorf, M.D. PhD: Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing), Sponsored research agreement (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing); Roche/Genentech: Consulting Fees (e.g., advisory boards) (Ongoing), Steering committee (Ongoing)

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12/8/2022

7:00 AM - 8:15 AM

P4-09-05

Characterization and validation of biologically-driven HER2-positive breast cancer subgroups in the ALTTO and NeoALTTO clinical trials

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Background: Tumor and microenvironment features, including luminal phenotype as well as metabolic, immune and stroma activation, impact prognosis and treatment response in HER2-positive breast cancer. Here, we aimed to identify subgroups depicting biological processes associated with prognosis in patients receiving adjuvant trastuzumab in the phase III ALTTO trial, and to validate their biological and prognostic characteristics in the phase III neoadjuvant NeoALTTO trial. Methods: By applying a case-control approach (1:2), we selected from the ALTTO trastuzumab arm 134 and 268 patients with and without a distant relapse respectively, matched for clinicopathological characteristics. In ALTTO, RNA was obtained from FFPE tumor cores from surgical samples. RNA sequencing (RNAseq) data available from 254 frozen pre-treatment samples were used for validation in patients receiving trastuzumab and/or lapatinib in NeoALTTO. The Absolute Intrinsic Molecular Subtyping (AIMS) was used to compute PAM50 subtypes. Prognostic genes were identified using a multivariable Cox proportional hazard model (controlling for clinicopathological characteristics and PAM50 HER2-enriched [HER2-E] vs others) for distant relapse-free survival (DRFS). Clusters were identified using non-negative matrix factorization (NMF) and k-means clustering, and characterized with gene expression profiling and Gene Set Variation Analysis (GSVA, hallmark gene sets from MSigDB). Aiming at identifying the subgroups in external cohorts, we identified relevant genes to develop group-specific signatures with LASSO regression, and used the derived scores to build a multinomial classifier. Results: The case-control cohort includes a high-risk population, with higher proportions of >2cm, node positive and G3 tumors compared to the whole ALTTO trastuzumab arm. RNAseq data were generated for 386/402 patients. NMF and k-means clustering performed on genes associated with DRFS (false discovery rate < 0.05) identified 4 groups with distinct biological characteristics and prognosis: immune-enriched (IM, N = 69), proliferative/metabolic (P/M, N = 87, characterized by glycolysis, cholesterol homeostasis and proliferation pathways), mesenchymal/stroma-enriched (M/S, N = 76, characterized by epithelial-mesenchymal transition, angiogenesis and TGF-beta signaling), and hormone receptor positive-enriched (N = 154), further divided into PAM50 HER2-E (N = 91) and non-HER2-E (N = 63, LUM, mainly luminal A/B tumors). The IM and LUM groups presented better DRFS (91% and 87% 5-year DRFS, respectively) compared to the others (5-year DRFS of

72%, 58% and 51% for HER2-E, M/S and P/M, respectively). The gene expression-based classifier identified the same 5 groups in NeoALTTO. GSVA analysis and comparisons among the 5 groups showed similar results in the two studies. Of interest, we observed significant differences in event-free survival in NeoALTTO ($P = 0.035$ and $P = 0.041$ in the whole population and in the subgroup with residual disease, respectively), with IM and LUM presenting better outcomes compared to the other groups. Sensitivity to neoadjuvant treatment as described by pathological complete response (pCR, ypT0/is ypN0) differed across the groups, with LUM presenting lower pCR rates (8%) compared to HER2-E (40%), IM (35%), P/M (32%), and M/S (32%). Conclusions: Five biologically-driven HER2-positive breast cancer subgroups were identified in ALTTO, highlighting the heterogeneity of this disease. Of note, their biological features and clinical behavior were validated in the NeoALTTO population, suggesting the robustness of our findings. IM and LUM tumors could be considered for treatment de-escalation approaches. Additional validation in cohorts receiving standard (neo)adjuvant therapies is warranted.

Disclosure(s):

Mattia Rediti, MD: No financial relationships to disclose

David Venet, PhD: No financial relationships to disclose

Andrea Joaquin Garcia, MS: No financial relationships to disclose

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Takayuki Ueno, MD, PhD: Astra Zeneca: lecture (Ongoing); Chugai Pharmaceutical: lecture (Ongoing); Eisai Co.Ltd: lecture (Ongoing); Novartis Pharma KK: lecture (Ongoing)

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Martine Piccart, MD, PhD: Astra-Zeneca: Contracted Research (Ongoing), Invited speaker (Ongoing); Camel-IDS/Precirix: Consulting Fees (e.g., advisory boards) (Ongoing); Frame Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); Immunomedics: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Immunetep: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Contracted Research (Ongoing), Invited speaker (Ongoing); Menarini: Consulting Fees (e.g., advisory boards) (Ongoing), Institutional funding (Ongoing); MSD: Invited speaker and institutional funding (Ongoing); NBE Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Invited speaker and institutional funding (Ongoing); Odonate: Consulting Fees (e.g., advisory boards) (Ongoing); Oncolytics: Member of Board of Directors, Scientific Board (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Institutional funding (Ongoing); Radius: Institutional funding (Ongoing); Roche-Genentech: Consulting Fees (e.g., advisory boards) (Ongoing), Invited speaker and institutional funding (Ongoing); SeaGen: Consulting Fees (e.g., advisory boards) (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing); Servier: Institutional funding (Ongoing); Synthon: Institutional funding (Ongoing)

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12/8/2022

7:00 AM - 8:15 AM

P4-09-07

Characterization of Immune Contexture in HR+/HER2- and Triple Negative Breast Cancer in a Real-world Cohort

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Background: Prior studies in breast cancer (BC) have demonstrated variability in the immune microenvironment of BCs across subtypes, with higher levels of immune infiltration observed in triple-negative (TN) BC. Clinical trials of immunotherapy in BC have largely targeted patients with TNBC, however many of these patients do not respond to treatment, suggesting heterogeneity across TN tumors. Further, immune infiltrated hormone receptor–positive, HER2-

negative (HR+/HER2-) tumors have been observed. Patients with these tumors may benefit from immune checkpoint blockade (ICB). Identification of patients with immunogenic tumors would be valuable for future patient selection and stratification in clinical trials. In this study, we conducted comprehensive molecular profiling of a set of commercially procured BC samples to characterize the tumor microenvironment (TME) of HR+/HER2- and TN tumors and to identify patient or tumor features associated with immune infiltration. Methods: 163 surgically resected BC samples were used for this study (93 HR+/HER2-, 70 TN). Clinically validated immunohistochemistry (IHC) assays were used to evaluate the expression of two immune checkpoint (IC) molecules, PD-L1 (by VENTANA PD-L1 (SP142) Assay and Agilent PD-L1 IHC 28-8 pharmDx) and LAG3 (antibody clone 17B4). The presence of CD8+ cells was measured by IHC (Dako/Agilent clone C8/144B) and used to derive the spatial location and density (topology) of CD8+ cells within the TME. RNA sequencing (RNA-seq) was used to construct gene expression signatures representative of immune cell types. Furthermore, RNAseq data was used to identify expressed somatic mutations and to calculate the total expressed tumor mutational burden ('eTMB'). Results: As previously reported, the prevalence of PD-L1 + tumors was higher in TN vs HR+/HER2- BC, however close to half (44.1% SP142 IC> 1%) of HR+/HER2- tumors showed some degree of PD-L1 expression. Similar patterns were observed for LAG3 IHC expression (32.3% and 64.7% of HR+ and TN tumors respectively with >1% expression). Concordant expression of the two markers (SP142 IC> 1% and LAG3 >=1% or < 1% and < 1%) was observed in approximately 80% of tumors in both subtypes. Less than 10% of tumors in both subtypes had high LAG3 (>1%) and low PD-L1(< 1%) expression. Most (82.4%) HR+/HER2- tumors in the dataset were deficient in CD8+ cells in both stroma and tumor parenchyma, however a subset (12.9%) were identified as having an 'excluded' CD8 pattern, and four (4.7%) were classified as 'inflamed'. The frequency of both the excluded and inflamed states was slightly higher among the TN tumors (20.6% and 15.9% respectively). Expression of PD-L1+ occurred more frequently among tumors with higher CD8 expression. Among both TN and HR+ tumors, most 'inflamed' tumors were grade 3. We also examined a range of gene expression signatures representative of various immune cell subpopulations, their distribution within each subtype, and relationships with other molecular data. For example, expression of a CXCL13+ T cell signature, a cell type that has been shown to be predictive of response to anti-PD-L1 + chemo combo therapy in TNBC, was significantly higher in TN vs HR+ tumors, however, a large subset of HR+ tumors had levels of expression of the signature above the median observed in TN tumors. In addition, we noted that eTMB, while low overall, was positively correlated with certain immune-related expression signatures across HR+/HER2- samples, including signatures previously associated with improved response to ICB, as well as PD-L1 positivity. Conclusions: We observed heterogeneity in the immune profile of the real-world HR+ and TN tumors in this cohort. A subset of tumors in both subtypes expressed markers or signatures previously reported to be associated with response to ICB. (1) Cancer Cell. 2021 Dec 13;39(12):1578-1593.e8.

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

P4-09-08

AI-based quantitation of cancer cell and fibroblast nuclear morphology reflects transcriptomic heterogeneity and predicts survival in breast cancer

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Background: Morphological features of cancer cell nuclei are routinely used to assess disease severity and prognosis, and cancer nuclear morphology has been linked to genomic alterations. Quantitative analyses of the nuclear features of cancer cells and other tumor-resident cell types, such as cancer-associated fibroblasts (CAFs), may reveal novel biomarkers for prognosis and treatment response. Here, we applied a pan-cancer nucleus detection and segmentation algorithm and a cell classification model to hematoxylin and eosin (H&E)-stained whole slide images (WSIs) of breast cancer specimens, enabling the measurement of morphological features of nuclei of multiple cell types within a tumor. Methods: Convolutional Neural Network models for 1) nucleus detection and segmentation and 2) cell classification were deployed on H&E-stained WSIs from The Cancer Genome Atlas (TCGA) breast cancer dataset (primary surgical resections; N=890). Separate models were trained to segment regions of stromal subtypes, such as inflamed and fibroblastic stroma. Nuclear features (area, axis length, eccentricity, color, and texture) were computed and aggregated across each slide to summarize slide-level nuclear morphology for each cell type. Next-generation sequencing-based metrics of genomic instability (N=774) and gene expression (N=868) were acquired and paired with TCGA WSIs. Gene set enrichment analysis was performed using the Molecular

Signatures Database. Spearman correlation compared nuclear features to genomic instability metrics. Linear regression was used to assess the relationship between nuclear features and bulk gene expression. Multivariable Cox regression with age and ordinal tumor stage as covariates was used to find association between overall survival (OS) and nuclear features. All reported results were significant ($p < 0.05$) when adjusted for false discovery rate via the Benjamini-Hochberg procedure. Results: Variation in cancer cell nuclear area, a quantitative metric related to pathologist-assessed nuclear pleomorphism, was calculated by the standard deviation of the nuclear area of cancer cells across a WSI. This feature was associated with genomic instability, as measured by aneuploidy score ($r=0.448$) and homologous recombination deficiency score ($r=0.382$), and reduced OS. In contrast, the variability in fibroblast and lymphocyte nuclear areas did not correlate with either metric of genomic instability (all $r < 0.1$, $p > 0.05$). Furthermore, an association between variation in cancer cell nuclear area with the expression of cell cycle and proliferation pathway genes was observed, suggesting that increased nuclear size heterogeneity may indicate a more aggressive cancer phenotype. Features quantifying CAF nuclear morphology were also assessed, revealing that CAF nucleus shape (larger minor axis length) was associated with lower OS, as well as the expression of gene sets involved in extracellular matrix remodeling and degradation. Conclusions: The nuclear morphologies of breast cancer cells and CAFs reflect underlying genomic and transcriptomic properties of the tumor and correlates with patient outcome. The application of digital pathology analysis of breast cancer histopathology slides enables the integrative study of genomics, transcriptomics, tumor morphology, and overall survival to support research into disease biology research and biomarker discovery.

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12/8/2022

7:00 AM - 8:15 AM

P4-09-10

Spatial protein and RNA expression in tumor, immune and stromal cells in BRCA1/2 mutated metastatic breast cancer

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Background: Spatial transcriptomics and proteomics are cutting-edge techniques that allow for quantification of RNA and protein expression within separate cell populations or regions of interest in a tissue biopsy specimen. We aimed to independently characterize the tumor cells and immune infiltrate in metastatic site biopsy specimens from patients with somatic or germline BRCA1/2 mutations. Methods: We performed spatial transcriptomics and proteomics using the Nanostring GeoMx Digital Spatial Profiler (DSP) on 9 formalin-fixed paraffin-embedded (FFPE) tissue biopsy specimens from 5 patients with metastatic breast cancer and a known somatic or germline BRCA1/2 mutation. Each patient had 1-3 separate metastatic site tissue biopsy specimens. Cell populations of interest were delineated with fluorescently labeled antibodies to pan-cytokeratin on tumor cells, CD45 of immune cells, and a nuclear stain. On each sample, 4-5 regions of interest (ROIs) were selected near the interface of the metastatic tumor deposit and surrounding normal tissue. Each ROI was segmented into 3 areas of interest (AOIs): pan-cytokeratin-positive tumor cells, CD45-positive immune cells, and the remaining stromal cells negative for both pan-cytokeratin and CD45. Data was background corrected and normalized with internal negative and positive internal controls. Relative abundance of immune cell subtypes was derived from CD45+ cell gene expression data using the TIMER algorithm. Results: The expression of 57 proteins and 84 RNAs was quantified in each of the 396 AOIs. Separate analysis of CD45+ cells, pan-cytokeratin cells, and stromal cell populations confirmed

expected differential expression of immune, tumor and stromal markers, respectively. Protein expression of the estrogen receptor (ER) and progesterone receptor (PR) on pan-cytokeratin-positive tumor cells using the DSP correlated with pathologist reviewed immunohistochemistry (IHC) for ER and PR. Significant differential expression was found within each cell population between hormone receptor (HR) positive and negative cohorts, including enrichment for S100B in HR negative samples. Comparison will be shown for expression of 14 overlapping genes/proteins. Immune cell compartment gene expression deconvolution showed heterogeneity in the relative proportion of infiltrating immune cell subtypes between samples and also between ROIs within a sample. Changes in gene and protein expression from a patient with 3 serial biopsy specimens can be tracked with substantial heterogeneity across distinct AOIs within individual specimens and across metastatic sites.. Conclusions: Spatial transcriptomics and proteomics is feasible for concurrent, relative quantification of protein and gene expression in tumor, immune, and stromal cells in FFPE tissue biopsies from patients with metastatic breast cancer harboring germline or somatic BRCA1 or BRCA2 mutations. Heterogeneity within individual samples and across serial time points offers opportunity for methods development in the analyses and interpretation of spatial transcriptomic/proteomic data.

Disclosure(s):

Katharine A. Collier, MD: No financial relationships to disclose

Katherine Miller, PhD: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

P4-09-11

Development of personalized medicine for breast cancer based on elucidation of resistance mechanisms to CDK4/6 inhibitors

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Background

CDK4/6 inhibitors are the latest and highly specific CDK inhibitors approved for metastatic and early estrogen receptor (ER)-positive breast cancer patients, improving the survival outcomes. Prior preclinical research has indicated various aberrations of cell cycle regulation and activated oncogenic signaling pathway as the mechanisms of resistance to CDK4/6 inhibitors. However, there is currently no available biomarker except ER and human epidermal growth factor receptor 2 (HER2) in clinical practice. The aim of our study is to elucidate diverse mechanisms of acquired resistance of ER-positive breast cancers to CDK4/6 inhibitors and develop personalized medicine in ER-positive breast cancer patients.

Materials and methods

To generate resistant lines, the ER-positive human breast cancer cell lines MCF7 and T47D were treated individually with increasing concentrations of the CDK4/6 inhibitors palbociclib and ribociclib until a target concentration of 3 μ M for six months. Cells were maintained in RPMI 1640 containing 10% fetal bovine serum, 100 U/ml penicillin/streptomycin at 37°C in a 5% CO₂ incubator. Western blot analysis was performed for whole cell extract proteins from resistant cells to CDK4/6 inhibitors and parental cells. Colony formation assay was done to observe cell viability.

Results

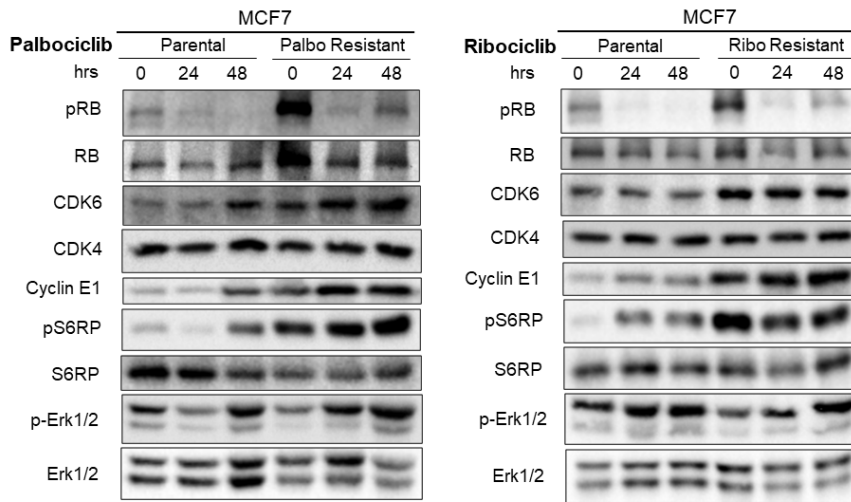
Western blot analysis showed elevated FGFR2, CDK6, pS6RP, and cyclin E1 in resistant cells

compared to parental cells. Specifically, cyclin E1 and pS6RP were increased in MCF7 palbociclib- and ribociclib-resistant cells, while FGFR2 and CDK6 in T47D palbociclib- and ribociclib-resistant cells. Notably, CDK6 was upregulated in MCF7 ribociclib-resistant cells, whereas increased cyclin E1 was detected in T47D palbociclib-resistant cells, respectively. Colony formation assay revealed acquired ability of resistance to CDK4/6 inhibitors in generated resistant cell lines.

Conclusions

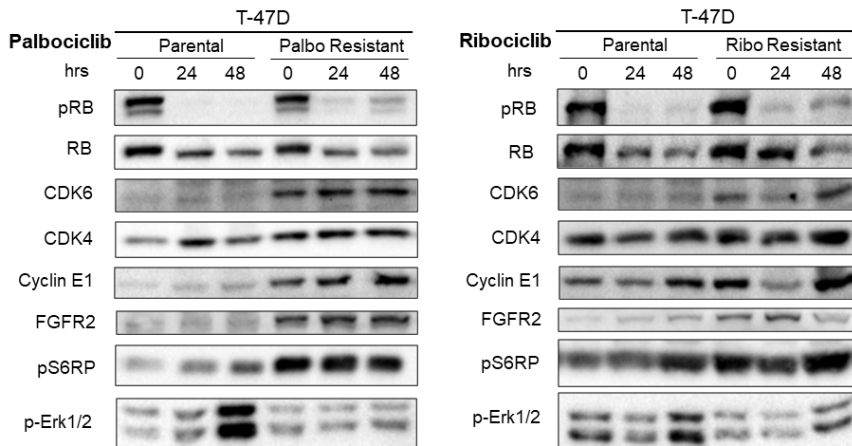
The tumors harboring resistance to CDK4/6 inhibitors have heterogenous mechanisms of therapeutic resistance to these agents. The novel combination treatment of targeted molecular therapy and CDK4/6 inhibition will lead development of personalized medicine for ER-positive breast cancer based on elucidation of diverse resistant mechanisms to CDK4/6 inhibition.

Western blot analysis of lysates from MCF-7 cells treated for 24 to 48 hours with palbociclib (Palbo) and ribociclib (Ribo)



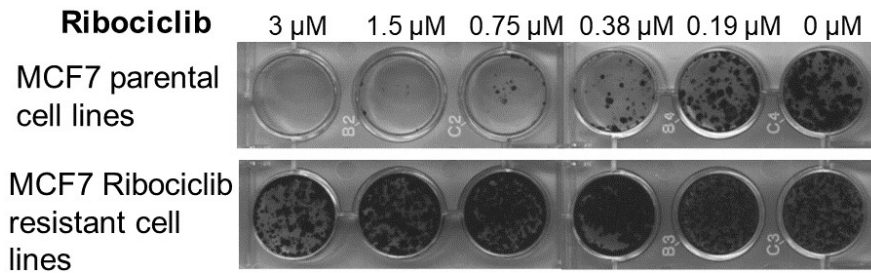
Cyclin E1 and pS6RP were increased in MCF7 palbociclib- and ribociclib-resistant cells, whereas CDK6 was upregulated especially in MCF7 ribociclib-resistant cells.

Western blot analysis of lysates from T47D cells treated for 24 to 48 hours with palbociclib (Palbo) and ribociclib (Ribo)



FGFR2 and CDK6 were increased in T47D palbociclib- and ribociclib-resistant cells, whereas increased cyclin E1 was detected especially in T47D palbociclib-resistant cells.

Viability in MCF7 ribociclib-resistant and parental cells by colony formation assay
Colony formation assay (Ribociclib)



Colony formation assay revealed acquired ability of resistance to CDK4/6 inhibitors in MCF7 resistant-cells.

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7:00 AM - 8:15 AM

P4-09-12

Baseline and End-of-Treatment Biomarkers in Patients With PIK3CA-Mutated, Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative Advanced Breast Cancer From BYLieve Study Cohorts A and B

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Introduction: Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA) is mutated in ~40% of patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (ABC). PIK3CA mutations are associated with resistance to endocrine therapy (ET) and worse overall survival. Alpelisib (ALP), an α -selective PI3K inhibitor and degrader, is indicated in combination with fulvestrant (FUL) for pts with PIK3CA-mutated (mut) HR+, HER2- ABC following progression on/after ET-based treatments. In the Phase 2, open-label, 3-cohort, noncomparative BYLieve study, clinical benefit of ALP in combination with ET was observed in the post-cyclin-dependent kinase 4/6 inhibitor (CDK4/6i) setting in pts with PIK3CA-mut, HR+, HER2- ABC. Here we report the results of a biomarker analysis using paired baseline (Cycle 1 Day 1) and end-of-treatment (EOT) circulating tumor DNA (ctDNA) samples from pts in BYLieve Cohorts A and B.

Methods: In the BYLieve study, pts with PIK3CA-mut, HR+, HER2- ABC had CDK4/6i + aromatase inhibitor (Cohort A; N=127) or CDK4/6i + FUL (Cohort B; N=126) as treatment immediately prior to receiving ALP + FUL and ALP + letrozole, respectively. In this biomarker analysis, gene alterations were detected in ctDNA at baseline and EOT using next-generation sequencing (PanCancer V2 panel). Pts included in this interim analysis had confirmed PIK3CA mutations and matched baseline/EOT samples with enough sequencing coverage and ctDNA fraction to detect mutations at both time points. ctDNA fractions, tumor mutation burden (TMB) distributions, genomic landscapes, gain/loss of PIK3CA and estrogen receptor 1 (ESR1), chromosome 8/11 amplification profiles, and alterations in PI3K pathway and potential CDK4/6i resistance markers were assessed across time points. Sample sizes were small; results should thus be interpreted with caution.

Results: Forty-three pts were included in the Cohort A biomarker population and 40 pts were included in Cohort B. ctDNA fraction was numerically higher at EOT compared with baseline in both cohorts; further analyses will be presented. In Cohort A, no significant differences were observed in TMB at EOT compared with baseline ($P=0.21$). In Cohort B, TMB was higher at EOT compared with baseline ($P=0.053$). Chromosome 8/11 amplifications were consistent between baseline and EOT for both cohorts. Small variations were observed in ESR1/PIK3CA mutations between baseline and EOT on both cohorts (Table). The status of potential CDK4/6i resistance markers was relatively unchanged at EOT (Table). Loss-of-function mutations in PTEN, a known PI3K inhibitor resistance marker, increased from 9% at baseline to 14% at EOT in Cohort A and from 12% at baseline to 22% at EOT in Cohort B.

Conclusions: Between baseline and EOT, only small variations in gene alterations in PIK3CA-mutated HR+, HER2- ABC were observed in the post-CDK4/6i setting. As the disease progressed, increases in loss-of-function mutations in PTEN at EOT in both Cohorts A and B suggested loss of PTEN in PI3K pathway may drive resistance to ALP. Early intervention with ALP, when the tumor is particularly driven by PIK3CA oncogenic mutations and before it develops more genomic complexity, may potentially provide better clinical outcomes.

Table. Gene Alteration Gain/Loss at Baseline/EOT Across Cohorts A and B

Gene	Mutation, n (%)	Cohort A (N=43)		Cohort B (N=40)		
		Baseline (C1D1)	EOT	Baseline (C1D1)	EOT	
ESR1	D273Y	1 (2.3)	0	0	0	
	M357I	0	0	0	1 (2.5)	
	E380Q	2 (4.7)	2 (4.7)	2 (5.0)	1 (2.5)	
	S395Y	0	0	1 (2.5)	0	
	S463P	1 (2.3)	0	0	0	
	L536H	1 (2.3)	1 (2.3)	0	1 (2.5)	
	Y537N	4 (9.3)	3 (7.0)	2 (5.0)	3 (7.5)	
	Y537D	0	0	1 (2.5)	1 (2.5)	
	Y537S	6 (14.0)	9 (20.9)	7 (17.5)	7 (17.5)	
	Y537C	1 (2.3)	1 (2.3)	1 (2.5)	0	
	D538G	6 (14.0)	7 (16.3)	7 (17.5)	7 (17.5)	
	R548S	0	0	0	1 (2.5)	
	E39K	0	0	1 (2.5)	0	
	I69N	0	0	1 (2.5)	1 (2.5)	
R108H	0	0	1 (2.5)	1 (2.5)		
PIK3CA	I112F	1 (2.3)	1 (2.3)	0	0	
	G118D	0	0	1 (2.5)	1 (2.5)	
	N284S	0	1 (2.3)	0	0	
	N345D	0	0	0	1 (2.5)	
	N345K	0	0	1 (2.5)	1 (2.5)	
	E418K	1 (2.3)	0	0	0	
	E453K	1 (2.3)	0	0	1 (2.5)	
	E542K	8 (18.6)	8 (18.6)	3 (7.5)	4 (10.0)	
	E542G	0	0	0	1 (2.5)	
	E545K	13 (30.2)	13 (30.2)	5 (12.5)	5 (12.5)	
	E545G	1 (2.3)	1 (2.3)	0	0	
	Q546K	0	0	1 (2.5)	1 (2.5)	
	Q546R	0	0	1 (2.5)	1 (2.5)	
	E726K	0	0	2 (5.0)	1 (2.5)	
D939G	0	0	1 (2.5)	1 (2.5)		
PI3K pathway	L1001V	1 (2.3)	1 (2.3)	0	0	
	G1007R	0	0	0	1 (2.5)	
	H1047Y	1 (2.3)	1 (2.3)	0	0	
	H1047R	16 (37.2)	14 (32.6)	19 (47.5)	18 (45.0)	
	H1047L	2 (4.7)	1 (2.3)	5 (12.5)	5 (12.5)	
	AKT1	0	1 (2.3)	1 (2.5)	1 (2.5)	
	AKT2	0	0	1 (2.5)	1 (2.5)	
	AKT3	0	0	1 (2.5)	1 (2.5)	
	PIK3R1	1 (2.3)	1 (2.3)	1 (2.5)	1 (2.5)	
	PTEN	4 (9.3)	6 (14.0)	5 (12.5)	9 (22.5)	
	CDKi resistance	ATM	2 (4.7)	1 (2.3)	2 (5.0)	0
		CDKN2A/B/C	1 (2.3)	1 (2.3)	2 (5.0)	2 (5.0)
		CHD4	1 (2.3)	1 (2.3)	7 (17.5)	5 (12.5)
		ERBB2	1 (2.3)	0	1 (2.5)	2 (5.0)
FAT1		3 (7.0)	3 (7.0)	4 (10.0)	5 (12.5)	
NF1		2 (4.7)	2 (4.7)	2 (5.0)	2 (5.0)	
RB1		4 (9.3)	4 (9.3)	5 (12.5)	3 (7.5)	

*Only missense, non-sense, frameshift alterations, and deletions are included.
 AKT1/2/3, AKT serine/threonine kinase 1/2/3; ATM, ATM serine/threonine kinase; C1D1, Cycle 1 Day 1; CDKi, cyclin-dependent kinase 4/6 inhibitor; CDKN2A/B/C, cyclin-dependent kinase inhibitor 2A/B/C; CHD4, chromodomain helicase DNA binding protein 4; EOT, end of treatment; ERBB2, ERB-B2 receptor tyrosine kinase 2; ESR1, estrogen receptor 1; FAT1, FAT atypical cadherin 1; NF1, neurofibromin 1; PI3K, phosphatidylinositol 3-kinase; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; PIK3R1, phosphoinositide-3-kinase regulatory subunit 1; PTEN, phosphatase and tensin homolog; RB1, RB transcriptional corepressor 1.

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12/8/2022

7:00 AM - 8:15 AM

Discussion 1 + Q&A: Biomarkers of Response and Resistance

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PD10-06, PD10-07, PD10-08, PD10-09 & PD10-10

12/8/2022

7:00 AM - 8:15 AM

Discussion 2 + Q&A: Mechanism of Resistance and New Treatment Strategies

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PD10-01, PD10-02, PD10-03, PD10-04 & PD10-05

12/8/2022

7:00 AM - 8:15 AM

Poster Spotlight Discussion 10: Endocrine Therapy and Resistance

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Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

PD10-01

PD10-01 Impact of ESR1 mutations on Selective Estrogen Receptor Degraders and Modulators: an integrated liquid-biopsy and pharmacodynamics approach.

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Background: ESR1 hotspot mutations (HS) (i.e. 380, 536, 537, and 538) are important drivers of resistance to aromatase inhibitors, but the differential impact of genomic variants (HS vs non-HS) on response to endocrine therapies (ET) under clinical development, such as novel oral Selective Estrogen Receptor Degraders and Modulators (SERDs and SERMs), is not known. The aim of the study was to evaluate the impact of non-HS ESR1 mutations on the pharmacodynamics of SERDs and SERMs as an additional ET resistance mechanism. Materials and Methods: The study analyzed a multi-institutional cohort of 1008 patients with hormone receptor positive metastatic breast cancer characterized by circulating tumor DNA (ctDNA). Pathway classification was defined based on previous work (i.e. RTK, RAS, RAF, MEK, NRF2, ER, WNT, MYC, p53, Cell Cycle, Notch, PI3K). Single nucleotide variations (SNVs) were annotated through OncoKB; co-occurrence was tested by Fisher's exact test. A structure-based computational strategy was used to create 3D-models of ESR1 mutants and predict changes in binding affinity (dAff) across approved and experimental drugs. A positive dAff reflects a lower affinity of the drug for mutant ESR1 compared with wild type and thus a

potential for a reduced response. Results: Among the total 680 detected ESR1 mutations, 633 were missense, and 631 were gain-of-function. The most frequent mutations were in codon 537 (N=305), followed by 538 (N=224). No significant MAF differences were observed across ESR1 variants (P=0.0829). The L391F mutation resulted in an increased binding affinity for Lasofoxifene (LAS) (dAff -0.34), Giredestrant (GIR) (dAff -0.18), Elacestrant (ELA) (dAff -0.08) and Amcenestrant (AMC) (dAff -0.41), while a decreased binding affinity was observed for 4OH-Tamoxifen (TAM) (dAff 0.01), Imlunestrant (IML) (dAff 0.15), Fulvestrant (FUL) (dAff 0.43), and Camizestrant (CAM) (dAff 0.02). V392F decreased binding affinity for TAM (dAff 0.05), LAS (dAff 0.13), IML (dAff 0.11), GIR (dAff 0.11), FUL (dAff 0.04), CAM (dAff 0.05), AMC (dAff 0.06) but not for ELA (dAff -0.01). F404L decreased binding affinity for FUL (dAff 0.07), ELA (dAff 0.73), and CAM (dAff 0.26), while it increased binding affinity for TAM (dAff -0.27), LAS (dAff -0.02), IML (dAff -0.05), GIR (dAff -0.69), and AMC (dAff -2.01). G415E increased binding affinity for LAS, (dAff -0.15) GIR (dAff -0.02) and ELA (dAff -0.08), while it decreased binding affinity for TAM (dAff 0.11), IML (dAff 0.09), FUL (dAff 0.29), CAM (dAff 0.19) and AMC (dAff 0.10). Mutations in codon 537 did not affect dAff for TAM, GIR, and ELA; a significant decrease in binding affinity was observed for FUL and AMC, whereas it was increased for LAS. Mutational co-occurrence was tested between ESR1 mutations in FUL docking sites and oncogenic pathways. Significant associations were observed for cell cycle SNVs (P=0.047), Notch SNVs (P=0.020), and ER SNVs (P< 0.001). Within these pathways, significant single-gene associations were observed for FBXW7 SNVs (P=0.020), ESR1 SNVs (P< 0.001), and GATA3 SNVs (P= 0.016). Given the highly significant co-occurrence of non-HS with other ESR1 mutations, combined models were examined. The Y537/F404 combination resulted in decreased binding affinity for FUL and increased binding affinity for LAS, while L536/F404 decreased binding affinity for TAM and increased binding affinity for IML, ELA, and AMC. Notably, L540/F404 restored the FUL-ESR1 interaction resulting in an increased binding affinity (dAff -2.1). Conclusions: The study suggests that genomic variability in drug targets detectable through ctDNA may modulate therapeutic response. Preclinical models are under development to investigate the combined endocrine resistance mechanism suggested by the significant co-occurrence between ESR1 mutations in SERDs/SERMs docking sites and ESR1 hotspot mutations and provide valuable additional insights for drug development and future treatment algorithms.

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12/8/2022

7:00 AM - 8:15 AM

PD10-02

PD10-02 Novel ER fusion detection method to gain insight in fusion prevalence and endocrine resistant mechanisms

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Breast cancer is a leading cause of female mortality and despite advancements in diagnostics and personalized therapeutics, metastatic disease largely remains incurable due to drug resistance. The druggable estrogen receptor (ER, ESR1), overexpressed in two-thirds of all breast cancer, evolves in 30% of tumors exposed to endocrine therapy consequently resulting in treatment resistance. A more recently discovered mechanism of ER mediated endocrine resistance is ER fusion proteins. ER fusions, found predominately in metastatic endocrine resistant disease, harbor ESR1 exons 1-6 fused to an in-frame gene partner due to an ESR1 intron 6 translocation break. Our lab has demonstrated that ER fusion proteins, which lack the C-terminal ligand-binding domain (LBD), recapitulate phenotypes of ER proteins harboring endocrine-resistant point mutations occurring in the LBD. Our research goals aim to 1) determine fusion prevalence and emergence, 2) understand fusion mechanisms of resistance and 3) explore alternative treatment options for our patients. The promiscuous nature of fusion partners hinders fusion detection by traditional sequencing and thus our research team has developed a novel ER fusion detection method, EnRich. The EnRich probe set (4,324 probes in total) is composed of two separate probe pools targeting at 2x tiling intronic and exonic ESR1, the upstream promoter region and select oncogenic genes. To optimize the EnRich pipeline,

DNA was extracted from a frozen tumor sample and a PDX model harboring ESR1-DAB2 and ESR1-LPP fusions, respectively. ESR1-DAB2 and ESR1-LPP were accurately detected by quantifying discordant paired-end or split reads mapped to chromosome 6. In addition, liquid biopsies from 15 patients with ER positive advanced breast cancer were also assessed through EnRich to uncover unidentified ESR1 structural variants. Two patient samples were detected to harbor ESR1 fusions (ESR1-CCDC170, ESR1-AKAP12 and ESR1-YAP1) and were further validated in corresponding mRNA. These recurrent and novel fusions were supported with more than 10 reads each, indicating that the EnRich pipeline is an effective and accurate sequencing approach to understanding ER fusion prevalence. Our lab, furthermore, has studied ER fusion proteins mechanistically. We have stably overexpressed ER fusions in transgenic breast cancer cell lines engineered with shRNA targeting the endogenous wildtype ER (ESR1-WT). In this ESR1-WT depleted cellular context, we found that ER fusions (notably ESR1-SOX9 and ESR1-YAP1) demonstrate ER hyperactivation through an estrogen response element (ERE) assay compared to ESR1-WT and a truncated exon 1-6 ESR1 (ESR1 Δ CTD). Importantly, fusion ERE activity was robust in the absence of the ER ligand, estradiol, as well as in the presence of endocrine therapies, implying ER fusion proteins function in a ligand independent, endocrine resistant mechanism. ER fusion positive cell lines were also enriched in oncogenic phenotypes such as enhanced 3D growth, cell survival via colony formation, and migration in a wound scratch assay. These enhanced metastatic potentials of the ER fusions were observed in both invasive ductal and lobular carcinoma cell lines, albeit at varying magnitudes depending on the 3' fusion partner and phenotype being assessed. Although the ER fusions harbored unique characteristics due to the C-terminal partner, transcriptomic profiling revealed that enhanced EMT and KRAS signaling signatures were shared among all fusions when compared to the ESR1-WT and ESR1 Δ CTD cell lines, which may serve as future exploitable drug targets. Comprehensive detection and functional evaluation of ER fusion proteins will provide clinicians and patients with better understanding of tumor endocrine-resistant prevalence and discovery of more effective treatment options.

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12/8/2022

7:00 AM - 8:15 AM

PD10-03

PD10-03 Super-enhancer-oriented integrative bioinformatics identifies aberrant KLF4 signaling in endocrine-resistant breast cancer (BC)

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Background: Recent studies suggest that enhancer reprogramming underlies heterogeneity and disease progression in estrogen receptor-positive (ER+) BC. Cell-type/state specific transcription is governed by high-order assemblies of master transcription factors (TFs) and epigenetically defined regulatory regions including super-enhancers (SEs). We previously showed that aberrant activation of the pioneer TF FOXA1 promotes enhancer and transcriptional reprogramming in endocrine-resistant BC, involving the ER and the AP-1 FRA1 and c-JUN TFs. As SEs maintain a robust cell-type/state specific core transcriptional regulatory

circuitry (CRC) in developmental and tumorigenic processes, we sought to identify key additional TFs in SE/FOXA1-driven CRCs in endocrine resistance, which could serve as attractive therapeutic targets. Methods: TF binding motif at the shared SEs (mapped by H3K27ac ChIP-seq) between MCF7-parental (P) cells with ectopic FOXA1 overexpression (OE) and the endogenous FOXA1-amplified tamoxifen-resistant (TamR) cells was analyzed by HOMER. ER-bound SEs distinguishing TamR vs. P cells were defined by integrating the SEs with our prior ER ChIP-seq data (PMID 28507152). KLF4 motif within these ER-bound SEs was scanned using FIMO and linked to nearby genes by intersection with the previously defined promoter-tethered regions (PTRs) (PMID 24141950). Differential gene expression in MCF7-TamR cells upon KLF4 knockdown (KD) by 3 unique siRNAs was analyzed using limma from edgeR. The biological and clinical significance of the KLF4-dependent genes was analyzed using Gene Ontology and survival modeling with METABRIC and the ER+ metastatic BC cohort (SABCS19-GS2-02). Cell migration was assessed by the wound-healing assay. Results: We identified KLF4 among the top enriched TF binding motifs at the shared SEs in FOXA1-overexpressing MCF7-P cells and the FOXA1-amplified TamR cells. Analysis of our prior RNA-seq data of MCF7-P and TamR cells upon OE or siRNA KD of FOXA1, FRA1, or c-JUN (PMIDs 27791031, 31826955, 32424275, SABCS21-PD1-05) revealed KLF4, the Yamanaka factor for induced pluripotent stem cells, as a common target activated by the FOXA1/FRA1/c-JUN axis. We next identified 44 genes commonly down-regulated upon KLF4 KD in the MCF7-TamR cells. This KLF4-dependent 44-gene set was enriched in biological processes of embryonic development and tumor progression, preferentially dependent on ER in MCF7-TamR vs. P cells, highly elevated in ER+ metastases vs. primary tumors, and associated with poor outcome in ER+ BC treated with endocrine therapy. KLF4 KD, using the 2 siRNAs that generated similar pathway perturbations in MCF7-TamR cells, reduced TamR cell migration. Notably, among the genes co-dependent on KLF4 and ER in TamR cells, PYGB was the only gene with a PTR residing in an ER-bound SE established in TamR but not P cells. Glycogen phosphorylase B, encoded by PYGB, is the rate-limiting enzyme in glycogen degradation and plays a role in the progression of various tumors. Expression of KLF4, FOXA1, and FRA1 are commonly activated during the differentiation of human embryonic stem cells into foregut endoderm and in the inner core of fibroblasts of first-trimester human placenta villi, suggesting a unique role of KLF4 in mediating lineage-specific CRC, possibly by engaging PYGB and the glycogen metabolic pathway in advanced ER+ disease. Conclusions: Using SE-oriented integrative bioinformatics, we identified KLF4 as a potential novel target in the FOXA1/AP-1 transcriptional axis. As KLF4 binding motif resides in the unique ER-bound SEs of TamR cells, KLF4 likely forms an auto-regulated loop amplifying CRC in transcriptional reprogramming, among which the PYGB/glycogen metabolic pathway merits further investigation in endocrine-resistant ER+ disease.

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7:00 AM - 8:15 AM

PD10-04

PD10-04 Combination of the next generation oral SERD camizestrant (AZD9833) with CDK4/6 and mTOR/AKT inhibitors delivers robust efficacy in a broad range of ER+ breast tumors.

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Next-generation oral selective estrogen receptor degraders (ngSERDs) are aiming to become the backbone endocrine therapy (ET) for patients with estrogen receptor positive (ER+) breast cancer (BC) by achieving greater ER signaling blockade than current therapies and tackling key mechanisms of resistance. Camizestrant (AZD9833) is an ngSERD for the treatment of ER+ BC which has demonstrated selective ER α degradation, pure ER antagonism and significant anti-tumor activity in ESR1 wild-type (ESR1wt) and mutant (ESR1m) tumors, as well as encouraging clinical activity in early phase trials. ER+ BC is responsive to therapies targeting ER α and CDK4/6 signaling in the adjuvant and metastatic settings. To explore camizestrant combination potential as a backbone ET, camizestrant was partnered with either palbociclib or abemaciclib in CDK4/6 inhibitor (CDK4/6i) naïve and resistant in vitro and in vivo models. Combination benefit was observed in vitro in 3 parental ER+ BC cell lines, moreover camizestrant plus abemaciclib showed activity in palbociclib-resistant cell lines including lines harboring CCNE1amp and RB1 loss. In vivo, combination of camizestrant and either CDK4/6i was well tolerated with the combinations promoting improved efficacy in ESR1wt and ESR1m PDX tumor models compared to monotherapy arms. ER+ BC has a high prevalence of alterations in the PI3K/AKT/PTEN pathway which provides opportunities for treatment with PI3K/AKT pathway inhibitors. Camizestrant delivered enhanced efficacy when combined with mTORC1 inhibitor everolimus and AKT inhibitor capivasertib in CTC-174, an ESR1m and PI3KCAm tumor model. Additionally, combination with capivasertib was more efficacious than single treatments, at clinically relevant dose and schedules, in both PI3Kwt and mutated pathway in PDX models. These data demonstrate the interplay between PI3K/AKT/PTEN pathway inhibition and camizestrant mechanism of action. Finally, we explored a potential triple combination of camizestrant, capivasertib and palbociclib in Palbociclib-resistant models representative of PI3KCA/AKT/PTEN wt and altered tumors. This strategy delivered robust efficacy across these models comparing to single treatments and double combinations. The triplet led to durable regressions at clinically achievable doses of all compounds, irrespective of genetic background and aligned to biomarker modulation of the three signaling axis. These preclinical data demonstrate the potential of camizestrant to become the backbone ET, with high combinability in vivo with inhibitors of CDK4/6, mTOR and AKT. These combinations demonstrate the opportunity to impact care of patients with early and metastatic ER+BC, delivering benefit to broad patient populations including those with ESR1wt or ESR1m tumors, independent of PI3K/AKT/PTEN pathway mutation status, and in patients with both CDK4/6i sensitive and resistant tumors.

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

PD10-05

PD10-05 Neoadjuvant tamoxifen therapy reactivates tumor suppressor protein p53 in luminal breast cancer patients: Results from a window-of-opportunity clinical trial

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Therapeutic effect of tamoxifen (Tam) against ER+ breast cancer (BC) is known to be mediated by its binding to estrogen receptor-alpha (ER α /ESR1) and inhibiting estrogen signaling leading to altered gene expression. Besides this canonical mode of function, our pre-clinical studies had revealed a novel mechanism wherein ESR1 directly binds wild type p53 (wt TP53) resulting in repression of its tumor suppressor functions, and Tam blocks this inactivation of TP53. Although patients with Luminal Tumors expressing wt TP53 are known to be more responsive to tamoxifen therapy, the underlying mechanism in tumors has remained unknown. To test the hypothesis that abrogation of the ESR1-mediated functional inactivation of TP53 is one of the major mechanisms that underlie the early effects of Tam therapy, we conducted a window of opportunity clinical trial in newly diagnosed luminal breast cancer patients undergoing surgical therapy. Methods: 59 women with ER+ invasive BC were randomized to 20mg Tam daily for 28 days prior to surgery or standard of care (SOC). TP53 status was confirmed by massively parallel sequencing. ER+ wt TP53 tumors were included in the study. IHC was performed on FFPE tissue from tumors to compare expression of ESR1 and TP53 along with their selected downstream targets. ESR1-TP53 interaction in situ was determined by Proximity Ligation Assay (PLA). 17 β -estradiol and Tam metabolites were measured in the plasma, tumor, and surrounding normal tissue using LC-MS/MS. Global transcriptome analysis in tumors was conducted by RNA-seq. Proteome expression in resected tumors was analyzed by reverse phase protein array (RPPA) with 216 proteins. Findings: Importantly, IHC on tumor tissues showed that the levels of ESR1 and TP53 were not altered in response to Tam therapy, whereas ESR1-TP53 interaction was considerably disrupted by Tam (in situ PLA data). Differential gene expression (DGE) analysis using DESeq2 R package followed by GSEA pathway analysis showed that 307 genes were differentially expressed ($p < 0.05$) ($\log FC > 1.5$) in tumors from Tam-treated versus untreated patients in response to Tam therapy. Pathways

representing TP53 signaling, stem cells, and low-grade luminal breast cancer were upregulated in the Tam treated group while those representing adipogenesis, invasive breast cancer, estradiol response, ras signaling, and E2F targets were downregulated. “Master Regulators” identified by iRegulon included several p53 targets. Integration of RNA-seq and RPPA data revealed that DEGs fall into three categories: (i) regulated by TP53, (ii) regulated by ESR1, and (iii) regulated by both TP53 and ESR1. Together, the data demonstrated that in addition to its conventional effects mediated by its binding to ESR1 and inhibiting estrogen signaling leading to altered gene expression, Tam disrupted the ESR1–TP53 interaction leading to functional reactivation of TP53 and reprogramming of gene expression. Conclusions: Our data 1) support ESR1–TP53 crosstalk in tumors as a novel mechanism underlying endocrine therapy response of luminal BC patients, and 2) highlight the importance of factoring TP53 into therapeutic strategies for ER+ BC patients, and 3) have implications in stratifying ER+ BC patients to those who will or will not be responsive to Tam therapy.

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PD10-06

PD10-06 Clinical outcomes and exploratory gene expression analysis of OPPORTUNE: a phase II window-of-opportunity study to evaluate pictilisib+anastrozole versus anastrozole alone in ER-positive breast cancer

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Background: Endocrine therapy (ET) is the mainstay of ER+ BC treatment. However; up to 20% of ER+ BC tumors progress into metastatic disease and develop ET resistance, underscoring the need for combination therapies. Preclinical data suggest that combining phosphatidylinositol 3-kinase (PI3K) inhibitors with ET may overcome resistance. OPPORTUNE, a preoperative phase II window trial, evaluated whether the combination of the PI3K inhibitor pictilisib with

anastrozole (PIC+ANA) can increase the antitumor effect of ANA in newly diagnosed operable ER+ BC. Early results showed greater suppression of tumor Ki67 in patients treated with PIC+ANA versus ANA alone. Here, we present gene expression analysis from tumors collected pre- and post-treatment, and their associations with Ki67 outcomes. Methods: Postmenopausal women with newly diagnosed operable ER+/HER2-negative BC were randomly allocated (2:1, favoring the combination) to 2 weeks of preoperative treatment with ANA 1 mg once per day (n = 47) or the combination of ANA 1 mg with PIC 260 mg once per day (n = 89). The primary end point was inhibition of tumor cell proliferation measured by change in Ki67 protein expression via IHC between tumor samples taken pre- and post-treatment. Samples were analyzed by RNA-sequencing—ER pathway activity, PAM50 intrinsic subtypes, and pathway analyses were assessed by Ki67 outcomes. Elastic net regression analysis and transcription factor activity inference with Dorothea were performed to identify features strongly associated with Ki67 outcomes. Results: 124 patients (ANA, n=43; PIC+ANA, n=81) had paired tumor samples at baseline/week 2 that were evaluable for both Ki67 and RNA-seq. PIC+ANA showed improved suppression of Ki67 compared to ANA alone (-83.78% vs -73.85%, p=0.012) and a greater proportion of patients achieved complete cell cycle arrest (CCCA, as defined by Ki67< 2.7%) in the PIC+ANA arm (45.68% vs 36.59%). ER pathway activity suppression was comparable between treatments. PAM50 classification based on RNA-seq showed that 83.0% of tumors were luminal (Lum) A at baseline and 12.9% were LumB, with the remainder being classified as Normal-like. PIC+ANA showed greater suppression of Ki67 in LumB tumors compared to LumA (-92.29% vs -81.62%). This effect was much greater in the PIC+ANA arm compared to LumB tumors treated with ANA alone (-92.29% vs -37.87%); however, given the low number of LumB tumors in the ANA arm (n=3), we could not determine statistical significance. Bioinformatic analysis of RNA-seq from baseline specimens showed that MYBL2 activity was associated with resistance to ANA (as defined by Ki67≥7.5% at week2). Tumors in the top quartile of MYBL2 activity at baseline showed improved Ki67 outcomes in the PIC+ANA arm compared to ANA alone (-91.71% vs -51.44%), while no differences were observed between treatments for tumors with lower MYBL2 activity (-79.16% vs -76.72%). Single-nucleus (sn)-RNA-seq from untreated ER+ BC tumors showed that MYBL2 was enriched in a single cluster of tumor cells, which also had the highest expression of a subset of actionable targets (including CDK1, CDK2, CDK4, EZH2, and AKT1), as compared to other tumor cells. Expression data from DepMap and drug-sensitivity data from ER+ BC cell lines show a positive trend between high MYBL2 expression and sensitivity to the ER degrader, giredestrant. Conclusions: PIC exhibited greater antiproliferative effects in combination with ANA in ER+/HER2- early BC compared to ANA alone, particularly in LumB and MYBL2-high tumors. Furthermore, the transcriptional profile and in vitro response of tumor cells with high MYBL2 expression suggest potential sensitivity to other combination therapies.

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12/8/2022

7:00 AM - 8:15 AM

PD10-07

PD10-07 Low plasma estradiol, low expression of estrogen responsive genes and TP53 mutations are associated with poor anti-proliferative response to aromatase inhibitors

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Background: Aromatase inhibitors (AIs) are highly effective at reducing recurrences and mortality in postmenopausal patients with estrogen receptor positive breast cancer (ER+ BC). Poor anti-proliferative (Ki67) response or ER+ BCs to AIs after 2 weeks is associated with worse long-term outcomes. Factors that relate to the degree of the response may identify markers and/or mechanisms of resistance. Methods: The PeriOperative Endocrine Therapy for Individualizing Care (POETIC) trial randomized 4,480 with ER+ BC to 2 weeks' AI before surgery or no presurgical treatment. All patients within the bottom 15% of Ki67 responders to AI (poor responders [PRs]; n=177 with RNA extracted) were selected from and matched to good responders (GRs) within the 50% showing the best response (n=190). Matching was based on baseline Ki67 levels as measured by immunohistochemistry (IHC). Response to AI was measured by the percentage change in Ki67 after 2 weeks' treatment. PRs were further divided into groups expressing high ESR1 (PRs ESR1HIGH; n=119) and low ESR1 (PRs ESR1LOW; n=58) levels since there were very few GRs with low ESR1. RNAseq, targeted exome DNA sequencing of 87 BC/resistance related genes and measurement of plasma estradiol levels by mass spectrometry were performed to understand mechanisms of de novo resistance. Intrinsic subtypes were estimated from RNAseq data. Results: More than 90% of PRs ESR1LOW were non-luminal subtypes with low expression of estrogen-responsive genes. In contrast, 11% of PRs ESR1HIGH were non-luminal compared to 4% of GRs but only HER2-enriched subtypes were significantly higher in PR ESR1HIGH (p=0.05, Fisher exact). While AI treatment had limited impact on Ki67 IHC values in PRs ESR1HIGH, PGR expression was more than 2-fold lower after 2 weeks of AI. Gene-set enrichment analysis showed significantly lower expression of estrogen-response genes in PRs ESR1HIGH compared to GRs (FDR < 10⁻⁹) at baseline despite similar percentage of Luminal subtypes in PRs ESR1HIGH and GRs. Plasma estradiol levels were correlated with expression of estrogen-response genes (FDR=0.01) and levels were significantly lower in PRs ESR1HIGH compared to GRs (p=0.003, Mann Whitney). PRs ESR1HIGH had significantly more mutations in RB1, TP53, ARID1B and DNAAH11 genes (p < 0.05, Fisher exact). TP53 mutations were significantly enriched in Luminal-A PRs ESR1HIGH compared to GRs (22% and 3% respectively; p=0.003, Fisher exact), but not in Luminal-B tumors (23% and 15% mutated respectively). Discussion and conclusions: In approximately 33% of PRs, de novo AI resistance was associated with and most likely due to low expression of ER/ESR1 and estrogen-responsive genes in non-luminal tumors. In the remaining tumors, AI treatment still impacted some estrogen responsive genes but had limited downstream impact on suppressing proliferation. This might be due to mutations including in TP53 that limit suppression of proliferation downstream of estrogen signaling. The proportion of Luminal tumors in GRs and PRs ESR1HIGH was similar, suggesting better outcome of Luminal-A tumors on AI is likely due to their better intrinsic prognosis rather than better response to endocrine therapy.

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12/8/2022

7:00 AM - 8:15 AM

PD10-08

PD10-08 Immune cell infiltration associated with poor anti-proliferative response to aromatase inhibitors in postmenopausal women with primary ER-positive HER2-negative breast cancer

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Background: Aromatase inhibitors (AIs) are one of the main treatment strategies for the clinical management of estrogen receptor-positive (ER+) breast cancer (BC). Despite prolonged time to recurrence and initial clinical responses, >20% of patients eventually relapse, and previous studies have shown an association of poor anti-proliferative response to AIs and worse outcome. High immune activity in ER+ tumors may be associated with worse outcome, in contrast to ER-negative BC where immune infiltration is a feature associated with better outcome. Our work focused on understanding the correlations between immune cell infiltration and response to AI. Methods: All patients with ER+ HER2- tumors within the bottom 15% of Ki67 anti-proliferative responders to AIs (poor responders [PRs]; n=177) were selected from the PeriOperative Endocrine Therapy for Individualizing Care (POETIC) trial and matched on baseline Ki67 levels to good responders (GRs) within the 50% showing the best response (n=190). Response to AI was measured by the Ki67 percentage change after 2 weeks of treatment. PRs were further divided into groups expressing high ESR1 (PRs ESR1HIGH; n=119) and low ESR1 (PRs ESR1LOW; n=58) levels to represent PR subgroups that showed partial or no response to AIs. The percentage of stromal tumor-infiltrating lymphocytes (TILs) was assessed. Multiple immunofluorescence was performed for ER, CD3, CD20, CD68, FOXP3, and CD3/FOXP3 in 15 baseline samples from each of the GR, PR ESR1HIGH, and PR ESR1LOW populations and immune cell density in stromal or tumor compartments was estimated. Spearman correlations of TILs with Consensus tumor microenvironment (TME) deconvolution and Molecular Signatures Database hallmark gene sets were conducted. The relationship between the immune markers' density and genes, hallmark gene sets and Consensus TME was assessed. Results: The percentage of TILs was significantly higher in the PR ESR1HIGH and PR ESR1LOW compared to the GRs (adjusted $p < 0.05$). As expected, TILs were highly correlated with T cells (particularly T-regulatory cells) and immune hallmark gene sets. There was a tendency for higher density of each of the immune markers in PRs compared to GRs, with significant differences being observed in stromal B-cell marker CD20 density ($p < 0.05$). Analysis showed a significant correlation between TILs and stromal FOXP3 marker density (FDR < 0.05), and stromal biomarker density was highly correlated to the gene expression of the encoding genes of the same tumors (CD3/CD3D, FOXP3/FOXP3, and CD20/MS4A1) (FDRs < 0.05). There was also a strong and significant correlation between the stromal expression of CD20, CD3, FOXP3, and CD3/FOXP3 with the immune hallmark gene sets (FDRs < 0.05). Finally, the immune phenotyping showed the expected correlations with TME deconvolution, with particularly strong correlations of CD20 and CD3 with B- and T-cell gene signatures, respectively (FDRs < 0.05). Conclusions: Different immune features indicated a broad involvement of several immune cell types in PRs to AIs, suggesting that the immune system might be associated with resistance of ER+ breast tumors to AI treatment. Spatial gene

expression profiling is ongoing to characterize these tumors further and investigate potential mechanisms of AI resistance.

Disclosure(s):

Anastasia Alataki, PhD: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

PD10-09

PD10-09 Multiomics analysis of matched ER+ primary and recurrent breast cancers on or after adjuvant endocrine therapy

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Background: 80% of all breast cancers (BCs) are ER-positive (ER+). Not all respond to adjuvant endocrine therapy (aET) and a significant number develop endocrine resistance and recur. The basis for primary and acquired endocrine resistance is poorly understood. A multiomics analysis of primary ER+ BCs matched with recurrences on or after completion of aET has been performed. Patients: A unique cohort of 520 women with matched primary and recurrent ER+, HER2-negative (HER2-) BC is being analysed. In the first subset of 75, all had surgery to clear margins, followed by aET. The endocrine therapy given was tamoxifen (66%), aromatase inhibitors (AI) (28%: 17% letrozole, 6% anastrozole, 2% exemestane, and 3% a succession of 2 different AIs), or a combination of tamoxifen and an AI (6%). aET duration was 5 years, unless the patient stopped treatment or developed a recurrence sooner. 16/75 patients (21%) had positive lymph nodes. All patients developed recurrences: local in 59/75, concurrent local and nodal in 13/75 and lymph node-only in 3/75. Median time to recurrence was 4.1 years (range: 0.7-29 years). 62% of patients were on aET at the time of recurrence. All patients have long-term follow-up. Methods: DNA and RNA were extracted from matched primary and recurrence BC tissue samples. Targeted DNA-exome and whole-genome expression analyses were performed. A custom targeted DNA panel was used to study genes implicated in endocrine therapy resistance (ETR): this included 73 different targets, selected based on our previous full-exome sequencing of sequential ET recurrences and those implicated in the literature and in curated somatic and cancer mutation databases. Somatic mutations and copy number alterations (CNA) were determined. Differential gene expression analysis was performed using two-class unpaired Significance Analysis of Microarrays (SAM). Validation of pathways implicated in ETR using NanoString GeoMx protein analysis is ongoing. Results: Targeted DNA-exome profiling identified 1 or 2 potential driver mutations in all but a few primary samples. Multiple aberrations and a highly diverse mutational landscape were observed in all the recurrences. Matched breast and lymph node samples from synchronous recurrences had very similar somatic profiles. Changes significantly enriched in recurrent samples included somatic aberrations in well-established drivers such as MAP3K1, PIK3CA,

TP53 and CDH1, as well as ESR1. Aberrations were also common in PTEN and in ER-associated factors FOXA1 and GATA3. Transcriptomic analysis revealed a number of pathways implicated in resistance, including ER, HER2, GATA3, AKT, RAS and p63 signalling. A panel-based, targeted DNA sequencing approach for mutational profiling allowed capture of relevant mutational profiles linked to ETR in a cost-effective manner compared with traditional whole-exome sequencing. Ongoing analysis has linked mutational profiles to specific endocrine agents and has allowed us to demonstrate significant differences between recurrences on aET compared with those after completion of aET. Multiomics profiling of the remaining samples in the cohort is underway. Discussion: This multiomics study provides the largest cohort to-date of matched early and recurrent ER+/HER2- BCs. It has shed new light on how different adjuvant endocrine agents can affect primary drivers and lead to complex somatic and transcriptomic changes in recurrent disease. This work confirms that the mechanisms of endocrine resistance are diverse and has already identified mechanisms underlying ETR and clinically meaningful biomarkers of ETR, including potentially actionable mutations and targets.

Disclosure(s):

Carlos Martinez-Perez, PhD: No financial relationships to disclose

Charlene Kay, MSc: No financial relationships to disclose

James Meehan, PhD: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

PD10-10

PD10-10 Single cell characterization of longitudinal biopsies from breast cancer patients treated with the aromatase inhibitors letrozole and exemestane in sequence

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Background About 70% of breast cancer cases are hormone receptor positive, indicating that cancer cells exploit estrogens for their growth. Postmenopausal estrogen receptor positive breast cancer patients are currently often treated with aromatase inhibitors suppressing serum and tumor tissue estradiol levels by >90%. Two widely used aromatase inhibitors are letrozole, a nonsteroidal inhibitor and exemestane, a steroidal aromatase inactivator. While the mechanisms of action of these two drugs are well studied, their effects on the tumor immune

microenvironment and mechanisms of resistance to these drugs are still not sufficiently elucidated. Study design The NEOLETEXE trial¹ was a neoadjuvant, randomized, open-label, intra-patient, cross-over, single center clinical trial aiming at treating postmenopausal patients with locally advanced breast cancer defined primarily as large T3/T4 and or N2/N3. However, patients with large T2 tumors were also eligible. Patients were randomized to neoadjuvant therapy with either letrozole (2.5 mg daily) or exemestane 25 mg daily for about 3 months, followed by a cross-over to the alternative drug for another 3 months prior to surgery. 102 patients were enrolled in NEOLETEXE. Methods Pre-treatment, on-treatment (3 months) and end-of-treatment (6 months of therapy) biopsies were subjected to single-cell transcriptome, T cell receptor and B cell receptor profiling using the Chromium Single-Cell v2 5' Chemistry (10x Genomics). Libraries were paired-end sequenced on a NovaSeq6000. Single cell gene expression matrices were analyzed with the Seurat package (v4.0.2). After filtering out stressed / dying cells or cells with low quality sequencing, gene expression of the remaining good quality cells was normalized and scaled to construct principal components and further cluster cells. Results We clustered 362.762 cells from 26 pre-treatment, 20 on-treatment and 19 end-of-treatment biopsies and identified 8 main cell types to be present: T cells, B cells, epithelial cells, fibroblasts, endothelial cells, macrophages, mast cells and dendritic cells. To further identify specific and specialized cell subtypes, we clustered the cells belonging to the above-mentioned cell types independently and annotated the clusters obtained using validated marker genes. Finally, we use statistical methods and algorithms to characterize how the proportion of the different cell types changes in tumors under treatment pressure. Specifically, we show changes in the proportion of CD8 effector memory cells under treatment pressure, with a significant increase in cytotoxic T cell proportions after two months of treatment with aromatase inhibitor. Conclusions We use single cell profiling to obtain a high-resolution map of the cell types found in tumor biopsies of the NEOLETEXE trial to characterize the effects of aromatase inhibitors on the tumor microenvironment and to identify the cancer cell signatures during treatment with letrozole or exemestane. 1. Bahrami N., Sauer T., Engebretsen S., Aljabri B., Bemanian V., Lindstrøm J., Lüders T., Kristensen V.N., Lorentzen A., Loeng M., Ødegård H.P., Kvaløy J.Ø., Vestøl I.B., Geisler S.B., Gravdehaug B., Gundersen J.M., Geisler J. The NEOLETEXE trial: a neoadjuvant cross-over study exploring the lack of cross resistance between aromatase inhibitors. *Future Oncology*, 15 (32), 3675-3682, 2019.

Disclosure(s):

Salim Ghannoum, n/a: No financial relationships to disclose

Chloé Steen, n/a: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

Discussion 1 + Q&A: PD11-01, PD11-02, PD11-03 & PD11-12

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12/8/2022

7:00 AM - 8:15 AM

Discussion 2 + Q&A: PD11-04, PD11-05, PD11-06 & PD11-07

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12/8/2022

7:00 AM - 8:15 AM

Discussion 3 + Q&A: PD11-08, PD11-09, PD11-10 & PD11-11

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12/8/2022

7:00 AM - 8:15 AM

Poster Spotlight Discussion 11: Improving Outcome for TNBC: New Directions in Immunotherapy

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12/8/2022

7:00 AM - 8:15 AM

PD11-01

PD11-01 Evaluation of the PD-1 Inhibitor Cemiplimab in early-stage, high-risk HER2-negative breast cancer: Results from the neoadjuvant I-SPY 2 TRIAL

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Background: I-SPY2 is a multicenter, phase 2 trial using response-adaptive randomization within biomarker subtypes defined by hormone-receptor (HR), HER2, and MammaPrint (MP) status to evaluate novel agents as neoadjuvant therapy for high-risk breast cancer. The primary endpoint is pathologic complete response (pCR). Cemiplimab (Cemi) is a PD-1 inhibitor approved for the treatment of NSCLC, cutaneous basal, and squamous cell cancer. Here, we report current efficacy rates of Cemi in combination with paclitaxel followed by AC.

Methods: Women with tumors ≥ 2.5 cm were eligible for screening. Only HER2 negative (HER2-) patients were eligible for this treatment; HR positive (HR+) patients had to be MP high risk. Treatment included paclitaxel 80 mg/m² IV weekly x 12 and Cemi 350 mg IV given q3weeks x 4, followed by doxorubicin/cyclophosphamide (AC) every 2 weeks x 4. The control arm was weekly paclitaxel x 12 followed by AC every 2-3 weeks x 4. All patients undergo serial MRI imaging; and imaging response (at 3 weeks, 12 weeks and prior to surgery) were used along with accumulating pCR data to continuously update and estimate pCR rates for trial arms. Analysis was modified intent to treat. Patients who switched to non-protocol therapy count as non-pCR. The goal is to identify (graduate) regimens with $\geq 85\%$ Bayesian predictive probability of success (i.e. demonstrating superiority to control) in a future 300-patient phase 3 neoadjuvant trial with a pCR endpoint within responsive signatures. Cemi was eligible to graduate in 3 pre-defined signatures: HER2-, HR-HER2-, and HR+HER2-. To adapt to changing standard of care, we constructed “dynamic controls” comprising ‘best’ alternative therapies using I-SPY 2 and external data and estimated the probability of Cemi being superior to the dynamic control.

Results: 60 HER2- patients (28 HR+ and 32 HR-) received Cemi arm treatment. The control group included 357 patients with HER2- tumors (201 HR+ and 156 HR-) enrolled since March 2010. Cemi graduated in HR-/HER2- signature. Estimated pCR rates (as of June 2022) are summarized in the table.

Immune-related endocrine disorders include: hypothyroid (14.5%), adrenal insufficiency (10%), hyperthyroid (4.8%), and thyroiditis (3.2%). Only one grade 3 adrenal insufficiency was observed. All immune related AE's were manageable. Additional biomarker analyses are ongoing and will be presented at the meeting. Response predictive subtypes (Immune+ vs Immune-) and additional predictive biomarkers were assessed. Associations with pCR will be presented at SABCS.

Conclusion: The I-SPY 2 study aims to assess the probability that investigational regimens will be successful in a phase 3 neoadjuvant trial. Anti-PD-1 therapy with Cemi resulted in a higher predicted pCR rate in HR-/HER2- 55 rate% disease compared to control at 29%. Immune-mediated AE's were observed. This data is consistent with previously published data using check point inhibitors in early-stage HR-/HER2- breast cancer.

Signature	Estimated pCR rate		Probability Cemi Superior to Control	Predictive Probability of Success in Phase 3	Probability Cemi Superior to Dynamic Control
	Cemi	Control			
HER2-	0.321	0.211	0.985	0.555	
HR-/HER2-	0.548	0.291	0.999	0.931	0.419
HR+/HER2-	0.132	0.145	0.377	0.088	0.013

Estimated pCR rates

Disclosure(s):

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12/8/2022

7:00 AM - 8:15 AM

PD11-02

PD11-02 A Phase II Randomized Window of Opportunity Trial Evaluating Cytotoxic and Immunomodulatory effects of Intratumoral INT230-6 in Early Stage Breast Cancer: the INVINCIBLE Trial

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Background: The majority of breast cancers outside of the triple negative subtype are considered immunological quiescent and are therefore minimally responsive to immunotherapies. One potential method to combat this is through local therapies that induce cell death, thereby exposing tumor antigens, providing adjuvants for anti-tumor immune priming, and potentially increasing responsiveness to immunotherapies. We have conducted a randomized, Phase 2 presurgical Window-Of-Opportunity trial for intratumoral (IT) INT230-6 (comprising VINblastine (VIN) Cisplatin (VIN)) evaluating clinical and BioLogical Effects in patients with early-stage operable Breast Cancer (the INVINCIBLE trial- <https://clinicaltrials.gov/ct2/show/NCT04781725>). INT230-6 contains a dispersion enhancer molecule (SHAO) with the cytotoxic agents and is designed to cause tumor necrosis by dispersion throughout the tumor and diffusion into cancer cells. Previous in vitro studies have demonstrated that INT230-6 halts cancer cell replication and induces cell death recruiting dendritic cells and T-cells to the tumor microenvironment. In this trial, IT injections of INT230-6 are conducted to 1) exploit the potential of regional cytotoxic chemotherapy on breast cancer in vivo and 2) assess the immune response within the tumor, microenvironment and systemically in the host blood prior to surgical resection. **Methods:** Women with newly diagnosed and awaiting surgery for early-stage intermediate or high-grade T1-T2 invasive breast cancers were recruited to the trial. The study has two parts. Part I was a randomized (2:1) open label trial comparing 1-3 doses of INT230-6 injected weekly versus no treatment prior to surgery to evaluate safety, feasibility, and optimal drug dosing. Part II was a double-blinded randomized (2:1) trial where patients received one IT dose of INT230-6 vs saline injection. The primary objective was to estimate the proportion of patients with tumor necrosis and complete cell cycle arrest (CCCA) at the time of surgery compared to control. In addition, we performed targeted sequencing and proteomic profiling in tumour samples from the INT230-6 clinical trial. **Results:** The study recruited 90 patients with age ranges of 40-77 yrs (mean = 60 yrs) with tumors ranging from 1.5-4.3 cm (mean = 2.4cm). No surgeries were delayed or altered as a result of trial participation and the most common (>10%) AEs were injection site pain, injection site reaction and nausea/vomiting. Compared to the control group, up to 95% tumor necrosis was present in varying biologic subtypes and histologies, including invasive lobular carcinoma. Preliminary gene expression analysis showed significant differential gene expression between the baseline biopsy and surgical specimens. Pathway analysis identified genes associated with TCR signaling, B cells, T cells, chemokine signaling and NF- κ B signaling were significantly changed in the post treatment samples. There was a relative increase in CD4 and CD8 T cells and B and NK cells within the tumor and in the tumour microenvironment. **Conclusion:** Preliminary evidence shows that a single dose of INT230-6 can cause substantial tumor necrosis and stimulate an immune response in breast cancers prior to surgery with minimal adverse effects and good tolerability. This window of opportunity clinical trial demonstrates that INT230-6 injection is a novel and simple method to convert traditionally immune quiescent breast cancers into immunogenic tumors. This can open the door to future potential immunotherapeutic options in early stage breast cancer.

Disclosure(s):

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PD11-03

PD11-03 Comparison of a mono Atezolizumab window followed by Atezolizumab and chemotherapy with Atezolizumab and chemotherapy in triple negative breast cancer – an interim analysis of the adaptive randomized neoadjuvant trial NeoMono

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Introduction: Improvement of systemic treatment of TNBC represents an unmet medical need. Targeted therapy of regulatory immune pathways has become an important option in the treatment of many malignant diseases including breast cancer. Neoadjuvant trials combining chemotherapy and checkpoint inhibitors (KEYNOTE-522 and IMpassion031) have demonstrated a meaningful benefit regarding pathological complete remission (pCR) for the addition of PD-1- or PD-L1-inhibitors to chemotherapy in patients with TNBC. In the KEYNOTE-522 trial, the addition of an immune checkpoint inhibitor (ICI) to neoadjuvant chemotherapy also had a beneficial impact on event-free survival even in patients who did not achieve a pCR. Of note, in the neoadjuvant GeparNuevo trial only those patients with TNBC who received a 2-week checkpoint inhibitor monotherapy window before the start of neoadjuvant chemotherapy in combination with checkpoint inhibition, achieved a significant pCR benefit from the addition of the PD-1 inhibitor Durvalumab to neoadjuvant chemotherapy alone. Methods: NeoMono is a phase 2 randomized multicenter trial recruiting male and female patients with primary TNBC (defined as ER/PR < 10% and HER2 negative). Neoadjuvant treatment in Arm A and B consists of Atezolizumab 1200 mg every 3 weeks in addition to neoadjuvant chemotherapy (i.e., 12 x Carboplatin and Paclitaxel q1w followed by Epirubicin and Cyclophosphamide q3w). Combination therapy in arm A is preceded by an Atezolizumab monotherapy window (i.e., 840 mg Atezolizumab once two weeks prior to initiation of combination therapy). Study goals are to compare the efficacy of neoadjuvant chemotherapy with Atezolizumab with and without an Atezolizumab two-week monotherapy window (primary endpoint: pCR) and the identification of biomarkers predicting (early) response to or resistance against Atezolizumab. The extensive translational program of the neoMono trial aims at identifying these biomarkers on tumor and patient level through analysis of sequential tissue and liquid biopsies. The NeoMono statistical design adapts the idea of a proof-of-concept trial and uses Bayesian posterior and predictive probabilities for inference about the primary hypothesis. Up to four planned efficacy interim analyses provide decision points for early stopping for success or futility. The expected maximum number of patients to be recruited is 458. Results: The predefined number of 50 patients in each arm being evaluable for the primary endpoint pCR has been reached and the results of the first planned interim analysis will be presented at the meeting. Conclusion: The addition of an ICI to state of the art neoadjuvant chemotherapy has recently been established as a new standard of care in TNBC. NeoMono has the potential to answer the question if the beneficial effect of the ICI can be increased by a chemotherapy free ICI monotherapy window prior to a combination with neoadjuvant chemotherapy.

Disclosure(s):

Hans-Christian Kolberg, MD PhD: Agendia: Consulting Fees (e.g., advisory boards) (Ongoing); Amgen: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Carl Zeiss Meditec: Consulting Fees (e.g., advisory boards) (Ongoing); Diichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Genomic Health/Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); GSK: Consulting Fees (e.g., advisory boards) (Ongoing); Janssen-Cilag: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); LIV Pharma: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Onkowissen: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Phaon Scientific GmbH: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Riemser: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Fees for lectures (Ongoing); SeaGen: Consulting Fees (e.g., advisory boards) (Ongoing); SurgVision: Consulting Fees (e.g., advisory boards) (Ongoing); Tesaro: travel expenses (Ongoing); TEVA: Consulting Fees (e.g., advisory boards) (Ongoing); Theraclion: Consulting Fees (e.g., advisory boards) (Ongoing); Theraclion

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12/8/2022

7:00 AM - 8:15 AM

PD11-04

PD11-04 Primary results of SOLTI-1503 PROMETEO phase 2 trial of Combination of Talimogene Laherparepvec (T-VEC) with Atezolizumab in patients with residual breast cancer after standard neoadjuvant multi-agent chemotherapy

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Background: Residual disease (RD) following neoadjuvant chemotherapy (NAC) in early HER2-negative breast cancer (BC) remains an unmet medical need. However, no therapies to date have tested their activity directly in chemo-resistant RD. Here, we hypothesized that combining an oncolytic virus such as T-VEC with atezolizumab may offer clinical benefit in patients (pts) with RD after standard NAC. To our knowledge, PROMETEO is the first trial that examines the activity of immunotherapy in pts with RD prior to surgery. Methods: PROMETEO (NCT03802604) is a single-arm, open-label, multicenter phase II trial. Women with triple-negative BC (TNBC) or hormone receptor-positive/HER2-negative (HR+/HER2-) BC with baseline (i.e., before NAC) ki67 \geq 20% were eligible. RD was confirmed with a magnetic resonance imaging (MRI) showing a tumor diameter \geq 10 mm and a core-biopsy detecting the presence of invasive cells. Before surgery, T-VEC was administered intratumorally on week 1 (106 pfu/mL), then in week 4 and every 2 weeks thereafter (108 pfu/mL) for 4 injections. Atezolizumab (840 mg) was administered intravenously every 2 weeks for 4 infusions, starting at week 4. Surgery was performed in $<$ 3 weeks after completing the treatment. The primary objective was to evaluate the efficacy of the combination, measured by the rate of residual cancer burden (RCB) class 0/1 at surgery. Tumor samples collected at 5 timepoints (before NAC, during screening period, after first dose of T-VEC, after first dose of T-VEC and atezolizumab and at surgery) were mandatory to assess gene expression, tumor-infiltrating lymphocytes (TILs), immune cells PD-L1 IHC (SP142), tumor mutational burden (TMB) by FoundationOne and other translational endpoints. Results: Between Dec 2018 to Feb 2022, 28 pts were enrolled: 20 pts with HR+/HER2- disease and 8 pts with TNBC. Median age was 47 (range 31-71) and 71% of pts were premenopausal. At diagnosis before NAC, clinical stage II disease represented 60.7%, cN+ 60.7%, median Ki-67 was 37.5% (range 20%-95%), high TILs (\geq 10%) 37%, median TMB was 3 (0-19) and only 1 of 27 pts (3.7%) had a PD-L1-positive

tumor. After NAC, mean tumor size by MRI was 28.3 mm (10-93). Two pts discontinued from the trial (1 withdrawal of consent and 1 COVID infection). The completion of 5 cycles of treatment was achieved by 73% of pts. The overall RCB-0/1 rate was 25% (7 of 28, 95% IC 10.7 – 44.9%), all with RCB 0 (pathologic complete response [pCR]). The pCR rate was 30% in HR+/HER2- disease and 12.5 % in TNBC. Radiological response by MRI was achieved by 3 of 28 pts (10.7%). Interestingly, none of the 7 pts with a pCR had radiological response (stable disease n=5, progressive disease [PD] n=2). Six pts (21.4%) had radiological PD and had RCB 2/3. Overall, 27 (96%) patients had at least one treatment-emergent adverse event (TEAE) of any grade. Most common grade 1 or 2 AEs were fever (11 pts, 39.3%), ALT increased (9 pts, 32.1%), AST increased (8 pts, 28.6%), arthralgia (6 pts, 21.4%) and anemia (6 pts, 21.4%). Grade 3 reversible neutropenia occurred in 1 patient. Across all pts, significant increases ($p < 0.001$) in TILs, immune genes and immune PDL1+ cells were observed after 1 dose of TVEC, 1 dose of the combination and at surgery. Intrinsic subtype changes at surgery occurred in 73.1% of cases, mostly (46.1%) Luminal A/B converting to Normal-like. At surgery, 19 of 26 (73.1%) of tumors were PDL1+. Conclusions: Two months of T-VEC in combination with atezolizumab induced a pCR in a subgroup of pts with chemoresistant HER2- breast cancer. This effect is probably related to the immune activation provoked by the combined treatment. Interestingly, a high discrepancy was observed between the pre-surgical radiological imaging and the actual surgical pathological report. Pre-operative window-of-opportunity trials in this context might provide important clues regarding the activity of novel treatment strategies.

Disclosure(s):

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7:00 AM - 8:15 AM

PD11-05

PD11-05 Gut microbiome signatures correlate with overall survival among patients receiving eribulin with or without pembrolizumab for hormone receptor-positive metastatic breast cancer

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Background: The gut microbiome modulates response and resistance to immune checkpoint inhibitors (ICI) across different cancer types. The objective of this study was to explore the association between fecal microbiome profiles and clinical outcomes in patients with hormone receptor-positive (HR+) metastatic breast cancer (MBC) treated with eribulin (E) + pembrolizumab (P) or E alone as part of a randomized phase II study (NCT03051659). **Patients and Methods:** Metagenomic shotgun sequencing was performed on fecal samples collected prior to randomization from a subset of 26 participating patients (E+P, n = 15; E, n = 11) collected prior to randomization. Sequencing data were processed with MetaPhlan3 to obtain diversity scores and taxonomic composition profiles. Associations between microbiome diversity, taxonomic composition, and clinical outcomes including survival metrics were assessed using Kaplan-Meier estimation methods and Cox proportional hazard models. **Results:** In this subset, median follow-up was 21.6 months and median overall survival (OS) was 17.9 months. OS was not statistically significant between two treatment arms as observed in the overall cohort. Metagenomic microbiome analysis revealed higher alpha diversity by inverse Simpson Index values associated with longer survival among all patients ($p = 0.004$), and in patients in the E + P arm ($p = 0.006$) but not in the E arm ($p = 0.2$). At the taxonomic level, longer OS among all patients was associated with a baseline lower relative abundance of *Blautia wexlerae* ($\leq 0.2\%$ vs $> 0.2\%$) (22.1 vs 16.6 months; $p = 0.01$) and a higher relative abundance of *Odoribacter splanchnicus*, a common short-chain fatty acid producing gut bacterium ($> 0.35\%$ vs $\leq 0.35\%$) (22.3 vs 11.3 months; $p < 0.0001$). These associations remained significant after controlling for age, ECOG-PS status, and use or not of prior lines of chemotherapy in the metastatic setting. **Conclusions:** These results suggest high diversity and composition of the gut microbiome are associated with prolonged OS in HR+ MBC pts receiving eribulin with pembrolizumab. Additional and larger clinical studies are needed to validate these findings and preclinical models are needed to interrogate the mechanisms by which gut microbiome diversity and composition may impact therapeutic response and clinical outcomes in this patient population.

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12/8/2022

7:00 AM - 8:15 AM

PD11-06

PD11-06 Circulating tumor DNA association with residual cancer burden after neoadjuvant therapy in triple negative breast cancer in TBCRC 030

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Background. Patients (pts) with early triple negative breast cancer (eTNBC) are at increased risk of breast cancer recurrence and death. Recent studies have focused on escalation of therapy, with current treatment standard of at least five drugs – and associated toxicities - for eTNBC. Though presence of residual disease after neoadjuvant therapy (NAT) as measured by

residual cancer burden (RCB) helps guide addition of adjuvant treatment, more effective tools to tailor therapy are limited. Persistence of circulating tumor DNA (ctDNA) in the setting of residual disease is associated with high risk of distant recurrence. However, more sensitive minimal residual disease (MRD) assays are needed to potentially guide optimization of systemic therapy.

Methods. TBCRC 030 is a phase II randomized study of 12 weeks of NAT single agent cisplatin or paclitaxel for stage II-III TNBC, followed by surgery. The primary objective of the parent study was to correlate baseline biomarker for homologous recombination deficiency and RCB by study arm. From this group, responders (RCB 0/1) and non-responders (RCB 2/3) from both study arms who did not receive additional NAT prior to surgery were selected for analysis from the study cohort, matched on baseline nodal status and tumor size. As a post hoc study amendment, available pts were followed for event free survival (EFS). Plasma samples were collected prior to treatment initiation (W0), at three weeks (W3), and at twelve weeks, prior to surgery (W12). Whole genome sequencing (WGS) was performed on primary tumor tissue to identify somatic mutations and design for each pt a tumor-informed, ctDNA assay tracking up to 1000 mutations to detect MRD. Detection limit was computed for each tested sample as previously described. For each sample assayed, we report tumor fraction (TFx) when MRD was detected and the detection limit at 90% power when MRD was not detected.

Results. Of 139 study pts, 68 had complete tissue and plasma samples and no receipt of additional NAT. Of these, 22 were responders. These responders, and 22 matched non-responders were identified for analysis. Data from 22 pts – 11 responders, 11 non-responders - are described here; full analysis on all 44 pts will be presented at the meeting. Personalized ctDNA assays were designed targeting 434 to 1000 variants (median 1000) and applied to 66 plasma samples. At W0, 100% (22/22) were positive for ctDNA; 73% (16/22) and 55% (12/22) were positive at W3, and W12, respectively. In pts with T1-T2 tumors median TFx was $4.1e-3$ ($7.8e-6$, $3.4e-2$) and $4.7e-1$ ($4.3e-2$, $9.0e-1$) in pts with T3-T4 tumors. TFx decreased from W0 to W3 and from W0 to W12 in responders (Table 1). By W12, ctDNA had cleared in 7/8 pts with RCB 0, 1/3 with RCB 1, 2/8 with RCB 2, and 0/3 with RCB 3. Overall, ctDNA levels were broad with median TFx of $1.5e-3$ (range $2.9e-6$ to 0.90). Detection limit at 90% power for all tested samples was a median of $8.8e-6$ (range $9.9e-7$ to $6.8e-3$).

To investigate whether ctDNA persistence after NAT was associated with BC recurrence, we analyzed a separate group of all 8 pts with known recurrence and with complete data and samples. All pts had persistent ctDNA at W12 (median TFx $6.8e-3$, [$2.9e-6$ to $6.6e-2$]).

Conclusions. After 3 weeks of NAT for eTNBC, ctDNA TFx decreased, with a 3900-fold change in responders and 18-fold change in non-responders. By W3, TFx for most pts with RCB 0/1 were below the 1 in 10,000 limit of detection for many currently available assays, emphasizing the need for sensitive tests to potentially guide therapy. Additional studies will determine if ctDNA-guided approaches in eTNBC can improve pt outcomes.

Table 1: Tumor Fraction and Tumor Fraction Fold Change by Response to Neoadjuvant Therapy

	Responders (N=11)	Non-Responders (N=11)
TFx		
Median (Min, Max)		
W0	7.0e-3 (2.4e-4, 9.0e-1)	3.0e-3 (7.8e-06, 4.3e-2)
W3	3.6e-6 (0, 1.1e-3)	2.0e-4 (0, 9.8e-3)
W12	0 (0, 1.2e-4)	2.4e-4 (0, 9.1e-3)
TFx Fold Change		
Median (Min, Max)		
From W0 to W3	3.9e-3 (3.2e-6, 6.6e-1)	1.8e-1 (3.0e-4, 7.2e-1)
From W0 to W12	1.0e-3 (7.5e-6, 7.8e-2)	2.9e-1 (4.1e-4, 1.7)

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PD11-07

PD11-07 Association of TNBC-DX scores with outcomes in triple-negative breast cancer (TNBC) treated with neoadjuvant pembrolizumab and chemotherapy: a correlative analysis from NeoPACT and NeoSTOP trials

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Introduction: The TNBC-DX risk score includes the 14-gene immunoglobulin (IGG) immune signature, tumor size, and nodal status and has shown prognostic value for survival in early-stage TNBC (B. Conte et al., ESMO Breast 2021). However, currently unknown are the value of the TNBC-DX risk score and IGG immune signature in 1) predicting pathologic complete response (pCR) following neoadjuvant therapy, and 2) predicting outcomes in the context of neoadjuvant anti-PD1 treatment. Here, we assessed the IGG immune signature and the TNBC-DX risk score in patients with TNBC treated with neoadjuvant chemoimmunotherapy (NeoPACT; NCT03639948) and neoadjuvant chemotherapy without immunotherapy (NeoSTOP; NCT02413320). **Methods:** NeoPACT trial enrolled 120 patients with stage I-III TNBC who received carboplatin (AUC 6) + docetaxel (75 mg/m²) + pembrolizumab (200 mg) every 21 days x 6 cycles. NeoSTOP randomized 100 patients with stage I-III TNBC to two chemotherapy regimens; Arm B of NeoSTOP was included in this correlative study as the chemotherapy regimen was identical to NeoPACT. RNA isolated from pretreatment tumor tissue was subjected to next-generation sequencing. The 14-gene IGG immune signature and TNBC-DX risk score were calculated *in silico* as previously described. Evaluation of stromal tumor-infiltrating lymphocytes (sTILs) was performed as previously described. Markers were tested for prediction of pCR. Logistic regression analysis was used to examine the effect of multiple variables. Event-free survival (EFS) curves were assessed by the Kaplan-Meier method and groups compared by the log-rank test, followed by Cox regression analysis. **Results:** In this analysis, 112 patients were treated with chemoimmunotherapy on NeoPACT (node-positive = 38%, pCR rate = 58%). In the NeoPACT trial, the 14-gene IGG immune signature (as a continuous variable) was significantly associated with improved pCR (odds ratio [OR]=1.105, 95% CI 1.019-1.197, P=0.015 for every 0.2 increment). The pCR rates in IGG-high (\geq median) and IGG-low (< median) groups were 71% and 44%, respectively (OR=3.152, 95% CI 1.420-6.996, P=0.005). In terms of EFS, the 14-gene IGG immune signature was not prognostic (hazard ratio [HR]=0.507, 95% CI 0.148-1.735, p=0.269). In contrast, TNBC-DX risk score was strongly associated with EFS (HR=5.684, 95% CI 1.226-26.356, P=0.012), even when adjusted for sTILs and pCR status (HR=8.415, 95% CI 1.054-67.169, P=0.044). Estimated 3-year EFS rates in TNBC-DX high and low risk groups (above and below median) were 77% and 89%, respectively (P=0.012). In 43 NeoSTOP patients treated with neoadjuvant chemotherapy only (node-positive = 33%, pCR rate = 53%), no association of IGG immune signature with pCR or TNBC-DX score with EFS was observed. Finally, we observed a moderate correlation between IGG immune signature and sTILs in both trial datasets combined (r=0.642, P< 0.001). **Conclusions:** High expression of the 14-gene IGG immune signature in baseline pretreatment tumor samples in early-stage TNBC is significantly associated with pCR following pembrolizumab-based neoadjuvant chemotherapy. The combination of this signature with tumor burden as assessed by TNBC-DX is prognostic for long-term outcomes. Availability of biomarkers that can predict both pathological response and survival with chemoimmunotherapy can optimize this therapy, and evaluation of this biomarker in larger studies is warranted.

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12/8/2022

7:00 AM - 8:15 AM

PD11-08

PD11-08 Trastuzumab deruxtecan (T-DXd) + durvalumab (D) as first-line (1L) treatment for unresectable locally advanced/metastatic hormone receptor-negative (HR-), HER2-low breast cancer: updated results from BEGONIA, a phase 1b/2 study

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Background: Patients with HR- advanced/metastatic breast cancer (a/mBC) with a low level of HER2 (immunohistochemistry [IHC] score 1+ or IHC 2+ and negative in situ hybridization [ISH]) have poor prognosis. Combining 1L chemotherapy with immune checkpoint inhibitors can modestly improve outcomes vs chemotherapy alone, but treatment benefit is largely seen in patients with PD-L1+ disease. BEGONIA (NCT03742102) is an ongoing 2-part, open-label platform study, evaluating safety and efficacy of D, an anti-PD-L1 antibody, combined with other novel therapies in 1L triple-negative a/mBC, including HR-, HER2-low disease. T-DXd is a trastuzumab-topoisomerase I inhibitor antibody-drug conjugate that improves survival in patients with previously treated HR-, HER2-low mBC (NCT03734029; Modi NEJM 2022). Here, we report updated results of the T-DXd + D combination from BEGONIA. Methods: Patients with unresectable HR-, HER2-low (per local testing, IHC 2+/ISH-, IHC 1+/ISH-, or IHC 1+/ISH untested) a/mBC were enrolled in the T-DXd + D arm. Patients eligible for 1L treatment, regardless of PD-L1 status, received intravenous T-DXd 5.4 mg/kg + D 1120 mg every 3 weeks until progression or unacceptable toxicity. PD-L1, assessed using the VENTANA PD-L1 (SP263) Assay, was defined as high if $\geq 5\%$ of the tumor area was populated by PD-L1-expressing tumor or immune cells. Primary endpoints were safety and tolerability. Secondary endpoints included investigator-assessed objective response rate (ORR; RECIST v1.1); progression-free survival [PFS]; and response duration. Patients included in the efficacy analysis had ≥ 2 on-treatment disease assessments, progressed, died, or withdrew from the study. Results: As of April 8, 2022, 56 patients received T-DXd + D (34 ongoing) and 46 were included in the efficacy analysis. Median (range) follow-up was 10.1 (0–22) months. Median age was 53.5 years, 71% had received prior treatment for early stage BC, and 64% had visceral metastases at baseline. Confirmed ORR was 26/46 (57%; 95% CI, 41–71) and unconfirmed ORR was 33/54 (61%; 95% CI, 47–74); 1/46 patients (2%) had complete and 25/46 (54%) had partial responses. Confirmed response occurred irrespective of PD-L1 expression (PD-L1 high ORR, 5/7 [71%]; PD-L1 low, 13/21 [62%]; PD-L1 missing, 8/18 [44%]). Median duration of response was not reached; however, 64% of patients remained in response at 12 month follow-up and 73% had an ongoing response at data cutoff. Median PFS was 12.6 months (95% CI, 8–not reached). Adverse events (AEs) were consistent with the agents' known safety, with treatment-related AEs occurring in 49 patients (88%), any Grade 3/4 AEs in 18 patients (32%), and any serious AEs in 10 patients (18%). The most common all-Grade AEs were nausea (41 [73%]), fatigue (26 [46%]), and vomiting (17 [30%]). Adjudicated treatment-related interstitial lung disease/pneumonitis occurred for 5 patients (9%), which were mostly Grade 1 or 2 and 1 case of Grade 5 associated with COVID pneumonia. Seven patients (13%) and 21 patients (38%) had T-DXd dose reduction and dose delay, respectively; 22 (39%) had D dose delay. Seven patients (13%) discontinued treatment due to AEs. Conclusions: For patients with HR-, HER2-low a/mBC, T-DXd in combination with D in the 1L setting shows manageable safety and promising efficacy including durable responses and an encouraging PFS. Although subgroups were small, responses were observed irrespective of PD-L1 expression. Analysis of additional translational data is ongoing. Funding: AstraZeneca/Daiichi Sankyo

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12/8/2022

7:00 AM - 8:15 AM

PD11-09

PD11-09 Datopotamab deruxtecan (Dato-DXd) + durvalumab (D) as first-line (1L) treatment for unresectable locally advanced/metastatic triple-negative breast cancer (a/mTNBC): updated results from BEGONIA, a phase 1b/2 study

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Background: Patients with a/mTNBC have limited treatment options and a poor prognosis (objective response rate [ORR] of 37%, median duration of response 6.5 months, median overall survival 15.5 months for 1L chemotherapy [Rugo, et al. Ann Oncol. 2021 LBA16]). Combining checkpoint inhibitors with 1L chemotherapy modestly improves outcomes but only in PD-L1–positive a/mTNBC, emphasizing a critical unmet need for patients with PD-L1–negative disease and for further improving outcomes in PD-L1–positive disease. BEGONIA (NCT03742102) is an ongoing 2-part, open-label platform study, evaluating safety and efficacy of D, an anti–PD-L1 antibody, combined with other novel therapies in 1L a/mTNBC, including Dato-DXd, an antibody-drug conjugate consisting of a humanized anti-TROP2 antibody covalently linked to a highly potent topoisomerase I inhibitor payload via a stable, tumor-selective, tetrapeptide-based cleavable linker. Early data from BEGONIA of D in combination with Dato-DXd showed promising responses. Here, we report updated results of Dato-DXd + D. Methods: Patients with unresectable a/mTNBC eligible for 1L treatment were enrolled, regardless of PD-L1 or TROP2 status, and received intravenous Dato-DXd 6 mg/kg + D 1120 mg every 3 weeks until progression or unacceptable toxicity. PD-L1, assessed using the VENTANA PD-L1 (SP263) Assay, was defined as high if $\geq 5\%$ of the tumor area was populated by PD-L1–expressing tumor or immune cells. Primary endpoints were safety and tolerability. Secondary endpoints included investigator-assessed ORR (RECIST v1.1) and duration of response. Patients included in the efficacy analysis had ≥ 2 on-treatment disease assessments, progressed, died, or withdrew from the study. Results: As of April 8, 2022, 47 patients received Dato-DXd + D (39 ongoing) and 33 of those were included in the efficacy analysis. Median (range) follow-up was 7.5 (0–11) months. Patient age was a median of 51 years, 57% received prior treatment for early stage TNBC, and 60% had visceral metastases at baseline. Confirmed ORR was 26/33 (79%; 95% CI, 61–91); 2/33 patients (6%) had a complete response and 24/33 (73%) had a partial response. Confirmed response was irrespective of PD-L1 expression (PD-L1 high ORR, 4/5 [80%]; PD-L1 low, 16/21 [76%]; PD-L1 missing, 6/7 [86%] patients). Median duration of response was not reached; 100% of patients with a complete or partial response remained in response at 6 month follow-up, and 96% had an ongoing response at data cutoff. Adverse events (AEs) were manageable and consistent with the known safety profiles of each agent, with treatment-related AEs occurring in 41 patients (87%), any Grade 3/4 AEs in 17 patients (36%), and any serious AEs in 7 patients (15%). The most common all-Grade AEs were gastrointestinal (nausea in 26 patients [55%] and stomatitis in 24 patients [51%]). A low rate of diarrhea was reported (6 patients [13%], all Grade 1 or 2); 4 patients had anemia and 1

had neutropenia. There were no cases of interstitial lung disease/pneumonitis or thrombocytopenia. Nine patients (19%) and 11 patients (23%) underwent Dato-DXd dose reduction and delay, respectively; 14 (30%) had D dose delay. Treatment was discontinued due to an AE for 3 patients (6%). There were no deaths due to treatment-related AEs. Conclusions: In this updated analysis with additional patients and longer follow-up, the combination of Dato-DXd + D in 1L a/mTNBC demonstrated a manageable safety profile and compelling high response rates with promising durability. Although subgroups were small, responses occurred irrespective of PD-L1 expression. Further investigation of this treatment combination is warranted. Analysis of translational data is ongoing. Funding: AstraZeneca/Daiichi Sankyo

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12/8/2022

7:00 AM - 8:15 AM

PD11-10

PD11-10 Efficacy, Safety, and Tolerability of KN046 (an anti-PD-L1/CTLA-4 Bispecific Antibody) in combination with Nab-paclitaxel in Metastatic Triple-negative Breast Cancer (mTNBC) : Final results of the Phase II trial

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Background: Despite recent FDA approval of immune checkpoint inhibitor pembrolizumab and drug-antibody conjugate in the treatment of mTNBC, the overall survival benefit of these patients remains modest. We conducted a phase 2 study to assess the efficacy and safety of

anti-PD-L1/CTLA-4 bispecific antibody KN046 in combination with nab-paclitaxel in mTNBC patients (pts) regardless of PD-L1 status. Preliminary results have been delivered in 2021 AACR[1], here we reported the final results of the progression-free survival (PFS) and overall survival (OS) analysis. Methods: This study enrolled pts with treatment-naïve locally advanced inoperable or metastatic TNBC. Eligible pts received nab-paclitaxel plus KN046 at two dose levels (DL1: KN046 3 mg/kg Q2W or DL2: KN046 5 mg/kg Q2W). Tumor response was evaluated Q8W per RECIST 1.1. The primary endpoint included objective response (ORR) and duration of response (DoR), secondary included disease control rate (DCR), clinical benefit rate (CBR), PFS, 1-year/2-year OS rate and safety/tolerability. Results: As of May 9, 2022 (cut-off date), 27 pts were enrolled into DL1 (n=16) and DL2 (n=11). Median patient age in the study was 50 years (range, 33-70 years). At baseline, 52% and 48% of patients had ECOG PS of 0 and 1, respectively. By the cut-off date, there are 1 pts under treatment and 16pts alive. The median study follow-up time was 26.3 months (95% CI, 20.7 - 29.8). Based on the intent-to-treatment (ITT) population, the confirmed ORR was 33.3% (95% CI, 16.5% - 54.0%), DCR was 88.9% (95% CI, 70.8% - 97.7%), and CBR was 48.1% (95% CI, 28.7% - 68.1%), which remained stable compared with last reported in 2021 [1]. The DoR was 11.9 (95% CI, 5.6 - NR) months. The median PFS was 7.3 (95% CI, 3.7 - 13.7) months. The median OS is immature, the preliminary result is 27.7 (95% CI, 14.8 - NR) months, and the 2-year OS rate was 60.1% (95%CI, 37.2% - 76.9%). Among the 11 pts with PD-L1 positive ($\geq 1\%$ IC), confirmed ORR was 45.5% (95%CI, 16.7% - 76.6%) and mPFS was 8.61 (95%CI, 1.6 - 13.8) months. Both PD-L1 positive and negative pts derived OS benefit from the combination treatment, with the 2-year OS rate of 57.14% (95%CI, 25.4% - 79.6%) and 62.5% (95%CI, 22.9% - 86.1%) respectively. Patients tolerated well to combination therapy in this trial. The most common reported treatment related adverse event (TRAEs) were ALT elevation (13 pts, 48%), AST elevation (12 pts, 44%), pyrexia (9 pts, 33%), neutropenia (8 pts, 30%), and anemia (7 pts, 26%). Grade ≥ 3 TRAEs ($\geq 10\%$) were neutropenia (7 pts, 26%), leukopenia (6 pts, 22%) and AST elevation (5 pts, 15%). 13 pts (48%) experienced immune related adverse events (irAEs), and only 3 irAEs (11%) were grade 3. The incidence of SAE was 33%, with no TRAE leading to death. Conclusions: The combination therapy of KN046 plus nab-paclitaxel has shown favorable clinical efficacy in mTNBC, especially in PD-L1 positive patients. By the cut-off date, the mOS is not mature and there is still more than half of pts alive, which demonstrated an encouraging 2-year OS rate. Pts in this trial tolerated well to the combination therapy and safety profile was manageable. Clinical trial information: NCT03872791 Reference 1. Cancer Res (2021) 81 (13_Supplement): 1660.

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7:00 AM - 8:15 AM

PD11-11

PD11-11 Results from ALICE – Atezolizumab Combined with Immunogenic Chemotherapy in Patients with Metastatic Triple Negative Breast Cancer, a Randomized Phase IIb Trial

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Background: Immune checkpoint inhibitors (CPI) have shown efficacy against metastatic triple negative breast cancer (mTNBC), but only for PD-L1 positive tumors. It is not known if so-called

immunogenic chemotherapies may yield clinical relevant synergies with CPI. We addressed these issues, by conducting a trial evaluating atezolizumab (anti-PD-L1) in combination with doxorubicin, which has been reported to provoke immunogenic cell death, and low-dose metronomic cyclophosphamide, which has been reported to counter immunosuppressive cells. The pegylated liposomal form of doxorubicin (PLD) was selected to avoid steroids and allow for long term therapy in responders. To our knowledge, this is the first randomized trial reporting on the concomitant addition of CPI to anticyclines in mTNBC. Methods: The trial enrolled patients with mTNBC and maximum one previous line of chemotherapy in the metastatic setting. Patients were randomized 2:3 into arm A (n=28), receiving chemotherapy alone, or arm B (n=40), receiving chemotherapy in combination with atezolizumab (840 mg every 2nd week). The chemotherapy consisted of PLD (20mg/m² every 2nd week) + oral cyclophosphamide (cyclo; 50mg/day, 2/4 weeks) in both arms. The per protocol (PP) population was defined as patients receiving > 3 doses of atezolizumab and >2 doses of PLD. The primary efficacy endpoint was progression-free survival (PFS) in the PP population. The protocol power analysis focused on durable response, as measured by 15 months PFS. Safety, a co-primary endpoint, was evaluated in all patients that started therapy (Full Analysis Set; FAS). Secondary endpoints included PFS in FAS, objective response rate (ORR), clinical benefit rate (CBR), durable response rate (>6 months; DRR), overall survival (OS) and biomarkers. PD-L1 status was determined retrospectively by the Ventana SP142 assay, as tumor-infiltrating immune cells with cut-off $\geq 1\%$. Efficacy data are given in the PP population unless stated otherwise. Hazard ratios (HR) are given with 95% confidence intervals (CI). Results: A total of 68 patients started therapy (FAS), of which 59 were in the PP population and 57% had not received previous chemotherapy in the metastatic setting. PFS was significantly improved in arm B compared to arm A in both the PP population (HR 0.57; CI 0.33-0.99; p=0.0477) and in the FAS (HR 0.56; CI 0.33-0.95; p=0.0326). Median PFS was 4.3 months in arm B versus 3.5 months in arm A. The progression-free proportion after 15 months was 14.7% (CI 6.4-30.1%) in arm B versus 0% in arm A. The ORR was 30.6%/21.7%, CBR was 52.8%/43.5% and DRR was 13.9%/4.3% in arm B/A. The PFS advantage was observed for both PD-L1+ (n=27; HR 0.58) and PD-L1- subjects (n=31; HR 0.66). All five patients without progression after 15 months belonged to arm B, and three out of these patients were PD-L1 negative. Serious adverse events occurred for 48% in arm B and 29% in arm A (FAS). The most common immune related adverse events of any grade in arm B/A were hypothyroidism (10.0%/7.1%), pneumonitis (10.0%/3.6%), hyperthyroidism (5.0%/7.1%) and rash (7.5%/3.6%). Further biomarker analyses and assessments of immunological changes during therapy are ongoing. Conclusions: The addition of atezolizumab to PLD and low-dose metronomic cyclophosphamide significantly improved PFS. A benefit was indicated also in patients with PD-L1 negative disease. The combination regimen was well tolerated with no new safety signals. Results from the ongoing analyses of consecutive tumor and blood samples will be important to assess the hypothesized immunological effects of the chemotherapy and to investigate biomarkers associated with the response to the combined treatment.

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7:00 AM - 8:15 AM

PD11-12

PD11-12 DORA: A Phase II, Multicenter, International, Non-Comparator Study of Olaparib (O) +/- Durvalumab (D) as a chemotherapy-free maintenance strategy in Platinum tReated Advanced Triple-Negative Breast Cancer (aTNBC)

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Introduction: A significant proportion of aTNBC patients carry homologous recombination defects associated with platinum sensitivity. Olaparib is an approved PARP inhibitor (PARPi) for germline BRCA (gBRCA) associated early and metastatic breast cancer as well as maintenance therapy in platinum-sensitive ovarian cancer irrespective of gBRCA status. PARPi enhances immune response via cGAS/STING activation and is synergistic with anti-PD-1 blockade in preclinical models without overlapping toxicities. Here, the efficacy of maintenance olaparib (O) +/- durvalumab (D) in aTNBC patients following clinical benefit from platinum chemotherapy is investigated (NCT03167619). Methods: Eligible pts had aTNBC with investigator-assessed clinical benefit (SD, PR, CR) after a minimum of 3 q3-weekly or 6 q1-weekly cycles of platinum-based chemotherapy in the 1st or 2nd line treatment setting. Patients were randomized 1:1 to receive O 300 mg BID daily or O 300mg BID daily + D 1.5g IV q4 wks. The study was a non-comparator trial; randomization aimed to reduce bias. Tumors were evaluated by RECIST1.1 at baseline and q8 wks. Known gBRCA carriers were limited to 10. The primary endpoint was progression-free survival (PFS). Secondary endpoints were disease control rate (DCR), clinical benefit rate (CBR), and overall survival (OS). Results: From 2/4/2019-12/24/2020, 45 pts were randomized (23 pts in O arm; 22 in O+D arm). 82.2%

received platinum as 1st line therapy and 82% received a platinum-doublet. As of data cutoff (6/30/2021), median follow-up of 9.8m (7.2-15.1), the median PFS was 3.95m (p= 0.0023; 95% CI 2.55-6.13) with O monotherapy. The median PFS was 6.1 mos (p= <.0001; 95% CI 3.68-10.11) in the O+D arm. CBR (CR, PR or SD ≥ 24 wks) was 39.1% (19.7%-61.5%) and 36.4% (17.2%-59.3%) in the O and O+D arms, respectively. DCR was 52.2% (30.6%, 73.2%) and 68.2% (45.1%, 86.1%) in the O and O + D arms, respectively. Currently, 7 pts (15.6%) remain on study treatment, only 2 have gBRCA alterations. No new safety signals were reported. Correlative analysis including germline/somatic BRCA, HRR genes, BRCA methylation, TMB and PDL-1 in association with clinical outcomes will be presented. Conclusions: A subset of non-gBRCA altered aTNBC pts who derived clinical benefit from platinum-based chemotherapy had a durable disease control with a chemotherapy-free maintenance strategy of olaparib +/- durvalumab.

Disclosure(s):

Tiffany A. Traina, MD: Astellas Pharma: Contracted Research (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Ayala Pharmaceuticals: Contracted Research (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Genentech: DSMB (Ongoing); Genentech/Roche: Contracted Research (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing)

Carey Anders, MD: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Athenex: Consulting Fees (e.g., advisory boards) (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Terminated, December 1, 2020); Elucida: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); G1-Therapeutics: Contracted Research (Ongoing); Genentech: Consulting Fees (e.g., advisory boards) (Ongoing); Immunomedics: Consulting Fees (e.g., advisory boards) (Ongoing); IPSEN: Consulting Fees (e.g., advisory boards) (Ongoing); Jones and Bartlett: Royalty (Ongoing); Lilly: Contracted Research (Ongoing); Merck: Contracted Research (Ongoing); Nektar: Contracted Research (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Pfizer: Contracted Research (Ongoing); Puma: Contracted Research (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Tesaro: Contracted Research (Ongoing); UpToDate: Royalty (Ongoing); ZION: Contracted Research (Ongoing)

Sung-Bae Kim, MD, PhD: Beigene: Consulting Fees (e.g., advisory boards) (Ongoing); CytomX Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Dae Hwa: Consulting Fees (e.g., advisory boards) (Ongoing), expert testimony (Ongoing); Daiichi-Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), expert testimony (Ongoing); DongKook Pharm Co: Research Grant paid to institution (Ongoing); Genopeak: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Inc: Consulting Fees (e.g., advisory boards) (Ongoing); ISU Abxis: Consulting Fees (e.g., advisory boards) (Ongoing), expert testimony (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), travel reimbursement and expert testimony (Ongoing); NeoGen TC: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Research funding to our institution, Honoraria for lecture (Ongoing); Pfizer: Honoraria for lecture (Ongoing); Roche-Genentech.: Consulting Fees (e.g., advisory boards) (Ongoing); Sanofi-Aventis: Research funding to our institution (Ongoing)

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12/8/2022

7:00 AM - 8:15 AM

Discussion 1 + Q&A: PD12-05, PD12-07, PD12-08 & PD12-09

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12/8/2022

7:00 AM - 8:15 AM

Discussion 2 + Q&A: PD12-01, PD12-06, PD12-04 & PD12-02

Presenting Author(s) and Co-Author(s):

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Disclosure(s):

Jennifer Ligibel, M.D.: No financial relationships to disclose

12/8/2022

7:00 AM - 8:15 AM

Poster Spotlight Discussion 12: Obesity and Breast Cancer

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12/8/2022

7:00 AM - 8:15 AM

PD12-01

PD12-01 Impact of obesity and post-diagnosis weight change on survival in women with breast cancer diagnosed at Smilow Cancer Hospital from 2013-2019

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Background: The association between obesity and breast cancer risk is well documented, but fewer studies have explored the impact of post diagnosis weight changes on survival especially in more contemporary contexts. The existing evidence has mainly focused on weight gain, been limited by small sample sizes and has evaluated prospective cohorts with restrictive eligibility criteria rather than population-based samples. Our study uniquely contributes to the literature by using a population-based approach and recent clinically measured weight data from the electronic health record (EHR) to explore the impact of weight change following a breast cancer diagnosis on survival. Methods: EHR weight measurements were extracted for women diagnosed with stages I-IV breast cancer at CT's Smilow Cancer Hospital and Care Network between 2013-2019 (N=6,934). During the follow-up period through April 26, 2020 (mean=3.2

years, standard deviation=1.8), there were 497 deaths. We used multivariable Cox regression models, adjusting for age at diagnosis, race/ethnicity, chemotherapy, radiation therapy, ER/PR subtype, to estimate the association between body mass index (BMI) at diagnosis and all-cause mortality from time since first post-diagnosis clinic visit (within 6 months of diagnosis). Percent weight change at 1-year post-diagnosis was categorized as a 5-level variable (weight stable – change within 5% of weight at diagnosis, moderate weight loss – 5% to < 10% change, large weight loss – ≥10% change, moderate weight gain – 5% to < 10% change, and large weight gain – ≥10% change) and evaluated in relation to all-cause mortality. A non-linear relationship between percent weight change at 1-year post-diagnosis and mortality was evaluated by comparing linear and cubic spline models. Results: Among these 6,934 breast cancer cases, the mean age was 61±13 years, BMI at diagnosis was 29±7 kg/m² and weight change from diagnosis to 1-year post-diagnosis was -0.47±5.4 kg. Being underweight (BMI< 18.5) or having class II obesity (BMI>35) at diagnosis were statistically significantly independently associated with higher all-cause mortality compared with normal BMI (Hazard Ratio [HR]=1.43, 95% Confidence Interval [CI]=1.11-1.85 and HR=3.32, 95% CI=1.90-5.80, respectively). At 1-year post-diagnosis, 64% of women remained weight stable since diagnosis, 12% gained moderate body weight, 5% had large weight gain, 12% lost moderate weight and 7% experienced a large weight loss. Compared with the weight stable group, there was a positive, non-significant association between moderate weight gain at 1-year post-diagnosis and overall mortality (HR=1.24, 95% CI=0.84-1.81). Greater than 10% weight loss at 1-year post-diagnosis was statistically significantly associated with higher mortality (HR=2.87, 95% CI=2.13-3.87). The test for curvature suggested a non-linear relationship between percent weight change at 1-year and mortality (p< 0.001). Conclusion: In this contemporary, population-based study of women with breast cancer from one large academic medical center, underweight and obesity at diagnosis were associated with poorer survival. Weight loss during the first-year post-diagnosis was also strongly associated with an increased risk of mortality. To further inform weight management strategies and future interventions for breast cancer survivors, we need to better understand changes in body composition in the post-diagnosis period.

Disclosure(s):

Leah Puklin, MPH: No financial relationships to disclose

Fangyong Li, MS, MPH: Yiviva Inc: Consulting Fees (e.g., advisory boards) (Ongoing)

Brenda Cartmel, PhD: No financial relationships to disclose

Tara B. Sanft, MD: No financial relationships to disclose

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Mona Sharifi, MD, MPH: No financial relationships to disclose

Melinda L. Irwin, PhD, MPH: No financial relationships to disclose

Leah Ferrucci, PhD, MPH: No financial relationships to disclose

12/8/2022

7:00 AM - 8:15 AM

PD12-02

PD12-02 Obesity is associated with poor breast cancer prognosis, particularly among women with low socioeconomic position

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Purpose: To examine the association between obesity and breast cancer outcomes and to describe socioeconomic position (SEP) in patients enrolled in the Malmö Diet and Cancer Study (MDCS) according to anthropometric measures. Patients and methods: The MDCS is a prospective cohort study that enrolled 17,035 female individuals in Malmö, Sweden from 1991 to 1996. The primary objective of the MDCS was to investigate associations between dietary patterns and cancer risk. Body mass index (BMI) and waist circumferences were measured upon enrollment, in the MDCS cohort. We identified all female MDCS participants with incident invasive breast cancer diagnosed between 1991 and 2014. The primary endpoint was breast cancer recurrence, defined as the time from breast cancer diagnosis until the earliest occurrence of invasive loco-regional recurrence or distant metastases. Follow-up time began at breast cancer diagnosis and continued until the first of breast cancer recurrence, death, emigration, or end of follow-up (June 8, 2020). BMI and waist circumference were categorized according to the World Health Organization guidelines as healthy weight (18.5-24.9 kg/m² or waist < 81 cm), overweight (25.0-29.9 kg/m² or waist 81-85 cm), and obese (≥ 30.0 kg/m² or waist > 85 cm). Consistent with the Swedish socioeconomic classification, we categorized labor status into two groups—manual labor and non-manual labor. We categorized socioeconomic position (SEP) as low if patients had unskilled manual labor with < 2 years post-high school education, low-middle if skilled manual labor with > 2 years of post-high school education, high-middle if assistant non-manual labor with < 3 years of post-high school education, and high if non-manual labor with > 3 years of post-high school education. We fit Cox regression models to compute crude and adjusted hazard ratios (HRs) with 95% confidence intervals (95% CI) of breast cancer recurrence as well as all-cause mortality according to BMI and waist circumference. To evaluate effect measure modification, we stratified the Cox models by labor

status, SEP, and smoking. Results: Among 1,099 breast cancer patients, 263 breast cancer recurrences were diagnosed over 12,810 person-years with a median follow-up of 11.1 years (interquartile range [IQR] was 6.6-16.2). The cohort consisted of 556 patients with healthy weight, 384 patients with overweight, and 159 patients with obesity. The median age at breast cancer diagnosis was 66.3 years (IQR: 61.2-72.8), and patients with obesity were older than patients with healthy weight (69.2 vs 64.9 years). In multivariable analyses, having obesity according to BMI was associated with increased rate of recurrence (HR= 1.44 [95% CI: 1.00-2.07]) and all-cause mortality (HR= 1.50 [95% CI: 1.13-1.98]) in comparison to having healthy weight. Similarly, having obesity according to waist circumference was associated with higher risk of recurrence (HR= 1.31 [95% CI: 0.98-1.77]) and all-cause mortality (HR= 1.72 [95% CI: 1.39-2.13]) in comparison to having healthy weight. When evaluating effect measure modification, we observed that obesity was associated with breast cancer recurrence in obese non-smoking women (HR= 1.66 [95% CI: 1.01-2.73]), in obese women with manual labor (HR= 2.45 [95% CI: 1.22-4.93]), and obese women with low SEP (HR= 2.55 [95% CI: 1.08-6.02]). We observed little evidence of an association between obesity and breast cancer recurrence among smokers (HR= 1.12 [95% CI: 0.43-2.92]), among patients with non-manual labor (HR= 0.94 [95% CI: 0.44-2.00]), or among patients with high SEP (HR= 1.47 [95% CI: 0.58-3.75]). Conclusion: Obesity defined by pre-diagnostic levels of BMI and waist circumference was associated with an increased risk of recurrence and all-cause mortality among breast cancer patients. The association between obesity and breast cancer recurrence seems dependent on patient characteristics such as labor status, socioeconomic position, and smoking.

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Deirdre Cronin-Fenton, BSc, PhD: No financial relationships to disclose

Susanne Dalton, MD, PhD: No financial relationships to disclose

Ann Rosendahl, MsC, PhD: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

PD12-04

PD12-04 Impact of Race and Body Mass Index on Breast Cancer Diagnoses

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Background

Breast cancer (BC) is the most common cancer among women and the second most common cause of cancer-related mortality among women. Much attention has been paid to factors that increase the risk of developing BC. Among these are weight, typically defined by body mass index (BMI), and race. Elevated BMI has not only been shown to increase the risk of BC in some patients but has also been associated with increased rates of hormone receptor (HR) positive BC, particularly among postmenopausal patients. In premenopausal patients, an inverse relationship has been established between obesity and BC. In fact, a 2008 meta-analysis of obesity and malignancy evaluated almost 8,000 cases of premenopausal BC and showed a BC risk reduction of 8% for every 5 kg/m². However, this study was not inclusive of African American (AA) patients. AA women are more likely to be obese than any other racial group in the US. They are also at higher risk of aggressive breast cancers, and at an earlier age. We sought to evaluate the relative risk of breast cancer diagnosis among obese vs nonobese patients of different races, as well as the rate of HR positivity in patients diagnosed with BC.

Methods

BMI, age, and self-declared race were collected from the electronic health record for all female patients presenting to our health system located in Louisiana and Mississippi between 2012 and 2022. This same data was collected for female patients who were diagnosed with BC in the same time period (n=9123), as well as HR positivity vs HR negativity. Patients less than 50 years old were considered premenopausal, and patients greater than 50 years old were considered postmenopausal. BMI greater than 30 was used to define obesity. The relative risk of BC was calculated for demographic groups according to premenopausal or postmenopausal status, White or Black/African American race, and BMI less than or greater than 30. The relative risk of HR positive BC was calculated among the same demographic groups.

Discussion

Data collected across the largest health system in Louisiana and Mississippi shows that a higher BMI is linked to an increased risk of BC, regardless of age or race. This was seen across both stratifications and was statistically significant except in postmenopausal AA women. This is contrary to what is frequently published in the literature that premenopausal obesity is protective against BC. Additionally, this data demonstrates that there is not a link between obesity and HR+ BC. This data did show that obesity in younger white patients may be protective against HR+ BC, which is aligned with prior research.

Conclusion

The association between obesity and BC incidence has been well-described in the literature, primarily in the postmenopausal setting. This large, retrospective analysis confirms that association, but also shows a strong association in premenopausal patients. Unlike other studies, this review did not show an association between obesity and HR positivity, and additionally did not show significant differences between AA patients and White patients. This provides needed insight into the inequities faced by AA women with BC. Further studies should be done to evaluate the association of socioeconomic status with BC subtypes.

Breast cancer cases (5/1/2012-5/1/2022) among women by BMI, age group, and race

Table 1: Breast cancer cases (5/1/2012-5/1/2022) among women, by BMI, age group, and race

Breast Cancer Age	Race	Number of cases (n=9123)	Standardized Risk Estimates		Risk Ratio (95% CL RR)
			BMI > 30	BMI ≤ 30	
< 50 years	African-American	672	0.00255	0.00140	1.83(1.57 - 2.13)*
< 50 years	White	978	0.00228	0.00147	1.55(1.36 - 1.76)*
≥ 50 years	African-American	2468	0.01164	0.01199	0.97(0.90 - 1.05)
≥ 50 years	White	5005	0.01114	0.00985	1.13(1.07 - 1.19)*

*statistically significantly difference

Hormone receptor positivity (5/1/2012-5/1/2022) among women with breast cancer by BMI, age group, and race

Table 2: Hormone Receptor positivity among women with breast cancer (5/1/2012-5/1/2022), by BMI, age group, and race

Hormone Receptor positive Age	Race	Number of cases (n=7196)	Standardized Risk Estimates		Risk Ratio (95% CL RR)
			BMI > 30	BMI ≤ 30	
< 50 years	African-American	443	0.63797	0.68953	0.93(0.83 - 1.03)
< 50 years	White	746	0.72682	0.78756	0.92(0.86 - 0.99)*
≥ 50 years	African-American	1774	0.72442	0.71182	1.02(0.97 - 1.07)
≥ 50 years	White	4233	0.85556	0.83827	1.02(1.00 - 1.05)

*statistically significantly difference

Disclosure(s):

Victoria Chung, DO: No financial relationships to disclose

Ruby Maini, MD: No financial relationships to disclose

Rabia Cattie, MD: OncoLive: Speaker and discussant (Ongoing)

Susan Olet, PhD: No financial relationships to disclose

Melanie Sheen, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing);

DaiichiSankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees

(e.g., advisory boards) (Ongoing)

12/8/2022

7:00 AM - 8:15 AM

PD12-05

PD12-05 Adipocyte directed vaccination to reduce the risk of breast cancer

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Background: Obesity is an important risk factor for breast cancer and women with metabolic syndrome may be at the highest risk. Infiltration of CD8 T-cells into fat is an early event in obesity. Type I cytokines secreted by CD8 T-cells upregulate costimulatory molecules on enlarged adipocytes. The adipocytes, now antigen presenting cells, further stimulate Type I T-cell activation. The resulting T-cells compete for glucose and fatty acids which leads to metabolic dysfunction in both the adipose tissue and the T-cells themselves. The T-cells are not able to maintain tumor immune surveillance and secretion of adipokines promotes malignant transformation. Immunologic memory prevents inflammation from resolving even if an individual becomes normal weight. Strategies to increase Type II (anti-inflammatory) T-cells in inflamed adipose could have clinical benefit. Methods: We developed a method of CD4 epitope identification that includes functional screening for Th1 or Th2 epitopes. We use a multi-algorithm approach to ensure responsiveness across diverse HLA alleles. We identified Th2 selective epitopes associated with high IL-10 secretion for 6 adipocyte associated antigens that become overexpressed in inflamed adipocytes (IGF-IR, HIF-1a, DUSP1, FABP4, PAI-1 and ATGL). The epitopes were highly homologous between mouse and man (median 100% (range-82-100%). When the epitopes were used to immunize mice, all antigens generated a significant IL-10 response compared to control ($p < 0.05$). We questioned whether our "adipocyte directed" vaccine (ADVac) could prevent the development of breast cancer in obese mice. Results: First, C57BL/6 mice were fed a high fat high sucrose (HFHS) diet or normal chow. When mice became obese, vaccination with ADVac or adjuvant alone (Alum) was initiated. Four weeks after the final vaccine, visceral adipose tissue showed significantly fewer CD8 T-cells in the obese mice immunized with ADVac as compared to the control, $p=0.0011$. The decrease in CD8 T-cells was specific for adipose tissue as no change was observed in matched spleen. There was a significant increase in T-regulatory cells in the adipose tissue of mice immunized with ADVac as compared to control, $p=0.031$. Two weeks after the final vaccine, a glucose tolerance test (GTT) and insulin tolerance (ITT) showed blood glucose concentrations were significantly lower at all time points for the ADVac-immunized obese mice as compared to the control obese mice ($p < 0.01$ for all). TgMMTV-neu develop aggressive breast cancer when made obese. Ten-week old TgMMTV-neu mice were fed a HFHS diet for 4 weeks, then randomized into 2 cohorts when obese, one cohort receiving the adjuvant only (Alum) and one receiving ADVac. Mice were sacrificed at 31 weeks of age when all controls had developed

tumor. ITT showed the glucose levels in the blood were significantly lower in the ADVac group as compared to control ($p < 0.0001$). Fewer CD8 T-cells were observed in mammary adipose tissue of AdVac immunized mice compared to control ($p = 0.001$). There was significantly less leptin detected in the serum of ADVac vaccinated mice compared to Alum immunized, $p = 0.024$. The median age of tumor development was 25 weeks in controls and 29 weeks in the immunized group ($p = 0.009$). Sixty percent (9/15) of the vaccinated mice were tumor free at study termination, whereas 100% of the control mice had developed tumor. Conclusions: ADVac represents the first vaccine to lower breast cancer risk in obesity. Vaccination corrected metabolic dysfunction as evidenced by reversal of diabetes and prevented breast cancer in the majority of obese ADVac immunized mice. Further studies are ongoing evaluating the systemic distribution of ADVac specific T-cells and the safety of the approach.

Disclosure(s):

Mary Disis, MD: Aston Sci: Contracted Research (Ongoing); Bavarian Nordisk: Contracted Research (Ongoing); Epthany: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Precigen: Contracted Research (Ongoing); University of Washington: Receipt of Intellectual Property Rights / Patent Holder (Ongoing); Veanna: Contracted Research (Ongoing)
Lauren Corulli, MS: Pfizer: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Terminated, May 12, 2022); Sage Therapeutics: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Terminated, November 20, 2020); ViewRay: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Terminated, August 10, 2020)

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Denise Cecil, PhD: No financial relationships to disclose

12/8/2022

7:00 AM - 8:15 AM

PD12-06

PD12-06 Longitudinal analysis of breast density change assessed by digital mammogram is associated with breast cancer

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Mammographic breast density is a well-established and strong risk factor for breast cancer. Widespread use of digital mammography has opened new potential for assessment of density changes over time. The underlying premise is that changes in breast tissue due to evolving structures that support cancer development should translate to quantifiable differences between the two breasts over time. To address this hypothesis, we draw on extensive digital mammography data and bring repeated measures over up to 10 years to evaluate the association between change in mammographic breast density and risk of breast cancer. Women were recruited from November 2008 to April 2012 through the mammography service at the Joanne Knight Breast Health Center at Washington University in St Louis. Baseline questionnaire risk factors and screening mammograms were collected from 12,153 women. Of these, 1,672 were excluded for prior history of any cancer (except non-melanoma skin) or diagnosis of breast cancer within 6 months of registration for the study, for a total of 10,481 women. Follow-up is through linking to electronic health records, tumor registry and death register. Routine screening mammograms are collected every 1 to 2 years. Follow-up of cohort participants through December 2020 was: 78% seen in 2019 or 2020; a further 4.4% seen most recently in 2018 and a further 2.4% in 2017 giving over 80% active follow-up for women seen within the last 36 months. The median number of mammograms is 5 (min = 1, max = 10; sd = 2.43). The average person-years of follow-up through most recent contact is 9.2 person-years. We have excluded women who are diagnosed within the first 6 month of baseline mammogram date in all analyses, leaving 259 cases and 695 controls with a total number of 8,966 craniocaudal (CC) view mammograms for analysis. For these 954 women, the mean number of years between mammograms is 1.3 (10th percentile: 1.0, 90th percentile: 2.0). For the cases, the mean number of years from last mammogram date to diagnosis date was 2.0 years (10th percentile: 1.0, 90th percentile: 3.9) after excluding mammograms that are within 6 months of diagnosis. The percentage volumetric density (MD) within each digital CC-view mammogram is estimated with an automated pixel-thresholding algorithm ADAPT implemented within the Division of Public Health at WashU. The skin around the breast is automatically removed using a boundary detection algorithm prior to estimating the dense areas. The percent density (MD) is then estimated using the dense area divided by the total breast area which normalizes the difference in breast size across women. The correlation between average MD generated from our automated algorithm with Volpara is 0.82. Initial analyses use linear mixed effects with average density between breasts (fitted with R package lmer). We performed test of assumptions for all linear mixed effects models, including the normality of residuals, linearity, and homogeneity of residual variance. Assessing the averaging density between 2 breasts

controlling for age, BMI, histology confirmed benign breast disease, family history, parity, and alcohol, MD decreases significantly over follow-up (time in years) ($P < 0.01$). At baseline, postmenopausal women had lower density than premenopausal women after controlling for the same set of risk factors. The average MD over all time points was significantly different for the case vs. control women ($P < 0.01$). For overweight women, the trajectory of MD over time was significantly different for the case vs. control women ($P < 0.01$). Drawing on over 10 years of follow-up we observe, for the first time, a dynamic effect for breast density such that divergence in density over time is related to risk for breast cancer.

Disclosure(s):

Graham A. Colditz, n/a: No financial relationships to disclose

Shu Jiang, n/a: No financial relationships to disclose

12/8/2022

7:00 AM - 8:15 AM

PD12-07

PD12-07 The effect of BMI on the pathological response after neoadjuvant systemic therapy in breast cancer patients: a nationwide retrospective study

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Background: Neoadjuvant systemic therapy is increasingly applied in breast cancer patients to improve surgical and oncological outcomes. There is only limited data from clinical practice on the relevance of body mass index (BMI) on the pathologic complete response (pCR) rate following neoadjuvant systemic treatment (NST). We aimed to retrospectively analyze the impact of BMI on pCR after NST for Dutch breast cancer patients.

Methods: Patients diagnosed with invasive breast cancer between 2019 and 2021 who were treated with NST followed by a surgical procedure, were selected from the Netherlands Cancer Registry (NCR). Patients were divided into three groups based on BMI: patients with underweight/normal weight (BMI < 25 kg/m²), patients with overweight (BMI 25-29.9 kg/m²) and patients with obesity (BMI > 30 kg/m²). Patients with unknown BMI, ER/PR/HER2 or pCR status were excluded for analysis. The primary outcome was pCR after NST. The association between BMI and pCR was estimated using logistic regression models with the expression of odds ratios (ORs).

Results: After applying in- and exclusion criteria, 4430 patients were included for analysis, stratified into four molecular breast cancer subtypes; HR+/HER2- (n=2256), HR+/HER2+ (n=722), HR-/HER2+ (n=405) and HR-/HER2- (n=1047). The predictors age, differentiation grade, histological type, clinical tumor (cT) and nodal (cN) stage and molecular breast cancer subtype were found significant for achieving pCR after NST. Multivariable regression analysis identified differentiation grade, cT and cN stage and molecular subtype as independent

predictors for pCR after NST. There was no association between pCR and (continuous or categorical) BMI. Above mentioned analyses performed by stratification according to molecular breast cancer subtype, also showed no statistically meaningful association between BMI and pCR.

Conclusion: In this nationwide retrospective cohort study, evaluating 3340 patients with invasive breast cancer, we found no evidence of BMI being a predictive factor for achieving pCR following NST in neither the whole cohort, nor stratified according to molecular breast cancer subtype.

Table 1. Multivariable regression analysis of the total cohort

	Odds ratio	95% CI	p-value
Age	0.987	0.980 - 0.993	0.000
Differentiation grade			
I	Ref		0.000
II	1.967	1.128 - 3.431	0.017
III	3.730	2.133 - 6.522	0.000
Unknown	7.230	3.807 - 13.706	0.000
Histology			
Ductal	Ref		0.000
Lobular	0.312	0.182 - 0.534	0.000
Other	0.652	0.474 - 0.897	0.009
Clinical T stadium			
1	Ref		0.001
2	0.926	0.759 - 1.131	0.453
3	0.586	0.430 - 0.799	0.001
4	0.556	0.358 - 0.863	0.009
Clinical N stadium			
1	Ref		0.059
2	0.812	0.673 - 0.981	0.031
3	0.665	0.408 - 1.084	0.102
4	1.029	0.773 - 1.369	0.845
Molecular subtype			
HR+/Her2-	Ref		0.000
HR+/Her2+	7.278	5.696 - 9.300	0.000
HR-/Her2+	41.443	30.582 - 56.161	0.000
HR-/Her2-	7.536	5.939 - 9.562	0.000
Constant	0.078		0.000

Disclosure(s):

Britt Jansen, MD: No financial relationships to disclose

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Marissa van Maaren, PhD: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

PD12-08

PD12-08 Randomized trial of exercise and nutrition on pathological complete response among women with breast cancer receiving neoadjuvant chemotherapy: the Lifestyle, Exercise and Nutrition Early after Diagnosis (LEANer) Study

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Background: Neoadjuvant chemotherapy is available to women with locally advanced breast cancer where chemotherapy is given prior to surgery. By examining resected tissue following neoadjuvant chemotherapy pathological complete response (pCR) can be determined. pCR is a favorable prognostic factor associated with longer survival compared to residual disease after neoadjuvant chemotherapy. Physical activity and diet may improve some side effects during treatment, but less is known about their effect on chemotherapy completion and more specifically on pCR in the neoadjuvant setting. Utilizing data from a randomized trial of diet and physical activity with a primary endpoint of chemotherapy completion in women with newly diagnosed breast cancer initiating chemotherapy, we evaluated the effect of a lifestyle intervention on pCR among the subset of women in the trial who received neoadjuvant chemotherapy. Methods: The Lifestyle, Exercise and Nutrition Early after Diagnosis (LEANer) Study enrolled 173 women with Stage I-III breast cancer who were randomized to usual care (n = 86) or a yearlong, 16-session, in-person or telephone-administered diet and physical activity intervention (n = 87) delivered by registered dietitians. Among study participants, 73 women received neoadjuvant chemotherapy and of these, 72 (98.6%) had complete follow-up pCR data (intervention = 40; usual care = 32). pCR, dates, doses and reason for dose-adjustments/delays of chemotherapy were abstracted from electronic medical records and confirmed with treating oncologists. A Chi-square test was used to examine the effect of the intervention versus usual care on pCR. Results: The 72 women receiving neoadjuvant chemotherapy with complete follow-up pCR data in LEANer were 49.4±11.6 years old, had a body mass index of 30.0±6.7 kg/m², and 37.0% and 49.3% had stage I or II breast cancer, respectively. Just over half (52.1%) of women had ER/PR positive cancers and 32.9% of tumors were HER2 positive, with no statistically significant differences in tumor type by study arm. 92.7% of the women randomized to intervention adhered to all of the counseling sessions during their neoadjuvant chemotherapy and had statistically significant improvements in mean physical activity (161 minute increase versus 40 minute increase, p-value = < 0.001) and fiber intake (0.21 gram/day increase versus -5.17 g/day decrease, p-value = 0.020), as well as median fruit and vegetable intake (0.6 serving/day increase versus -0.5 serving/day decrease, p-value = 0.041) compared to usual care. There was a benefit of the intervention on pCR compared to usual care (52.5% with pCR in the intervention arm versus 28.1% with pCR in the usual care arm, p-value = 0.037). The intervention effect on pCR did not appear to be impacted

by chemotherapy completion (relative dose intensity of 92% in intervention versus 90% in usual care) or chemotherapy dose delays as these were similar in the two study arms. In mediation analyses, results suggested that the changes in physical activity mediated, at least partially, the intervention effect on pCR. Conclusions: A primarily telephone-based diet and physical activity intervention led to improved pCR compared to usual care among the subset of women with breast cancer in the LEANer Study who received neoadjuvant chemotherapy. As pCR is an important prognostic factor for breast cancer, additional lifestyle interventions focusing on the neoadjuvant treatment setting with pCR as the primary outcome are necessary to confirm the potential benefits of lifestyle changes on pCR.

Disclosure(s):

Leah Ferrucci, PhD, MPH: No financial relationships to disclose

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12/8/2022

7:00 AM - 8:15 AM

PD12-09

PD12-09 Serum Advanced Glycation End-Products are Associated with Breast Cancer Prognosis

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Background: Tumor characteristics such as grade, stage and receptor status are associated with breast cancer (BC) prognosis. Less is known about modifiable factors and BC prognosis. Advanced glycation end-products (AGEs) are reactive metabolites produced as a by-product of sugar metabolism, generated in conditions of increased oxidative stress. AGEs irreversibly accumulate in our tissues over time with pathogenic effects on genetic fidelity, protein function, cell signaling pathways, and chronic inflammatory diseases. The total body AGE pool is composed of endogenous AGEs and exogenous AGEs (consumed mainly through processed foods and those cooked at high temperatures). Serum AGE (sAGE) levels, a reflection of total body AGE, are higher in people with poor diet quality, lower levels of physical activity, and in women with BC compared to healthy controls. AGEs promote growth, migration and invasion in BC cell lines and activate prognostic inflammatory mediators such as interleukin-6 and C-reactive protein. Dietary AGEs have been associated with increased BC risk and increased mortality after BC diagnosis whereas lifestyle interventions can lower dietary and sAGE levels. The impact of sAGE levels, a better estimate of total body AGE than dietary AGE, on BC prognosis has not been previously evaluated. Methods: The Women's Healthy Eating and Living (WHEL) study randomized 3088 BC patients stage I-III who completed their primary therapy to a high-vegetable, low-fat diet or control and followed for a median of 7.3 years. Main

outcomes were invasive BC events (recurrence or new primary N=518), death due to BC (N=262) and deaths from any cause (N=315). sAGE was measured as the AGE metabolite carboxymethyllysine (ug/ml) from WHEL fasting blood specimens at study entry. sAGE was logged and corrected for plate batch effect via linear regression and analyzed in continuous scale and in quintiles. The Kaplan-Meier method and Cox regression model were performed for risk impact of sAGE on overall survival (OS), recurrence free survival (RFS), breast cancer specific survival (BCSS) and distant metastasis free survival (DMFS). We additionally adjusted in Cox models for potential confounding variables (age, race, BMI, smoking, alcohol use, physical activity, tumor characteristics). Results: 2564 participants had sAGE available. After excluding samples for excessive variabilities, 2315 samples were analyzed. Raw corrected sAGE ranged from 0.0-48.15 ug/ml (median 7.39); logged and corrected range -5.04-1.67. sAGE was positively associated with BMI ($p < .0001$, r_s 0.10) and negatively associated with physical activity ($p < .001$, r_s -.006). sAGE was not significantly associated with tumor stage, grade, receptor status, or race or menopausal status. Comparing the highest quintile (logged and corrected range=0.33~1.67) to the lowest quintile (range=-5.04~-0.30), sAGE was significantly associated with all survival outcomes (Table 1). As a continuous variable, AGE was associated with worse OS (HR 1.38, $P = .031$, β .32) and RFS (HR 1.29, $P = .028$, β .25) with a trend towards worse DMFS (HR 1.28, $P = .067$, β .25) and BCSS (HR 1.36, $P = .06$, β .31). Conclusions: Higher sAGEs are associated with worse survival outcomes in BC and may represent a novel, lifestyle-linked, modifiable prognostic biomarker in BC. Interventions aimed at lowering sAGE levels should be tested for their impact on known prognostic biomarkers as well as clinical outcomes. Individualized cancer-specific lifestyle recommendations are a crucial but currently lacking component of personalized cancer medicine.

Disclosure(s):

Lindsay L. Peterson, MD, MSCR: No financial relationships to disclose

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Jingqin Luo, PhD: No financial relationships to disclose

Graham A. Colditz, n/a: No financial relationships to disclose

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12/8/2022

8:30 AM - 8:45 AM

GS3-01

GS3-01 EMERALD phase 3 trial of elacestrant versus standard of care endocrine therapy in patients with ER+/HER2- metastatic breast cancer: Updated results by duration of prior CDK4/6i in metastatic setting

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Background: In patients (pts) with ER+/HER2- metastatic breast cancer (MBC) following progression on prior endocrine and CDK4/6i therapy, the EMERALD trial demonstrated significantly prolonged progression-free survival (PFS) and a manageable safety profile for elacestrant versus standard of care endocrine therapy (SoC). Benefit was observed in all pts and in pts with ESR1 mutant MBC (ESR1-mut). EMERALD is the only oral SERD monotherapy

pivotal trial where all pts were pretreated with CDK4/6 inhibitor (CDK 4/6i). Here, we examine the impact of duration of prior CDK4/6i on PFS.

Methods: EMERALD (NCT03778931) is a randomized, open-label, phase 3 trial that enrolled pts with ER+/HER2- MBC who previously had 1-2 lines of endocrine therapy, mandatory CDK4/6i, and ≤ 1 chemotherapy; prior treatment with fulvestrant was allowed. Patients were randomized 1:1 to elacestrant (400 mg orally daily) or SoC (investigator's choice of aromatase inhibitor or fulvestrant). If randomized to the control arm, patients who received prior fulvestrant were to receive an aromatase inhibitor, and vice versa. If two CDK4/6i were used in the metastatic setting (n=40), the cumulative duration was calculated.

Results: A total of 478 pts were randomized (228 with ESR1-mut) between Feb 2019 – Oct 2020 (n=239, elacestrant; n=239, SoC). Overall survival was not yet mature, as of September 2nd 2022. Updated PFS results show statistically significant results in favor of elacestrant, both in all pts and in pts with ESR1-mut. The duration of prior CDK4/6i in the metastatic setting was positively associated with PFS, the longer the duration of prior CDK4/6i in the metastatic setting (n=465), the longer the PFS on elacestrant versus SoC (Table 1).

Table 1: PFS estimates in the elacestrant and SoC arms based on different cut-off points for the duration of prior CDK4/6i.

Updated safety data were consistent with previously reported results. Most of the adverse events (AEs), including nausea, were grade 1 and 2, and only 3.4% and 0.9% of the pts discontinued trial therapy because of an AE on elacestrant and SoC, respectively. A low percentage of pts received an antiemetic; 8.0%, 3.7%, and 10.3%, on elacestrant, fulvestrant, and AI, respectively. No hematological safety signal was observed and none of the patients in either of the two treatment arms had sinus bradycardia.

Conclusions: EMERALD is the first phase 3 trial to demonstrate a significant PFS improvement versus SoC in all pts and in the subgroup with ESR1 mutations in pts with ER-positive/HER2-negative MBC with 1-2 prior lines of endocrine treatment \pm one line of chemotherapy. Elacestrant demonstrated longer PFS versus SoC that was positively associated with the duration of prior treatment with CDK4/6i, which was more pronounced in pts with ESR1-mut MBC. In this 2nd and 3rd line setting, elacestrant was well tolerated with significantly longer PFS versus SoC, highlighting its potential role as a therapeutic option for pts with ER+/HER2-MBC.

Table 1: PFS estimates in the elacestrant and SoC arms based on different cut-off points for the duration of prior CDK4/6i.

Duration on CDK4/6i in the metastatic setting	≥6.0 months		≥12.0 months		≥18 months	
	Elacestrant (n=202)	SoC (n=205)	Elacestrant (n=150)	SoC (n=160)	Elacestrant (n=98)	SoC (n=119)
Median PFS (months)	2.8	1.9	3.8	1.9	5.5	3.3
PFS rate						
6-mo	34.4%	19.9%	41.6%	21.7%	44.7%	25.1%
12-mo	21.0%	6.4%	25.6%	7.4%	26.7%	8.2%
18-mo	16.2%	3.2%	19.3%	3.7%	21.0%	4.1%
Hazard ratio	0.69 (0.54-0.88)		0.61 (0.45-0.83)		0.70 (0.48-1.020)	
ESR1-mut	(n=103)	(n=102)	(n=78)	(n=81)	(n=55)	(n=56)
Median PFS (months)	4.1	1.9	8.6	1.9	8.6	2.1
PFS rate						
6-mo	42.4%	19.2%	55.8%	22.7%	58.6%	27.1%
12-mo	26.0%	6.4%	35.8%	8.4%	35.8%	7.7%
18-mo	20.7%	---	28.5%	---	30.7%	---
Hazard ratio	0.52 (0.36-0.74)		0.41 (0.26-0.63)		0.47 (0.20-0.79)	

Disclosure(s):

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12/8/2022

8:30 AM - 11:00 AM

General Session 3

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12/8/2022

8:45 AM - 9:00 AM

GS3-02

GS3-02 Camizestrant, a next generation oral SERD vs fulvestrant in post-menopausal women with advanced ER-positive HER2-negative breast cancer: Results of the randomized, multi-dose Phase 2 SERENA-2 trial

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12/8/2022

9:00 AM - 9:15 AM

GS3-03

GS3-03 ARV-471, a PROTAC® estrogen receptor (ER) degrader in advanced ER-positive/human epidermal growth factor receptor 2 (HER2)-negative breast cancer: phase 2 expansion (VERITAC) of a phase 1/2 study

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Background: ARV-471 is a selective, orally administered PROteolysis TArgeting Chimera (PROTAC®) protein degrader that targets wild-type and mutant ER. ARV-471 is being evaluated in patients with ER+/HER2- locally advanced or metastatic breast cancer in a first-in-human phase 1/2 study (NCT04072952). In the phase 1 dose escalation, ARV-471 monotherapy (dose range: 30–700 mg total daily dose) showed a manageable safety profile in patients who had previously received endocrine therapy and a cyclin-dependent kinase (CDK) 4/6 inhibitor. The clinical benefit rate (CBR; rate of confirmed complete or partial response or stable disease ≥ 24 weeks) was 40% (95% CI: 26–56) in 47 evaluable patients. The phase 2 expansion portion of the study (VERITAC) evaluated 2 doses of ARV-471. Methods: In VERITAC, ARV-471 monotherapy was administered at doses of 200 mg once daily (QD) or 500 mg QD to patients with ER+/HER2- locally advanced/metastatic breast cancer who had received ≥ 1 prior endocrine therapy for ≥ 6 months, ≥ 1 CDK4/6 inhibitor, and ≤ 1 chemotherapy regimen. The primary endpoint of CBR was evaluated in patients enrolled ≥ 24 weeks prior to the data cutoff. Results: As of June 6, 2022, 71 patients received ARV-471 (200 mg QD [n=35]; 500 mg QD [n=36]) in VERITAC. Across all treated patients, 69 (97.2%) were female and median age was 60 y (range: 41–86). Patients had received a median of 4 prior regimens in all settings (range: 1–10); 100% had prior CDK4/6 inhibitors, 78.9% had prior fulvestrant, and 73.2% had prior chemotherapy. ARV-471 was well tolerated at both doses, with most treatment-related adverse events (TRAEs) grade 1/2; the most common TRAEs were fatigue and nausea (Table). In all, 3 patients (1 in the 200 mg QD cohort and 2 in the 500 mg QD cohort) discontinued ARV-471 due to treatment-emergent adverse events (TEAEs); 3 patients had ARV-471 dose reductions due to TEAEs (all from 500 mg QD to 400 mg QD). CBR was 37.1% (95% CI: 21–55) in 35 evaluable patients treated at 200 mg QD and 38.9% (95% CI: 23–57) in 36 evaluable patients treated at 500 mg QD. CBR in evaluable patients with mutant ESR1 in the 200 mg QD (n=19) and 500 mg QD (n=22) cohorts was 47.4% (95% CI: 24–71) and 54.5% (95% CI: 32–76), respectively. Conclusions: In the phase 2 VERITAC expansion cohorts of patients with ER+/HER2- locally advanced/metastatic breast cancer and prior CDK4/6 inhibitor treatment, ARV-471 monotherapy showed evidence of clinical activity based on CBR, which was further enhanced in the subgroup with ESR1 mutations. The manageable AE profile observed in the phase 1 portion of the study was maintained during cohort expansion at doses of 200 mg QD and 500 mg QD. Additional analyses are ongoing. Table. TRAEs reported in $\geq 10\%$ of patients overall ^aNo grade 3/4 TRAE occurred in >1 patient.

AST=aspartate aminotransferase

Disclosure(s):

Sara Hurvitz, MD, FACP: Ambrx: Contracted Research (Ongoing); Amgen: Contracted Research (Ongoing); Arvinas: Contracted Research (Ongoing); Astra Zeneca: Contracted Research (Ongoing); Bayer: Contracted Research (Ongoing); Cytomx: Contracted Research

(Ongoing); Daiichi-Sankyo: Contracted Research (Ongoing); Dignitana: Contracted Research (Ongoing); Eli Lilly: Contracted Research (Ongoing); Genentech/Roche: Contracted Research (Ongoing); Gilead: Contracted Research (Ongoing); GSK: Contracted Research (Ongoing); Ideal Implant: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Immunomedics: Contracted Research (Ongoing); MacroGenics: Contracted Research (Ongoing); Novartis: Contracted Research (Ongoing); OBI Pharma: Contracted Research (Ongoing); Orinove: Contracted Research (Ongoing); Pfizer: Contracted Research (Ongoing); Phoenix Molecular Designs, Ltd.: Contracted Research (Ongoing); Pieris: Contracted Research (Ongoing); PUMA: Contracted Research (Ongoing); Radius: Contracted Research (Ongoing); Sanofi: Contracted Research (Ongoing); Seattle Genetics/Seagen: Contracted Research (Ongoing); Zymeworks: Contracted Research (Ongoing)

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12/8/2022

9:15 AM - 9:30 AM

GS3-04

GS3-04 Capivasertib and fulvestrant for patients with aromatase inhibitor-resistant hormone receptor-positive/human epidermal growth factor receptor 2-negative advanced breast cancer: results from the Phase III CAPItello-291 trial

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Background: AKT pathway activation has been implicated in the development of endocrine therapy resistance in hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) advanced breast cancer (ABC). In the Phase II, placebo (PBO)-controlled FAKTION trial, the addition of the pan-AKT inhibitor capivasertib to fulvestrant significantly improved progression-free survival (PFS) and overall survival in postmenopausal women with aromatase inhibitor (AI)-resistant HR+/HER2- ABC. The Phase III, randomized, double-blind, PBO-controlled CAPItello-291 trial (NCT04305496) investigated the efficacy and safety of capivasertib + fulvestrant in patients with AI-resistant HR+/HER2- ABC. Methods: Eligible pre/peri or postmenopausal women or men with HR+/HER2- ABC that had recurred or progressed on or after AI therapy with or without a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor were randomized 1:1 to receive fulvestrant (per standard dosing schedule) with either PBO or capivasertib (400 mg twice daily; 4 days on, 3 days off). Randomization was stratified by the presence of liver metastases, prior use of CDK4/6 inhibitors, and geographic location. AKT pathway alteration status (at least one qualifying PIK3CA, AKT1, or PTEN alteration) was determined using next-generation sequencing in tumor tissue. The dual primary endpoint was investigator-assessed PFS in the overall population and in patients with AKT pathway-altered tumors. **Results:** A total of 708 patients were randomized: 355 to capivasertib + fulvestrant and 353 to PBO + fulvestrant. Overall, 41% of patients had AKT pathway-altered tumors (48% [n=289/602] of patients with tumor sequencing results), 22% were pre/perimenopausal and 77% postmenopausal, with 1% male. Prior therapy for advanced disease included: 87% of patients with ≥1 line of prior treatment, 69% with a prior CDK4/6 inhibitor, and 18% with prior chemotherapy. Demographic and baseline characteristics were broadly balanced between the overall and altered populations and by treatment groups. At primary analysis (data cut-off Aug 15, 2022), 551 and 236 PFS events had occurred in the overall and pathway-altered

populations, respectively. Overall, the median PFS was 7.2 months with capivasertib + fulvestrant and 3.6 months with PBO + fulvestrant (hazard ratio [HR] 0.60; 95% confidence interval [CI] 0.51–0.71; $p < 0.001$). In patients with AKT pathway-altered tumors, median PFS was 7.3 months with capivasertib + fulvestrant and 3.1 months with PBO + fulvestrant (HR 0.50; 95% CI 0.38–0.65; $p < 0.001$). The objective response rate in patients with measurable disease was 22.9% for capivasertib + fulvestrant vs 12.2% for PBO + fulvestrant overall and 28.8% vs 9.7% in the AKT pathway-altered population. The most frequent all-grade adverse events (AEs) with capivasertib + fulvestrant were diarrhea (72.4% vs 20.0% PBO + fulvestrant arm), rash (group term of rash, rash macular, rash maculo-papular, rash papular, rash pruritic; 38.0% vs 7.1%) and nausea (34.6% vs 15.4%). The most frequently reported grade ≥ 3 AEs were rash (group term; 12.1% vs 0.3%), diarrhea (9.3% vs 0.3%), and hyperglycemia (2.3% vs 0.3%); grade ≥ 3 stomatitis was 2.0% vs 0%. AEs leading to discontinuation of capivasertib/placebo were reported in 13.0% and 2.3% of patients, respectively. **Conclusions:** Capivasertib + fulvestrant significantly improved PFS compared to fulvestrant alone in the overall population, and in patients with AKT pathway-altered tumors, and may become a future treatment option in this setting. The safety profile of capivasertib + fulvestrant was generally manageable and consistent with prior data. **Funding:** CAPItello-291 is sponsored by AstraZeneca. **Editorial acknowledgment:** AstraZeneca-funded medical writing support was provided by Suzanne Patel, Ph.D., from BOLDSCIENCE Inc. Capivasertib was discovered by AstraZeneca subsequent to a collaboration with Astex Therapeutics (and its collaboration with the Institute of Cancer Research and Cancer Research Technology Limited).

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12/8/2022

9:30 AM - 9:45 AM

GS3-05

GS3-05 Discussant for GS3-01, GS3-02, GS3-03 and GS3-04

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12/8/2022

9:45 AM - 10:00 AM

GS3-06

GS3-06 Palbociclib After CDK4/6i and Endocrine Therapy (PACE): A Randomized Phase II Study of Fulvestrant, Palbociclib, and Avelumab for Endocrine Pre-treated ER+/HER2-Metastatic Breast Cancer

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Background CDK4/6 inhibitors (CDK4/6i) in combination with endocrine therapy (ET) have a well-established role in the management of hormone receptor-positive (HR+)/HER2- metastatic

breast cancer (MBC). The benefit of continuing CDK4/6i beyond progression in combination with a different ET has not been confirmed. Preclinical data suggest synergy between CDK4/6i and PD-L1 inhibition. The PACE trial prospectively evaluates whether continuation of the CDK4/6i palbociclib beyond progression on prior CDK4/6i and aromatase inhibitor (AI), with a change in ET to fulvestrant, improves outcomes beyond change to fulvestrant alone, as well as explores the activity of the palbociclib, fulvestrant, and avelumab triplet. Methods PACE is a multicenter randomized open-label investigator-initiated phase II trial, open at 11 U.S. sites. Eligible patients (pts) had HR+/HER2- evaluable MBC with prior progression on AI and any CDK4/6i after > 6 months (mo) of therapy in the MBC setting, or during/within 12 mo in the adjuvant setting, with no more than 1 prior line of chemotherapy for MBC. Pts were randomized 1:2:1 to fulvestrant alone (F); fulvestrant and palbociclib (F+P); or fulvestrant, palbociclib, avelumab (F+P+A), with tumor assessments every 8 weeks. Blood for circulating tumor DNA (ctDNA) analysis was collected at baseline, at times of tumor assessments, and at progression. The primary objective was to evaluate progression-free survival (PFS) with F+P vs F; secondary objectives included PFS with F+P+A vs F, objective response rate (ORR) in all arms, and safety. A sample size of 220 patients was planned to provide 80% power to detect an improvement in PFS with HR 0.6154 with F+P vs F (6.5 vs 4 mo; $\alpha(1)=0.05$). Results A total of 220 pts were randomized from 9/2017-2/2022 (F: n=55, F+P: n=111, F+P+A: n=54); median age 57 years (range 25-83), 85% non-Hispanic (7.7% non-Hispanic black), 8.6% Hispanic, 6.4% unknown. 40% had de novo MBC, 60% had visceral disease, and 14% bone-only disease. 16% had 1 prior line of chemotherapy for MBC, 90% had received prior palbociclib, 4.5% ribociclib, 4.1% abemaciclib, 1.4% palbociclib and ribociclib. Pts entered the trial after a median 19 mo of prior CDK4/6i plus AI (interquartile range 12-31 mo). A total of 10 (5%) pts received protocol therapy as first line ET for MBC, 169 (77%) as second line, and 41 (17%) as beyond second line. 88% entered the trial directly after progression on CDK4/6i. After a median follow-up of 24 mo, 18 pts remained on protocol treatment. PFS was not improved with F+P vs F (median 4.6 vs 4.8 mo; HR=1.11, 90% CI 0.79-1.55; 2-sided p=0.62). Median PFS was 8.1 mo with F+P+A (HR=0.75 vs F, 90% CI 0.50-1.12; 2-sided p=0.23). ORR was 7.3% (90%CI 1.5-13.0) with F, 9.0% F+P (4.5-13.5%) and 13.0% F+P+A (5.4-20.5%). No new safety signals have been observed. Analysis of ctDNA panel sequencing encompassing 70 genes from 184 baseline samples, including correlation with known and hypothesized resistance genes, will be presented. Conclusions For ER+/HER2- breast cancer, combining palbociclib with fulvestrant beyond progression on prior CDK4/6i and AI did not significantly improve PFS compared with using fulvestrant alone. The observed longer PFS when a PD-L1 inhibitor was added to fulvestrant plus palbociclib is an intriguing signal in this ER+ population. Translational studies of blood and tumor tissue are ongoing and will be presented.

Disclosure(s):

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12/8/2022

10:00 AM - 10:15 AM

GS3-07

GS3-07 Clonal evolution and mechanisms of acquired resistance to CDK4/6 inhibitors in ER-wild type and ER-mutant breast cancer

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Background Despite the remarkable activity of CDK4/6 inhibitors (CDK4/6i) in the treatment of estrogen receptor positive (ER+) metastatic breast cancer (BC), most patients eventually develop resistance to these drugs. The ctDNA analysis of the PALOMA-3 trial showed that the estrogen receptor (ER) mutation Y537S is a potential mechanism of acquired resistance to the combination of endocrine therapy (ET) with CDK4/6i. To date, the role of the ER mutations in the clonal evolution and the mechanisms of acquired resistance to CDK4/6i is unknown. Moreover, it is not known if the development of resistance to CDK4/6i in the presence or absence of ER mutations is due to the expansion of pre-existing resistant clones or to the de novo acquisition of resistance mechanisms. **Methods** To explore the clonal evolution and the mechanisms of resistance to CDK4/6i in ER-wild type (ER-WT) and ER-mutant (ER-Mut) BC, we transduced doxycycline (DOX)-inducible Y537S ER-Mut MCF7 cells with the ClonTracer library, a high-complexity DNA barcode library, and cultured the barcoded cells without DOX (MCF7), or with DOX to induce the expression of the Y537S ER mutation (MCF7-YS). To develop Palbociclib (Palbo)-resistant (PDR) and Abemaciclib (Abema)-resistant (ABR) cell models, the barcoded MCF7 and MCF7-YS cells were passaged in culture with increasing concentrations of Palbo and Abema until the acquisition of resistance. The clonal dynamics and the molecular characteristics of the PDR and ABR models were investigated by barcode sequencing, whole-exome sequencing (WES), bulk and single cell RNA sequencing (RNAseq) and protein analyses. Finally, using an ER-Mut barcoded mice model, we compared the in vitro clonal evolution of ER-Mut CDK4/6i-resistant cells with the in vivo clonal evolution of ER-Mut metastases. **Results** The analysis of the barcodes revealed that during the acquisition of resistance to either Palbo or Abema there is a strong clonal selection of pre-existing resistant clones. The PDR clones were different in the presence of the Y537S mutation versus WT-ER. In contrast, the clones enriched in the ABR cells were comparable between WT and mutant ER. Furthermore, the ER mutations led to decreased diversity of the enriched clones in the PDR but not in the ABR cells. Interestingly, the barcodes enriched in the PDR and ABR models did not overlap. Unsupervised analyses showed that the samples clustering based on the barcodes fractions and the mutations were similar, suggesting that the clonal selection was driven by cellular populations with specific mutational landscapes. All the ER-WT and ER-Mut resistant models had different transcriptional profiles and by single-cell RNAseq showed various degrees of intra-sample heterogeneity. At the protein level, the PDR and the ABR cells displayed downregulation of ER, Rb and p27 and upregulation of p21. In the ER-Mut conditions Cyclin D1 was upregulated in the PDR cells, while Cyclin E was upregulated in the ABR cells. Finally, the barcode sequencing of the mice metastases revealed that the clonal selection in ER-Mut metastases and in ER-Mut CDK4/6i-resistant cells is different. **Conclusion** Our study suggests that the development of resistance to CDK4/6i is due to the selection of pre-existing resistant

clones. We also demonstrate that the expression of the Y537S ER mutation impacts the clonal evolution and the mechanisms of acquired resistance to Palbo but not to Abema. Finally, we show that the clonal evolution and mechanisms are disparate in Palbo and Abema resistance. These results support the addition of a third drug to CDK4/6i and ET, early in treatment, to delay the selection of pre-existing resistant clones and prolong the response to treatment and highlight differences between Palbo and Abema.

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12/8/2022

10:15 AM - 10:30 AM

GS3-08

GS3-08 Discussant for GS3-06 and GS3-07

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12/8/2022

10:30 AM - 10:45 AM

GS3-09

GS3-09 Circulating Tumor Cells-driven choice of first line therapy for ER+ HER2-metastatic breast cancer: overall survival analysis of the randomized STIC CTC trial

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Frédérique Berger, MSc: No financial relationships to disclose

William Jacot, MD PhD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Travel expenses (Ongoing); BMS: Consulting Fees (e.g., advisory boards) (Ongoing); Chugai: Consulting Fees (e.g., advisory boards) (Ongoing), Travel expenses (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Travel expenses (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Ongoing), Travel expenses (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Travel expenses (Ongoing); GlaxoSmithKline: travel reimbursement (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Travel expenses (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Travel expenses (Ongoing); Pierre Fabre: travel reimbursement (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Travel expenses (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing)

Jean-Yves Pierga, MD PhD: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichy Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing)

12/8/2022

10:45 AM - 11:00 AM

GS3-10

GS3-10 Discussant for GS3-09

Presenting Author(s) and Co-Author(s):

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Country: United States

Disclosure(s):

Daniel F. Hayes, MD: /TRANSFERRED to Menarini Silicon Biosystems: Contracted Research (Ongoing), Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Royalty (Ongoing); Artiman Ventures (Cellworks), East Palo Alto, CA: Diagnostics (tissue predictive factors) (Terminated, August 7, 2018); Astra Zeneca: Contracted Research (Ongoing); BioVeica: Diagnostics (liquid biopsies) (Terminated, December 7, 2020); Cepheid: Contracted Research (Terminated, November 7, 2017), Diagnostics (tissue prognostic and predictive factors) (Terminated, November 7, 2017); EPIC Sciences, Inc.: Diagnostics (liquid biopsies) (Terminated, October 7, 2019); Freenome Inc: Diagnostics (liquid biopsies) (Terminated, July 7, 2018); Guardant: Diagnostics (liquid biopsies) (Ongoing); Janssen R&D, LLC (Johnson & Johnson)/TRANSFERRED to Menarini Silicon Biosystems: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); L-Nutra: Therapeutic diet product (Terminated, May 7, 2020); MacroGenics: Diagnostics (tissue) (Terminated, December 7, 2021); Merrimack Pharmaceuticals, Inc. (Parexel Intl Corp): Contracted Research (Terminated, February 2, 2020); OncoCyte: Diagnostics (immune-oncology predictive factor) (Terminated, January 7, 2021); Pfizer: Contracted Research (Terminated, July 14, 2022); Predictus BioSciences: Diagnostics (tissue prognostic factor) (Ongoing); Tempus: Diagnostics (tissue and liquid biopsies) (Terminated, July 21, 2021); Turnstone Biologics: Therapeutics (none breast cancer) (Ongoing); Xilis: Diagnostics (tissue predictive factors) (Terminated, January 7, 2021)

12/8/2022

10:00 AM - 5:00 PM

Exhibits

12/8/2022

11:00 AM - 11:20 AM

Pro

Presenting Author(s) and Co-Author(s):

Debra Patt, MD, MBA - *Texas Oncology*

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12/8/2022

11:00 AM - 12:00 PM

Debate: Are All CDK4/6 Inhibitors the Same or Different?

Presenting Author(s) and Co-Author(s):

Sung-Bae Kim, MD, PhD - *University of Ulsan College of Medicine*

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Country: Republic of Korea

12/8/2022

11:20 AM - 11:40 AM

Con

Presenting Author(s) and Co-Author(s):

Ruth O'Regan, MD, *Charles A. Dewey Professor & Chair of Medicine - University of Rochester Medical Center*

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12/8/2022

11:40 AM - 12:00 PM

Debate Discussion

Presenting Author(s) and Co-Author(s):

Sung-Bae Kim, MD, PhD - *University of Ulsan College of Medicine*

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Country: Republic of Korea

12/8/2022

12:00 PM - 12:30 PM

Plenary Lecture 2: Premenopausal ER+ Breast Cancer: Past, Present, and Future

Presenting Author(s) and Co-Author(s):

Carlos Arteaga, MD - *UT Southwestern Medical Center, Simmons Comprehensive Cancer Center*

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Country: United States

Prudence Francis, MD - *Peter MacCallum Cancer Centre*

City: Victoria

Country: Australia

Adjuvant endocrine therapy for premenopausal ER+breast cancer had a relatively challenging initial pathway. The earliest trials testing adjuvant ovarian ablation in premenopausal breast cancer were hampered by the lack of ability to test for the relevant target, namely the estrogen receptor (ER). Therefore, trials testing adjuvant ovarian ablation and subsequently ovarian suppression with gonadotropin releasing hormone agonists (GnRHa) were diluted by the inclusion of women with estrogen receptor negative tumors. The subsequent demonstration of the effectiveness of adjuvant chemotherapy, initially with the CMF regimen, diverted some attention away from adjuvant endocrine therapy in premenopausal women, notwithstanding the fact that CMF, initially given for 12 months, resulted in permanent ovarian function suppression in many premenopausal women. Use of adjuvant CMF made it even more challenging to discern the added value of ovarian ablation or suppression. Oral adjuvant endocrine therapy with the selective estrogen receptor modulator tamoxifen became recommended for postmenopausal women, subsequently refined to only those with ER+ breast cancer, but the value of tamoxifen in premenopausal women was initially considered uncertain. Eventually, 5 years of adjuvant tamoxifen became a standard recommendation for premenopausal ER+ early breast cancer, although it took some time for evidence to emerge on the value of adding tamoxifen in women who received chemotherapy. The value of extending adjuvant endocrine therapy beyond 5 years was subsequently studied. More recent randomized premenopausal adjuvant endocrine therapy trials have focused on delineating the value of ovarian function suppression (OFS) added to tamoxifen or to an aromatase inhibitor. There are now a range of options for adjuvant endocrine therapy for premenopausal ER+ breast cancer, and identifying the clinical-pathologic features most appropriate for intensification of adjuvant endocrine therapy can assist with optimizing recommendations for an individual patient.

Disclosure(s):

Virginia Kaklamani, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Daiichi Sankyo: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Genentech: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Genomic Health: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Gilead Sciences: Honoraria (Ongoing); Novartis: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Pfizer: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents

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Prudence Francis, MD: No financial relationships to disclose

12/8/2022

12:30 PM - 1:00 PM

Brinker Award for Scientific Distinction in Basic Science

Presenting Author(s) and Co-Author(s):

Jennifer Pietenpol

12/8/2022

12:30 PM - 1:00 PM

Guardian at the Gates: Genome Stability, Cell State Plasticity, and Breast Cancer

Presenting Author(s) and Co-Author(s):

Geoffrey M. Wahl, PhD - *Salk Institute for Biological Studies*

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Country: United States

12/8/2022

1:00 PM - 1:20 PM

Fungal regulation of breast tumor radiation response

Presenting Author(s) and Co-Author(s):

Stephen Shiao, MD, PhD - *Cedars-Sinai*

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12/8/2022

1:00 PM - 2:00 PM

Forum 3: Modifying Tumor Response: Microbiome, Diet, and Fasting

Presenting Author(s) and Co-Author(s):

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Disclosure(s):

Sangeetha Reddy, MD, MSc: No financial relationships to disclose

12/8/2022

1:20 PM - 1:40 PM

Fasting and microbiotic

Presenting Author(s) and Co-Author(s):

Guido Kroemer, MD, PhD, PU-PH - *University of Paris Descartes*

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Fasting and caloric restriction mimetics stimulate anticancer immunosurveillance

Guido Kroemer

University of Paris, INSERM U1138, Centre de Recherche des Cordeliers, Hôpital Européen George Pompidou, Gustave Roussy Cancer Campus, Villejuif/Paris, France

Fasting and caloric restriction induce metabolic and neuroendocrine changes that have major anti-inflammatory and immunostimulatory effects. Some of these effects are mediated by a raise of ketone bodies (such as 3-hydroxybutyrate) and a decrease in circulating insulin-like growth factor-1 (IGF1), meaning that administration of 3-hydroxybutyrate and pharmacological inhibition of IGF1 receptor can mimic some of the beneficial effects of fasting on anticancer immunosurveillance. "Caloric restriction mimetics" (CRMs) are small molecules that induce autophagy through the same pathways that are activated by fasting, including the reduction of cytoplasmic protein acetylation. We have accumulated evidence that CRMs can stimulate anticancer immunosurveillance either as single agents (for the prevention of malignant disease) or in combination with chemotherapy and/or immune checkpoint blockade (for the treatment of established cancers). In preclinical experiments, fasting and CRMs have also been used for the prevention or treatment of hormone-induced breast cancer, and these effects are coupled to an increase in the T lymphocyte-mediated anticancer immune response. We have developed an in vitro screening assay to identify novel pharmacological agents that act as CRMs. Such neo-CRMs can be successfully employed to improve anticancer immunosurveillance in preclinical experiments.

12/8/2022

1:40 PM - 2:00 PM

Microbiome and response to immunotherapy

Presenting Author(s) and Co-Author(s):

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12/8/2022

1:00 PM - 2:00 PM

Molecular Tumor Board

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12/8/2022

2:00 PM - 2:20 PM

CDK4/6 inhibitor resistance: Biological mechanisms and novel approaches

Presenting Author(s) and Co-Author(s):

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CDK4/6 inhibitors (CDK4/6i) in combination with antiestrogens have revolutionized the treatment of ER+ metastatic breast cancer (MBC), significantly prolonging survival. However, this combination is not curative in MBC, and resistance to CDK4/6i represents a major challenge. A diverse array of mechanisms of CDK4/6i resistance have been described, including deregulation of the G1/S cell cycle checkpoint (i.e. Rb, Cyclin E/CDK2, CDK6, INK4s), activation of growth factor signaling pathways (receptor tyrosine kinases, Ras/MAPK pathway, PI3K/AKT pathway), and contributions from the tumor microenvironment. A detailed understanding of these mechanisms is critical for overcoming CDK4/6i resistance. In this presentation, I will discuss recent advances in defining novel biomarkers that are causally associated with CDK4/6i resistance, therapeutic vulnerabilities linked to distinct mechanisms of resistance, and potential strategies to improve clinical responses to CDK4/6i in ER+ MBC.

12/8/2022

2:00 PM - 3:00 PM

Forum 4: Demystifying CDKs in Breast Cancer: Beyond CDK4/6

Presenting Author(s) and Co-Author(s):

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2:20 PM - 2:40 PM

Current status of CDK2 inhibitors in (pre-)clinical development

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2:40 PM - 3:00 PM

Inhibiting transcriptional CDKs in breast cancer

Presenting Author(s) and Co-Author(s):

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12/8/2022

2:00 PM - 2:20 PM

RIP MTD

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2:00 PM - 3:00 PM

Translational Controversies

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12/8/2022

2:20 PM - 2:40 PM

Randomized trials vs real world evidence

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12/8/2022

2:40 PM - 3:00 PM

Ki 67

Presenting Author(s) and Co-Author(s):

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Ki67 – a clinically relevant biomarker or just *nice to have* information?

Nadia Harbeck

Breast Center, Dept. OB&GYN, LMU University Hospital, Munich, Germany

Ki67 is an immunohistochemical marker indicating the growth fraction of cycling cells from G1 to S-phase in tumor specimens. In breast cancer, Ki67 is a prognostic marker with high values indicating poor outcome. Over the last decades, obstacles for its wide-spread use in clinical practice included lack of methodological standardization and lack of specific cut-off values for clinical decision making, i.e. discrimination of luminal A vs. B early breast cancer (EBC), chemotherapy indication in HR+/HER2- EBC. However, recently, the International Ki67 working group has put forward consensus statements for a standardized methodology. In general, reproducibility of Ki67 values at extreme sides of the spectrum such as 10% or > 35% is much higher than in the intermediate range and quality assurance programs substantially improve laboratory performance. Moreover, clinical utility has also become apparent in two specific settings of HR+/HER2- EBC.

First, the monarchE trial evaluating adjuvant abemaciclib in node-positive high-risk disease used a Ki67 cut-off of 20% as a criterion for aggressive disease and as a sole inclusion criterion for patients with 1-3 lymph nodes (cohort2). While data for this cohort have not yet been reported, Ki67 was a strong prognostic factor in the overall trial population with patients with high Ki67 having worse outcome than those with Ki67 < 20%. Benefit from abemaciclib was independent of Ki67 index. Nevertheless, some health authorities included Ki67 in their abemaciclib label as the absolute benefit was greater in tumors with Ki67 \geq 20%.

Second, Ki67 response after a short (2-4 week) preoperative endocrine therapy allows endocrine response assessment by determining Ki67 in the surgical specimen. This information is widely used in drug development. Ki67_{post} 10% has been defined as endocrine response. In the POETIC trial, endocrine response was associated with improved outcome compared to tumors with Ki67 > 10% after 2-weeks of preoperative AI in postmenopausal patients. In the WSG ADAPT trial, patients with 0-3 lymph nodes, Recurrence Score 25 and endocrine response had excellent outcome with adjuvant endocrine therapy alone independent of menopausal status (5-year dDFS > 95%). In postmenopausal women, probability of endocrine response with an AI is around 80% whereas in premenopausal patients with tamoxifen it is only

around 40%. Yet, in premenopausal women addition of GnRH substantially improves endocrine response probability reaching about 80% with GnRH and AI as recently shown by interim analysis of the WSG ADAPTcycle trial (about 2500 patients). Endocrine response probabilities seen in the ADAPT trial (> 5000 patients) were validated in ADAPTcycle demonstrating clinical validity of this biomarker.

In conclusion, Ki67 is a clinically relevant biomarker that can be used for clinical decision making, particularly in HR+/HER2- EBC. As there is no single generally accepted Ki67 cut-off value to discriminate prognostically favorable from aggressive EBC, Ki67 needs to be used in the context of tumor burden and tumor biology. Currently, next to its use in allocating patients to adjuvant abemaciclib in countries where Ki67 index is included in the label, it provides clinically important information after short-term preoperative endocrine therapy regarding endocrine response in HR+/HER2 EBC. Given its easy and inexpensive determination method, its analytical validity within quality assurance programs, and its clinical usefulness, Ki67 needs to be integrated in our biomarker portfolio in EBC.

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12/8/2022

3:00 PM - 3:30 PM

Pathologic aspects

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12/8/2022

3:00 PM - 5:00 PM

Educational Session: Challenging Types of Breast Cancer

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12/8/2022

3:30 PM - 4:00 PM

Metaplastic Breast Cancer

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Metaplastic breast cancer (MPC) is a less common subtype of breast cancer, representing approximately 0.2-0.5% of breast cancer diagnoses, which is often associated with poor outcomes. MPC is an overarching term for breast tumors which demonstrate differentiation toward epithelial or mesenchymal components, or a mixture of these. In the context of challenging subtypes of breast cancer, this educational discussion will review epidemiology and clinical course of these tumors. Molecular characteristics of MPC and how this might impact current, as well as possible future, management strategies will be discussed. Finally, opportunities for laboratory investigations and clinical trial approaches to further understand and better treat MPC will also be discussed.

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12/8/2022

4:00 PM - 4:30 PM

Inflammatory Breast Cancer

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Inflammatory Breast Cancer (IBC) has an incidence of 1-5% among all breast cancers diagnosed within the USA, yet it accounts for a disproportionately high rate of mortality, leading to up to 10% of all breast cancer related deaths. Although IBC can present with any receptor status in terms of estrogen, progesterone, and human epidermal growth factor 2 (HER2), there is a higher proportion of HER2 positive cases compared to non-IBC. Given the distinct difference in outcome, it is important to differentiate IBC from more indolent locally advanced non-IBC with secondary inflammatory features. Despite ongoing efforts to identify molecular markers specific for IBC, the underlying tumor biology and genomic drivers of progression remain largely unknown. In this session we will review tumor-intrinsic signaling pathways, the role of the tumor microenvironment and clinical trials with combination therapies to inform future biomarkers of disease progression in IBC.

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12/8/2022

4:30 PM - 5:00 PM

Lobular/pleomorphic Breast Cancer

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Lobular Cancer

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Invasive lobular carcinoma (ILC) accounts for up to 15% of all invasive breast cancers. The general marker to identify lobular cancer is the loss or low expression of E-cadherin which is the result of genetic alterations of the *E-cadherin* gene which accounts for about 95%. The majority of classical ILCs are of low grade and express both hormone receptors strongly and rarely any HER2. Those not expressing the hormone-receptors are categorised as apocrine breast cancers which is a small group.

Recently it has been shown that ILC is a breast cancer type which has unique genomic features. Desmedt and colleagues genomically profiled 430 ILCs, to characterize the genomic alterations present in these tumors compared to invasive ductal carcinoma (now cold unfortunately NST non-specific subtype). The most frequent altered gene was CDH1 which results in a mRNA or protein loss of the cell adhesion molecule E-cadherin. Amongst the genes found to be altered at a high frequency are ESR1 and PIK3CA/PTEN. Currently those have little or no clinical impact in early breast cancer there might be consequences for metastatic breast cancer.

The molecular alterations result in a less cohesive tissue connection and influence imaging as well as surgical procedures and in the end the prognosis in those patients.

The size and extend of ILC is often underestimated by imaging and clinical examination. MRI thought to be the optimal imaging turned out to have no influence on positive margins and is no longer considered standard for all ILCs.

Several data suggest that ILCs have an improved outcome the first 5 years after primary diagnosis but thereafter the survival curves in general lie below those for non lobular breast cancer. ILC has a distinct metastatic pattern and often metastasise into the GI tract and the ovaries and less frequently to the lung.

Breast conserving surgery as well as mastectomy can be used when indicated based on tumor size and patients preference. Because ILC more often presents at higher stage, mastectomy is more frequently performed. But even after neoadjuvant chemotherapy we could demonstrate, despite response even resulting in pCR, mastectomy was more frequently conducted in ILC patients compared to non-ILC. In this analysis 71% of the non-ILC did receive BCS compared to only 59% in ILC (p

Systemic therapy follows the general recommendations based on stage and histopathological profile.

Neoadjuvant chemotherapy results in significantly lower rates of pathological responses. All analyses showed response rate in single digit numbers (far below 10%) but the less classical ILCs with either grade 3 or hormone-receptor negativity have a higher chance of achieving a pCR. Those ILCs with grade 3 and hormone-receptor negativity (apocrine cancer) have a pCR rate comparable to invasive ductal carcinoma (IDC). It is not surprising that lobular breast cancer does not respond as well as IDC to neoadjuvant chemotherapy because their biological features are, as described above, more luminal A like (high hormone receptor positivity, low grade, low proliferation). Because many patients with ILC present with extended diseases, they might still benefit from neoadjuvant chemotherapy even if they do not achieve a pathologic complete response, downstaging is an option and would potentially lead to less mastectomies.

Because of the luminal A like type of the majority of ILCs endocrine therapy seems to be the treatment of choice. Some data even suggested a better outcome for ILC breast cancer when treated with an aromatase inhibitor compared to tamoxifen. But other data are controversial in this regard and did not confirm the data from BIG 1-98.

In conclusion the molecular profile of ILC seems to be distinct but does not result in different treatment paradigms. We should not underestimate the necessity of optimal treatment, including chemotherapy for invasive lobular breast cancer patients.

Disclosure(s):

Sibylle Loibl, MD, PhD: Abbvie: Contracted Research (Ongoing), Other financial benefit paid to institute (Ongoing); Amgen: Other financial benefit paid to institute (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Other financial benefit paid to institute (Ongoing); BMS: Other financial benefit paid to institute (Ongoing); Celgene: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), paid to institute (Ongoing); Daiichi-Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Other financial benefit paid to institute (Ongoing); Eisai Europe Ltd.: Other financial benefit paid to institute (Ongoing); EP14153692.0, EP21152186.9, EP15702464.7, EP19808852.8: Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Royalty (Ongoing); GBG Forschungs GmbH: Salary (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Other financial benefit paid to institute (Ongoing); GSK: Other financial benefit paid to institute (Ongoing); Lilly: Other financial benefit paid to institute (Ongoing); Merck: Other financial benefit paid to institute (Ongoing); Molecular Health: Contracted Research (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Other financial benefit paid to institute (Ongoing); Olema Pharmaceuticals: Other financial benefit paid to institute (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Other financial benefit paid to institute (Ongoing); Pierre Fabre: Other financial benefit paid to institute (Ongoing); Relay Therapeutics: Other financial benefit paid to institute (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Other financial benefit paid to institute (Ongoing); Sanofi: Other financial benefit paid to institute (Ongoing); Seagen: Other financial benefit paid to institute (Ongoing); VM Scope GmbH: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Royalty (Ongoing)

12/8/2022

3:00 PM - 3:40 PM

Cancer risks in patients with moderate penetrance gene mutations

Presenting Author(s) and Co-Author(s):

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Cancer risks in patients with moderate penetrance gene mutations

The genetic landscape of inherited breast cancer is broad, spanning from high and moderate penetrance pathogenic variants in breast cancer susceptibility genes, to polygenic risk associated with the cumulative impact of single nucleotide polymorphisms (SNPs). This educational session will review the landscape of inherited breast cancer. The discussion will then focus on breast cancer susceptibility genes associated with moderately elevated risks of breast cancer including *PALB2*, *ATM*, *CHEK2* and others. Recent data informing quantitative and qualitative cancer risk estimates, management recommendations, therapeutic implications, and reproductive considerations will be reviewed. Emerging issues and treatment strategies under investigation will also be discussed.

12/8/2022

3:00 PM - 5:00 PM

Educational Session: Management of Hereditary Risk: Moderate-Risk Genes and New Approaches

Presenting Author(s) and Co-Author(s):

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Seema Khan, MD: No financial relationships to disclose

12/8/2022

3:40 PM - 4:20 PM

Screening for high risk patients: Does everyone need annual MRI with mammogram?

Presenting Author(s) and Co-Author(s):

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Introduction:

To reduce mortality, all guidelines advice women with very high breast cancer (BC) risk, due to a pathogenic variant (PV) in genes like BRA1/2 or chest wall irradiation between age 10-30 yrs., annual screening with Magnetic Resonance Imaging (MRI) and 2 or 3D mammography (Mm).¹⁻⁶ For MRI, starting age for this group is usually 25 years. However for Mm some guidelines advise annual from age 30 yrs.^{1,2}, others 10 yr. younger than the youngest family member^{4,5}, or for BRCA1 biennial from age 40 yrs.⁷

USA and Canadian but not European guidelines advice MRI screening also for women with a \geq 20% lifetime breast cancer (BC) risk, while the European Eusobi guideline, unlike the US and Canadian, now advises to screen women with extremely dense breasts with MRI although not yearly.⁸

Considerations and evidence:

We need to balance the possible benefit with the disadvantages of screening, like false positive rate, possible overdiagnosis and cost. We therefore have to use the optimal frequency of screening, depending on the expected tumor growth rate, which varies with a woman's age and the cause of the increased risk.⁹

Two recent randomized trials one in women with familial risk the other for extremely dense breasts showed how much MRI advances BC detection compared to mammography, at which side effects.^{10,11}

Observational and modelling studies show varying additional value of Mm to MRI-screening for different risk – and age groups.¹²⁻¹⁷

Conclusion: Screening for women at high risk can be better tailored to the age and risk-group.

References:

1. American College of Radiology (ACR) Appropriateness Criteria. Breast Cancer Screening: High risk women. www.cancer.org. Assessed 2022-9-17
2. American Cancer Society Guideline High risk. Last Revised Jan. 2022. www.cancer.org
3. Mulder RL, Hudson MM, Bathia S et al. J Clin Oncol. 2020 Dec 10;38(35):4194-4207. Updated Breast Cancer Surveillance Recommendations for Female Survivors of

Childhood, Adolescent, and Young Adult Cancer From the International Guideline Harmonization Group.

4. Cancer Care Ontario's (CCO) "Magnetic Resonance Imaging Screening of Women at High Risk for Breast Cancer", practice guideline; https://www.easternhealth.ca/wp-content/uploads/sites/2/2018/06/Breast-Magnetic-Resonance-MRI-and-High-Risk-Guideline_2017.pdf. and www.cancercare.on.ca

5. William J, Benjamin OA et al. Breast cancer screening and Diagnosis Version 1 2019.2. NCCN clinical practice guidelines in oncology. J Natl. ComprCaNetwork 2020;18(4):452-78. www.nccn.org. version 1 2022

6. National Institute for Health and Care Excellence (NICE). Familial breast cancer:

Classification and care of people at risk of familial breast cancer and management of breast cancer and related risks in people with a family history of breast cancer. www.guidance.nice.org.uk/CG80/Guidance.

7. The Dutch guideline breast screening outside the National screening scheme: https://richtlijnendatabase.nl/richtlijn/borstkanker/screening/screening_buiten_het_bob/screening_buiten_het_bevolkingsonderzoek.html. Assessed 19 September 2022.

8. Mann EM, Athanasiou A, Baltzer PAT et al. Breast cancer screening in women with extremely dense breasts recommendations of the European Society of Breast Imaging (EUSOBI). *European Radiology* 2022;32: 4036-45.

9. Tilanus-Linthorst MMA, Obdeijn AIM, Hop WCJ et al. Age and a BRCA1 or-2 mutation predict breast cancer growth rates in the UK, Dutch and Canadian MRI-screening studies. *Clin Ca Res* 2007.

10. Saadatmand S, Geuzinge HA, Rutgers EJT, et al. MRI versus mammography for breast cancer screening in women with familial risk (FaMRIsC): a multicentre, randomised, controlled trial. *Lancet Oncol.* 2019;20(8):1136-1147.

11. Bakker MF, de Lange SV, Pijnappel RM et al. Supplemental MRI screening for women with extremely dense breast tissue. *N Engl. J Med* 2019; 381;22:2091-2102.

12. Geuzinge HA, Obdeijn IM, Rutgers EJT et al. Cost-effectiveness of breast cancer screening with magnetic resonance imaging for women at familial risk. *JAMA Oncology* 2020;6(9):13-81-1389.

13. Geuzinge HA, BakkerMF, Heijnsdijk EAM et al. Cost-Effectiveness of Magnetic Resonance Imaging Screening for Women With Extremely Dense Breast Tissue. *J Natl Cancer Inst.* 2021 Nov 2;113(11):1476-1483.

14. Chiarelli AM, Blackmore et al. Performance measures of Magnetic Resonance Imaging plus Mammography in the high risk Ontario breast screening program. *JNCI* 2020;112(2):136-144.

15. Obdeijn IM, Heijnsdijk EA, Hunink MG et al. Mammographic screening in BRCA1 mutation carriers postponed until age 40: Evaluation of benefits, costs and radiation risks using models. *Eur J Ca* 2016; 63:135-42.

16. Obdeijn et al. The supplemental value of mammographic screening over MRI alone in BRCA2 screening. *Br Ca Res Treat* 2020 ; 181 :581-88.

17. Vreemann S, v Zelst JC, Mann RM et al. Breast Cancer Res 2018;20(1):84 The added value of mammography in different age-groups of women with and without BRCA mutation screened with MRI.

12/8/2022

4:20 PM - 5:00 PM

Hormonal exposure and risk in BRCA1/2 carriers

Presenting Author(s) and Co-Author(s):

Joanne Kotsopoulos, PhD - *University of Toronto*

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Women who inherit a pathogenic variant (*mutation* hereafter) in the *BRCA1* or *BRCA2* gene face extremely high lifetime risks of developing breast and ovarian (or fallopian tube) cancer. More than two decades since the discovery of these genes, and primary prevention with bilateral mastectomy and salpingo-oophorectomy remain the most effective options to manage cancer risk in this population. Understanding the impact of exogenous hormone use is important for both the clinical management of high-risk women and for furthering our knowledge of the pathogenesis of *BRCA*-associated disease. In this session, I will review the current epidemiologic data surrounding the role of exogenous (anti)hormone use on *BRCA*-cancer risk. Specifically, I will discuss the role of tamoxifen in preventing *BRCA*-associated breast cancer and I will describe whether use of oral contraceptives or hormone replacement therapy (HRT) increase the risk of breast cancer. Where possible, I will present data by gene mutation. Potential associations with the risk of ovarian cancer will also be referred to, given that managing *BRCA*-cancer risks is a balancing act. Finally, I will review how the epidemiologic information has contributed to the discovery of novel targets for the non-surgical prevention of *BRCA1*-associated breast cancer and gaps in the literature to be addressed in future research.

12/8/2022

3:00 PM - 3:40 PM

Which is the best technique

Presenting Author(s) and Co-Author(s):

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12/8/2022

3:00 PM - 5:00 PM

Educational Session: What ctDNA Can Tell Us

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Disclosure(s):

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12/8/2022

3:40 PM - 4:20 PM

Can ctDNA substitute tissue testing

Presenting Author(s) and Co-Author(s):

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Circulating tumor DNA (ctDNA) is at the forefront of liquid biopsy technology. A key advantage of ctDNA is being able to achieve genomic profiling from a blood test rather than from a more invasive tissue biopsy, reducing risk and discomfort for patients as well as costs and logistical complexity. Increasing evidence supports ctDNA as a useful clinical tool in specific indications, for example in the detection of *PIK3CA* mutations to identify patients suitable for alpelisib plus fulvestrant. The expectation is that indications for routine ctDNA testing will expand as more data become available and ctDNA is embedded into clinical trials and paired with novel therapies.

Biological and technical factors both contribute to the feasibility of ctDNA expansion into the clinic. Representation of heterogeneity might be a key strength of ctDNA analysis over tumour biopsy analysis, as sampling the circulation compartment can in principle allow representation of a wider array of disease sites than a tumor sample acquired with a single needle.

However, the factors influencing how different metastases might contribute to the circulating compartment are poorly understood, presenting a challenge to clinical interpretation. Moreover, the limit of detection of ctDNA assays, the timing of treatment and stochastic effects can contribute to uncertainty, particularly in the interpretation of negative results. Recent work analyzing tumor mutational burden using ctDNA has highlighted these challenges as applied to biomarker development.

Circulating tumour DNA is likely to complement tissue biopsy in the future, and may substitute tumor biopsy in specific indications supported by the data. Ultimately, clinical utility for different ctDNA indications, as opposed to tissue biopsy, will need ongoing confirmation within clinical trials.

12/8/2022

4:20 PM - 5:00 PM

Using ctDNA in detecting disease

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12/8/2022

5:00 PM - 6:15 PM

Ongoing Trials 3

12/8/2022

5:00 PM - 6:15 PM

OT3-01-01

A single-arm confirmatory study to evaluate the efficacy of non-surgical therapy for HER2 positive early breast cancer with clinical complete response after primary systemic therapy: (JCOG1806)

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Background: The surgical treatment is the standard therapy for early breast cancer (EBC) after primary systemic therapy (PST). In more than half of HER2 positive (HER2(+)) breast cancer, pathological complete response (pCR) is achieved by PST with HER2 inhibitors and chemotherapy. However, non-surgical therapy is not an option for EBC with cCR after PST because of little evidence. We planned a single-arm confirmatory study to evaluate the efficacy and safety of the non-surgical therapy for HER2(+) EBC with cCR after PST. Methods: The key eligibility criteria are as follows: 1) Histologically confirmed as invasive ductal carcinoma of the breast, HER2(+). 2) cT1-2, N0, M0 (UICC 8th). 3) No ipsilateral BC. 4) Women aged 20-74 years. 5) ECOG performance status 0 or 1. 6) Adequate hematologic and organ function. 7) Ejection fraction as cardiac function is over 50%. 8) Written informed consent. HER2 inhibitors

(trastuzumab and pertuzumab) and cytotoxic drugs as PST are administered to all patients (pts). After completion of PST, cCR is diagnosed by breast imaging and physical examination. cCR is defined as 1) Not palpable breast mass by physical examination, 2) No enhanced breast mass by enhanced MRI, and 3) No breast mass by ultrasonography. 4) For hormonal receptor (+) EBC, needle biopsy after PST must be done to evaluate the pCR. After a diagnosis of cCR, conventional radiotherapy for whole breast and boost radiation for tumor bed is mandatory, followed by pertuzumab and trastuzumab every 3 weeks for 9 months. In non-cCR cases, surgical resection is performed and adjuvant therapy is not specified. The primary endpoint is a distant metastasis-free survival (DMFS) at 3 years, the secondary endpoints are DFS, OS, RFS, the proportion of local recurrence, and cosmetics outcome. Given that the threshold and expected DMFS at 3-year is 93% and 98% with a significance level of 2.5% (one-sided) and 80% power, 170 cCR cases are required. Assuming half of the HER2 pts reach cCR, 350 pts are required as the sample size started PST. Enrollment launched in January 2020, and 260 pts are enrolled as of July 12, 2022. This clinical trial has been registered at the Japan Registry of Clinical Trials as JRCTs031190129 and conducted by the Japan Clinical Oncology Group (JCOG) Breast Cancer Study Group under a public fund (National Cancer Center Research and Development Fund).

Disclosure(s):

Tomomi Fujisawa, MD, PhD: No financial relationships to disclose

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Taro Shibata, n/a: No financial relationships to disclose

12/8/2022

5:00 PM - 6:15 PM

OT3-03-01

Phase I study of intratumoral administration of CF33-hNIS-antiPD-L1 (CHECKvacc) in patients with metastatic triple negative breast cancer

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Background: Despite recent FDA approvals of immune checkpoint inhibitor pembrolizumab and drug-antibody conjugate in the treatment of metastatic triple negative breast cancer (mTNBC), the overall survival benefit of these therapies remains modest. Oncolytic virotherapy (OV) utilizes genetically modified viruses to infect and kill cancer cells while sparing healthy cells. CF33-hNIS-anti-PD-L1 (CHECKvacc) is a novel chimeric orthopoxvirus with robust anti-cancer activity in TNBC xenografts. Cells infected with CHECKvacc were shown to express functional human sodium-iodide symporter (hNIS) and anti-PD-L1 proteins. hNIS gene transfer allows tracking of virus by 99mTc single-photon emission computed tomography (SPECT). Our preliminary animal studies demonstrated that tumor cells infected with CHECKvacc successfully secrete functional hNIS and anti-PD-L1. CHECKvacc administered by intratumoral injection appears safe and is generally well-tolerated. CHECKvacc detects and effectively kills TNBC at doses several magnitudes lower than other OVs in xenograft models. Methods: This study is a first-in-human phase I, single center, single arm clinical trial evaluating the safety and tolerability of CHECKvacc intratumoral injection in patients with mTNBC. Key eligibility criteria include patients with unresectable or metastatic TNBC; progressed on at least 2 prior chemotherapies including an immune checkpoint inhibitor-containing regimen; ECOG 0-1; RECIST 1.1 measurable disease; and at least one tumor amenable to repeated intratumoral injections. Eligible patients receive CHECKvacc intratumorally at one of 8 assigned dose levels (1 x 10⁵ PFU, 3 x 10⁵ PFU, 1 x 10⁶ PFU, 3x 10⁶ PFU, 1 x 10⁷ PFU, 3 x 10⁷ PFU, 1 x 10⁸ PFU, 3 x 10⁸ PFU) on Days 1 and 15 of each 28-day cycle for a total of 3 cycles of treatment. The primary objective is to evaluate the safety and tolerability of CHECKvacc by CTCAE v5.0.

Secondary objectives are to determine optimal biological dose, recommended phase II dose (RP2D), and response rate by RECIST1.1. The first 3 subjects of dose level 1 were enrolled sequentially for safety monitoring. Once the initial 3 subjects were treated sequentially, the study followed the Phase I Queue 3+3 (IQ 3+3) design which expands a dose level up to 8 subjects after a single DLT has been observed. Enrollment to the final RP2D may be expanded to include up to 12 patients for efficacy assessment. The estimated targeted accrual is 33 patients (minimum) to 78 patients (maximum). Correlative aims include assessing viral kinetics, viral plaque assay, 99mTc SPECT imaging for virus tracking, peripheral blood and tumor tissue for antiviral immune activation, and tumor microenvironment changes in association with response to therapy. Results: From October 2021 to June 2022, 6 patients were enrolled and received at least 1 dose of CHECKVacc injection at dose level 1 (1×10^5 pfu) and 2 (3×10^5 pfu). The intratumoral CHECKVacc injections were well tolerated. No DLTs were observed. No treatment emergent AEs (TEAEs) have been reported for the 6 patients so far. 99mTc SPECT imaging for virus tracking is on-going. Baseline and on treatment tumor biopsies were submitted for spatial immune profiling. Peripheral blood at baseline, on treatment and EOT were subjected for flow cytometry analysis. Conclusion: CF33hNIS-antiPD-L1 administered by intratumoral injection in patients with mTNBC is safe and well tolerated at the dose levels tested. Clinical trial information: NCT05081492

Disclosure(s):

Yuan Yuan, MD PhD: AstraZeneca: Speaker's bureau (Ongoing); Celgene: Contracted Research (Ongoing); Daiichi Sankyo: Speaker's bureau (Ongoing); Eisai: Contracted Research (Ongoing), Speaker's bureau (Ongoing); Genentech: Contracted Research (Ongoing), Speaker's bureau (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), Speaker's bureau (Ongoing); Merck: Contracted Research (Ongoing); Novartis: Contracted Research (Ongoing), Speaker's bureau (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Puma: Consulting Fees (e.g., advisory boards) (Ongoing)

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OT3-04-01

A Phase 3 study evaluating ovarian suppression following three-month leuprolide acetate in combination with endocrine therapy in premenopausal subjects with HR+, HER2-negative breast cancer (OVELIA)

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Background: In US clinical practice, GnRH agonists are widely used to suppress ovarian function in pre/perimenopausal patients with breast cancer that is moderate-to high-risk for recurrence. Despite extensive use of leuprolide acetate (LA) for ovarian suppression, regulatory approval for this indication has not been established in the US. Additionally, existing three month formulations may not reliably provide ovarian suppression, as demonstrated by escapes in estradiol (E2). An extended-release LA product with a 3-month dosing period specifically developed for ovarian suppression in patients with breast cancer could fill this unmet need. TOL2506 is a 3-month, extended-release formulation of 30 mg of LA. This combination of active drug and in situ polymeric extended release technology is expected to deliver higher exposure to drug than the currently available 3-month (22.5 mg) formulations of LA marketed for advanced prostate cancer and potentially reduce escapes in E2 over the dosing period. Methods: TOL2506A (OVELIA) is a phase 3, single arm, open-label study evaluating the effectiveness of TOL2506 to suppress ovarian function in premenopausal women with HR+, HER2-negative breast cancer. Approximately 250 subjects will be enrolled targeting 220 evaluable subjects, with 30% aged 40 years or younger. Subjects must be premenopausal women, age 18-49 (inclusive), with a diagnosis of Stage I, II, or III HR+, HER2-negative breast cancer (ER>1% and/or, PR>1%, HER2-negative per ASCO CAP guidelines), who are candidates for ovarian suppression with endocrine therapy. For subjects receiving chemotherapy, premenopausal status will be determined prior to initiating chemotherapy. Male subjects with HR+, HER2-negative breast cancer may also be eligible, but will be evaluated for safety analyses only. Eligible subjects will enter the 48 week Treatment Period in 2 groups: those receiving tamoxifen concurrently with TOL2506 or those who initiate therapy with an aromatase inhibitor (AI; letrozole, anastrozole, or exemestane) beginning 6 weeks after the first administration of TOL2506, if E2 < 20 pg/mL has been achieved. After Week 12, subjects will be allowed to switch from receiving an AI to receiving tamoxifen or from tamoxifen to AI at the Investigator's discretion. Subjects will receive 4 doses of TOL2506 every 12 weeks over the 48 week study duration. The primary endpoint to be evaluated is ovarian suppression, defined as \geq

90% of subjects with LH levels < 4 IU/L at Week 6. Secondary endpoints include suppression of LH, E2 (< 20 pg/mL for tamoxifen cohort and < 2.72 pg/mL for AI cohort) and absence of menses at weeks 6, 12, 24, 36, and 48. NCT04906395

Disclosure(s):

Ryan Turncliff, PhD: Tolmar Inc: Salary (Ongoing)

Erika Hamilton, MD: Abbvie: Research Funding - Paid to Institution (Ongoing); Accutar Biotechnology: Research Funding - Paid to Institution (Ongoing); Acerta Pharma: Research Funding - Paid to Institution (Ongoing); ADC Therapeutics: Research Funding - Paid to Institution (Ongoing); AKESOBIO Australia: Research Funding - Paid to Institution (Ongoing); Amgen: Research Funding - Paid to Institution (Ongoing); Aravive: Research Funding - Paid to Institution (Ongoing); Arcus: Consulting Fees to Institution (Ongoing); ArQule: Research Funding - Paid to Institution (Ongoing); Artios: Research Funding - Paid to Institution (Ongoing); Arvinas: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); AstraZeneca: Study sponsor, consulting fees and research grant paid to institution (Ongoing); AtlasMedx: Research Funding - Paid to Institution (Ongoing); Black Diamond: Consulting and Research Funding - Paid to Institution (Ongoing); Bliss BioPharmaceuticals: Research Funding - Paid to Institution (Ongoing); Boehringer Ingelheim: Consulting and Research Funding - Paid to Institution (Ongoing); Cascadian Therapeutics: Research Funding to Institution (Ongoing); Clovis: Research Funding to Institution (Ongoing); Compugen: Research Funding to Institution (Ongoing); Cullen-Florentine: Research Funding to Institution (Ongoing); Curis: Research Funding to Institution (Ongoing); CytomX: Consulting Fees and Research Funding to Institution (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Dana Farber Cancer Inst: Research Funding to Institution (Ongoing); Dantari: Consulting Fees and Research Funding to Institution (Ongoing); Deciphera: Consulting Fees and Research Funding to Institution (Ongoing); Duality Biologics: Research Funding to Institution (Ongoing); eFFECTOR Therapeutics: Research Funding to Institution (Ongoing); Eisai: Consulting Fees to Institution (Ongoing); Ellipses Pharma: Research Funding to Institution (Ongoing); Elucida Oncology: Research Funding to Institution (Ongoing); EMD Serono: Research Funding to Institution (Ongoing); Fochon: Research Funding to Institution (Ongoing); FujiFilm: Research Funding to Institution (Ongoing); G1 Therapeutics: Research Funding to Institution (Ongoing); Greenwich Lifesciences: Consulting Fees to Institution (Ongoing); H3 Biomedicine: Consulting Fees and Research Funding to Institution (Ongoing); Harpoon: Research Funding to Institution (Ongoing); Hutchinson MediPharma: Research Funding to Institution (Ongoing); Immunogen: Research Funding to Institution (Ongoing); Immunomedics: Research Funding to Institution (Ongoing); Incyte: Research Funding to Institution (Ongoing); Infinity Pharmaceuticals: Research Funding to Institution (Ongoing); InvestisBio: Research Funding to Institution (Ongoing); iTeos: Consulting Fees to Institution (Ongoing); Jacobio: Research Funding to Institution (Ongoing); Janssen: Consulting Fees to Institution (Ongoing); Karyopharm: Research Funding to Institution (Ongoing); Leap Therapeutics: Research Funding to Institution (Ongoing); Lilly: Consulting Fees and Research Funding to Institution (Ongoing); Loxo: Consulting Fees to Institution (Ongoing); Lycera: Research Funding to Institution (Ongoing); Mabspace Biosciences: Research Funding to Institution (Ongoing); MacroGenics: Research Funding to Institution (Ongoing); MedImmune: Research Funding to Institution (Ongoing); Merck: Consulting Fees and Research Funding to Institution (Ongoing); Mersana: Consulting Fees and Research Funding to Institution (Ongoing); Merus: Research Funding to Institution (Ongoing); Millennium: Research Funding to Institution (Ongoing); Molecular Templates: Research Funding to Institution (Ongoing); Myraid Genetic Laboratories: Research Funding to Institution (Ongoing); Novartis: Consulting Fees and Research Funding to Institution (Ongoing); Nucana: Research Funding to Institution (Ongoing); Olema: Research Funding to Institution (Ongoing); OncoMed: Research Funding to Institution (Ongoing); Onconova Therapeutics: Research Funding to Institution (Ongoing); ORIC

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OT3-05-01

Adaptive Multi-Drug Treatment of Evolving Cancers (AMTEC): A Phase II, Open-Label, Study of Olaparib in Combination with either Durvalumab, Selumetinib or Capivasertib, or Ceralasertib Monotherapy in Patients with Metastatic TNBC

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BACKGROUND PARP inhibitors (PARPi) afford a rational therapeutic strategy in metastatic TNBC (mTNBC) due to the high incidence of dysregulated DNA damage repair mechanisms and high-level genomic instability that resemble tumors originating in germline BRCA-mutated carriers. However, PARPi monotherapy has limited efficacy in BRCA wild-type mTNBC; in BRCA mutant disease following initial response, compensatory mechanisms inevitably restore replication fork protection. AMTEC leverages pre- and on-therapy biopsies from a 4-week PARPi monotherapy run-in period for personalized biomarker-driven patient selection to interdict adaptive resistance to the PARPi. Data from our pilot study (NCT03544125) and from Arm 1 of AMTEC (olaparib + durvalumab) identified PI3K-AKT, RAS-MEK, and ATR/CHK1/WEE1 as targetable pathways contributing to PARPi adaptive resistance in individual participants. Clinically validated assays (DNA, RNA, and protein) enable the identification of cellular mechanisms of PARPi sensitivity and resistance in individual patients and further reveal combined drug treatments that could prevent emergence of PARPi resistance. METHODS AMTEC is a non-comparative, multi-arm, open-label, phase II study to assess the efficacy of combining olaparib (ola) with durvalumab (dur), or MEKi, selumetinib (sel), or AKTi, capivasertib (cap), or monotherapy with ATRi, ceralasertib, (cer mono) in mTNBC patients. Participants with biopsy proven mTNBC (ER< 10%, PR< 10%, and HER-2 non-amplified), AR< 80% are eligible. - Participants undergo a pre-treatment biopsy, then start a 28-day induction with ola (300 mg PO BID, D1-28). On C1D14, patients undergo a repeat, on-treatment biopsy. Clinically validated assays (DNA, RNA, protein) from both biopsies inform patient assignment to a specific ola combination arm starting on C2D1: - Arm 1 tumor immune

activated: ola + dur (1500 mg IV Q4W) - Arm 2 RAS-MEK-ERK pathway activation: ola + sel (BSA-based BID D1-28) - Arm 3 PI3K-AKT pathway activation: ola + cap (400 mg PO BID, 4 days on/3 days off) - Arm 4: If not eligible for Arms 1-3 (per biomarker selection criteria): Cer mono (240 mg PO BID D1-14) Endpoints: The primary endpoint is objective response rate (ORR per RECIST 1.1). Secondary endpoints include safety and toxicity, clinical benefit rate, duration of response, and survival. Statistical Methods: - Arm 1 will enroll 28 patients to detect an ORR difference of 20% ($H_0: \pi = 0.15$ and $H_a: \pi = 0.35$). Arm 1 will continue on to stage 2 if ORR ≥ 3 of the first 15 patients. The null hypothesis for Arm 1 is rejected if $\geq 7/28$ patient achieve a response. - Arms 2, 3, and 4, will each enroll 22 patients to detect an ORR difference of 25% ($H_0: \pi = 0.15$ and $H_a: \pi = 0.40$). Arms 2, 3, and 4 will each continue on to stage 2 if ORR ≥ 2 of first 11 patients in each arm, respectively. The null hypothesis for Arm 2, 3, and 4 is rejected if $\geq 7/22$ patients achieve a response in each arm, respectively. For arms 2 and 3, if there are $\geq 5/11$ responses, the trial will open a biomarker negative expansion cohort for each arm (N = 19 patients/arm). ENROLLMENT The study was activated on 1/7/2019. Arm 1 met pre-specified interim analysis criteria in 12/2020, and accrual to stage 2 began in 1/2021. Arms 2, 3, and 4 start enrolling in Q4 of 2022. Up to 132 patients will be enrolled. Clinical trial information: NCT03801369 Contact information: For more information or to refer a patient, email hobbev@ohsu.edu

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OT3-06-01

Diminishing Chemotherapy Related Side Effects through Patient Education

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Background At the Penn State Cancer Institute (PSCI), there is currently a lack of patient education materials regarding self-management of cytotoxic chemotherapy related side effects, thus leading to use of disreputable sources (online searches) by cancer patients. A standardized brochure developed by our team aims to educate patients about commonly experienced chemotherapy related side effects. It also provides patients with tools to address these problems themselves, information on when to contact their medical oncologist, and brief guidance on when it is appropriate to visit the Emergency Department. We hypothesize that effective patient education through the brochure will improve patient related outcomes and quality of life. Moreover, empowering patients with such a trustworthy resource will decrease anxiety and distress related to their treatments. If this intervention is found to be impactful, it could be expanded to other cancer types within PSCI and eventually to other institutions across the country. Trial design • Recruitment and Screening: Chemotherapy naïve patients with breast cancer are recruited from our institution, screened, and enrolled on a rolling basis • Baseline Visit: Consent, receive the brochure, and complete the following questionnaires: the Patient Education Material Assessment Tool (PEMAT), Emotional Thermometer Scales (ETS), and Memorial Symptom Assessment Scale (MSAS) • PEMAT is utilized to evaluate if a teaching material is understandable and promotes action, which will help determine if the

brochure itself is an effective education tool • ETS is utilized to evaluate the mental health, specifically measuring distress, anxiety, depression, and anger • MSAS is a validated patient rated instrument for evaluation of diverse group of symptoms commonly seen with chemotherapy • Follow Up Visits: Fill out the same 3 surveys again at their 6-week and 12-week visits • Patients will fill out the same questionnaires to assess changes over time, a surrogate for effectiveness of the brochure • Surveys take about 12 minutes to complete on average Eligibility Criteria 1. Adult with Breast cancer >18 years of age 2. Chemotherapy naive, will either start cytotoxic chemotherapy in the next 6 weeks or have started cytotoxic chemotherapy in the past 6 weeks prior to enrollment 3. May receive multiple forms of therapy such as immunotherapy, targeted treatment, endocrine therapy or radiation as long as they receive concurrent cytotoxic chemotherapy 4. Ability to understand and read written English or Spanish without any functional difficulty 5. ECOG performance status 0-3 6. May be involved with other cancer trials being offered at the PSCI Specific Aims • Primary Outcome: Determine if effective patient education through a standardized brochure will improve patient related outcomes and quality of life • Secondary Outcome: Drop-out rate after the baseline visit Statistical methods • Outcome variables from survey-based questionnaires will be measured at all three time points • Their distribution at time points will be summarized using numerical and graphical methods • Paired-sample tests will be used to compare the difference between visits' data • Linear mixed-effect models for repeated measures will be used to examine the overall pattern by using data from all three time points • All tests will be two-sided with a significance level of 0.05 • We do not plan to do adjustments for multiple testing Present accrual and target accrual: • 24 total accrued, 14 completed • 60 target accrual • Plan to approach 70-75 patients and anticipate a 10-15% dropout rate which was considered in determining accrual goals Contact: • Corresponding Author: Shelby Labe SLabe1@pennstatehealth.psu.edu • PI: Monali Vasekar, MD MVasekar@pennstatehealth.psu.edu

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Real-World Data on First-line Treatment of HR-positive, HER2-negative, Metastatic Breast Cancer in Brazil (BRAVE Study / LACOG 0221)

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Background: It is estimated that 50 thousand patients live with metastatic breast cancer (MBC) in Brazil. A recent Brazilian registry (LACOG 0312) on MBC demonstrated a median overall survival (OS) by breast subtype of 15 months for triple negative, 23 months for HER2 positive, and 42 months for Luminal tumors, which are very similar to developed countries except the HER2 positive group which have limited access to targeted agents in the public health system. Recently, CDK 4/6 inhibitors were approved for the treatment of HR+ HER2-negative MBC with an improvement in progression-free survival (PFS) and ribociclib and abemaciclib demonstrating benefit in OS over endocrine therapy alone, establishing the standard of care in first-line setting for this BC subtype. In Brazil, disparities exist in the incorporation of novel anticancer agents between public and private health systems limiting treatment options for patients with HR+ HER2- negative MBC in the public system, which covers most of the population. The BRAVE study aims to describe the patient journey and current patterns of care for HR+ HER2-negative MBC to identify possible gaps and how health insurance type influences treatment patterns in Brazil. Trial Design: This is an observational, retrospective cohort study. All patients diagnosed with mBC (either de novo or recurrent) in the period of January 2018 to December 2020 at participating centers will be included. Data will be collected from medical records. No interventions are proposed. Enrollment of a total of 300 patients (150 patients from public health care system and 150 patients from private health care system) is planned. ClinicalTrials.gov identifier: NCT05034393. Eligibility: Inclusion criteria: women ≥ 18 years old; histologically confirmed HR-positive HER2-negative invasive breast cancer; HR-positive, defined as 1% to 100% of tumor nuclei positive for ER and/or PgR as per ASCO/CAP Guideline 2020 or Allred score of ≥ 3 ; HER2-negative, defined as IHC result is 0/1+ or 2+ with ISH negative as per ASCO/CAP Guideline 2018; diagnosed with de novo or recurrent metastatic breast cancer between January 2018 and December 2020. Exclusion criteria: male BC; first-line treatment for mBC received through clinical trial. Specific Aims: Primary objective is to describe the first-line (1L) treatment of HR-positive, HER2-negative mBC in Brazil. Secondary objectives are to describe progression-free survival (PFS) in the 1L setting until

month 24; describe and compare the 1L treatment of HR-positive, HER2-negative mBC and PFS until month 24 according to the health care coverage (public vs. private); describe timelines from symptoms, histopathological diagnosis, molecular test, and treatment; describe the mBC pathological characterization; describe frequency of diagnostic tests to define breast cancer molecular subtypes; describe the subsequent line of treatment and corresponding PFS; describe overall survival (OS); evaluate PFS and OS according to visceral vs. non-visceral metastatic disease, primary endocrine resistance vs. acquired endocrine resistance, de novo versus recurrent disease, public vs. private health system and pre vs postmenopausal status. Statistical Methods: No a priori sample size calculation was performed. The expected sample size of 150 patients in each group allows description of the proportion of patients using CDK 4/6 inhibitors with two-sided 90% confidence interval ranging from 53.4% to 66.6% when the expected proportion is 60% in the private health system. Present Accrual and Target Accrual: A total of 12 sites of 14 planned were activated. The first patient was enrolled on February 8, 2022. As of June 24, 2022, a total of 122 patients were enrolled, 86 from public and 36 from private health system. The target accrual of 300 patients is expected to be completed by November 2022. Results are expected to be presented by April 2023. Funding: Novartis. Acknowledgements: SAS.

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A phase 1 trial of LOXO-783, a potent, highly mutant-selective, brain-penetrant allosteric PI3K α H1047R inhibitor in PIK3CA H1047R-mutant advanced breast cancer (aBC) and other solid tumors (PIKASSO-01, trial in progress)

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Background: Phosphoinositide 3-kinase alpha (PI3K α) H1047R mutations are activating oncogenic events that occur in ~15% of breast cancers (BC). Available PI3K α inhibitors target both wild-type (WT) and mutant PI3K α and, as a result, their efficacy may be limited by on-target WT PI3K α -mediated toxicities, including hyperglycemia, skin rash, and diarrhea. LOXO-783 is an oral, potent and highly mutant-selective, brain-penetrant allosteric PI3K α H1047R inhibitor. Preclinically, LOXO-783 is highly selective for PI3K α H1047R over WT PI3K α and other PI3K isoforms and induces single-agent tumor regressions in ER+, HER2- PI3K α H1047R-mutant BC models without causing hyperglycemia or increases in plasma insulin / C-peptide. LOXO-783 also demonstrates brain penetration in vivo with dose-dependent tumor growth inhibition in brain metastasis models. This trial investigates LOXO-783 alone and in combination with other anticancer therapies in patients with PIK3CA H1047R-mutant aBC and

other solid tumors.

Trial Design: This global, first-in-human phase 1a/b study of LOXO-783 includes dose escalation of LOXO-783 monotherapy followed by dose expansion of LOXO-783 alone and in combination with other anticancer therapies (Table). Monotherapy dose escalation will be evaluated using a modified toxicity probability interval-2 (mTPI-2) design. In dose expansion (Parts A-E), each combination cohort will include a safety lead-in of 3-6 patients. Men and premenopausal women with ER+ aBC must receive concomitant treatment with a GnRH agonist. An optional pharmacodynamic (PD) biomarker sub-study will be conducted at select dose levels during dose escalation in patients with ER+, HER2- aBC with soft tissue disease amenable to safe repeat tumor biopsies.

Eligibility criteria: Eligible patients must have PIK3CA H1047R-mutant aBC or other solid tumors with measurable disease or non-measurable bone-only disease (aBC patients only). In dose escalation, patients may have received up to 5 prior regimens. In dose expansion, prior therapy requirements are outlined in the Table below. Key exclusion criteria include prior inhibitor(s) of PI3K/AKT/mTOR (except in dose escalation or in select patients with prior intolerance of these inhibitors), colorectal cancer, endometrial cancer with concurrent PI3K/AKT/mTOR and/or RAS/RAF alterations and diabetes mellitus (DM) requiring medication (except in Part C).

Study objectives: Recommended phase 2 dose (RP2D) determination; safety and tolerability assessment, PK and PD evaluation, objective response rate and clinical benefit rate assessment per RECIST v1.1. Recruitment is ongoing (PIKASSO-01, NCT05307705).

Table. Dose Expansion (Phase 1b)

Patient Subgroup	Key Eligibility	Study Drugs (Cohort)
Part A: ER+, HER2- aBC	<ul style="list-style-type: none"> ≤2 prior regimens for aBC Prior CDK4/6 inhibitor (CDK4/6i) required 	<ul style="list-style-type: none"> LOXO-783 + Fulvestrant (FUL) LOXO-783 + Imlunestrant (selective estrogen receptor degrader)
Part B: ER+, HER2- aBC	<ul style="list-style-type: none"> ≤2 prior regimens for aBC 	<ul style="list-style-type: none"> LOXO-783 + aromatase inhibitor + Abemaciclib LOXO-783 + FUL + Abemaciclib LOXO-783 + Imlunestrant + Abemaciclib
Part C: ER+, HER2- aBC	<ul style="list-style-type: none"> ≤5 prior regimens for aBC Prior CDK4/6i required Stable Type 2 DM (HbA1c ≤ 8% and not requiring insulin) 	<ul style="list-style-type: none"> LOXO-783 + FUL
Part D: aBC	<ul style="list-style-type: none"> ≤5 prior regimens for aBC 	<ul style="list-style-type: none"> LOXO-783 + Paclitaxel
Part E: Solid tumors	<ul style="list-style-type: none"> ≤3 prior regimens for aBC 	<ul style="list-style-type: none"> LOXO-783

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Clinical Trial of Alpelisib and Tucatinib in Patients with PIK3CA-Mutant HER2-Positive Metastatic Breast Cancer

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Phosphatidylinositol 3-kinase (PI3K) pathway plays a key role in resistance to the drugs targeting human epidermal growth factor receptor 2 (HER2). Activating mutations in the gene encoding alpha catalytic subunit of PI3K (PIK3CA) are present in approximately 30% of HER2+ tumors. PIK3CA mutations are linked to drug resistance and decreased survival in patients with HER2+ breast cancer. To overcome this resistance mechanism, we designed a phase IB/II clinical trial to evaluate the combination of HER2 small molecule inhibitor tucatinib with PI3K inhibitor alpelisib in patients with HER2+ metastatic breast cancer (NCT05230810). This multicenter clinical trial is conducted through the Academic Breast Cancer Consortium (ABRCC), with the University of Colorado Cancer Center as the lead site. Target enrollment: 40 patients. This is a run-in phase IB / roll-over phase II study. Phase IB will follow Time-to-Event Bayesian Optimal Interval design and enroll from 9 to 19 patients to find the maximum tolerated doses (MTDs) of tucatinib and alpelisib. From 21 to 31 patients will be enrolled in phase II part, for a total of 40 patients in the final efficacy analysis. Main inclusion criteria: 1. Women and men \geq 18 years old 2. Eastern Cooperative Oncology Group (ECOG) performance status 0-1 3. Presence of activating PIK3CA mutation in the tumor 4. Patients with HR-/HER2+ or HR+/HER2+ breast cancer may enroll; ovarian suppression is mandatory for premenopausal patients with HR+/HER2+ disease 5. HR+/HER2+ patients should be agreeable to concomitant treatment with fulvestrant 6. Prior treatment with at least two FDA-approved HER2-targeted agents 7. Measurable or evaluable disease. Bone only disease is allowed. 8. Subjects with untreated central nervous system (CNS) metastases not needing immediate local therapy, and subjects with previously treated stable or progressive brain metastases may enroll, provided that there is no indication for immediate re-treatment. For patients with treated CNS metastases: time from treatment of CNS disease until the first dose of study drugs should be as follows: WBRT \geq 21 days, surgical resection \geq 14 days, SRS \geq 7 days. 9. Adequate organ and marrow function Main exclusion criteria: 1. Contraindications to undergo contrast brain MRI 2. Leptomeningeal disease 3. Poorly controlled seizures 4. Diabetes mellitus type I, or uncontrolled diabetes mellitus type II 5. Acute pancreatitis within 1 year of screening, or history of chronic pancreatitis 6. History of severe cutaneous hypersensitivity reactions 7. Toxicities of prior cancer therapies that have not resolved to grade 1 or less, except peripheral neuropathy, which must have resolved to grade 2 or less, and alopecia 8. Previous treatment with EGFR or HER2 tyrosine kinase inhibitors, or PI3K/mTOR/AKT inhibitors. 9. Systemic anti-cancer therapy, palliative radiation to extracranial sites, or surgery within 2 weeks of the first dose of study drugs 10. Active bacterial, fungal, or viral infections, hepatitis B, C, or HIV 11. Clinically significant cardio-vascular disease Primary objectives: • Phase IB: safety and tolerability of combination therapy • Phase II: efficacy by progression free survival Exploratory assessment of biomarkers will be performed in the liquid biopsy samples. Study contact: Elena Shagisultanova, MD, PhD, elena.shagisultanova@cuanschutz.edu

Disclosure(s):

Elena Shagisultanova, MD, PhD: Novartis: Funding for investigator initiated clinical trials (Ongoing); Pfizer: Funding for investigator initiated clinical trials (Ongoing); Seagen: Funding for investigator initiated clinical trials (Ongoing)

Kari B. Wisinski, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Context: Contracted Research (Ongoing), Contracted Research (Ongoing); DSI: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Genentech/Roche: Contracted Research (Ongoing), Contracted Research (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing);

Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Relay Therapeutics: Contracted Research (Ongoing), Contracted Research (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); Seagen: Contracted Research (Ongoing), Contracted Research (Ongoing)

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Farrah M. Datko, MD: No financial relationships to disclose

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12/8/2022

5:00 PM - 6:15 PM

OT3-11-01

TK IMPACT: Treatment Monitoring of Hormone Receptor Positive (HR+), HER2 Negative (HER2-) Metastatic Breast Cancer (MBC) Patients Receiving CDK 4/6 Inhibitors (CDK4/6i) with DiviTum® Thymidine Kinase 1 Activity

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Background: CDK 4/6i have altered the therapeutic landscape of HR+, HER2- MBC, improving progression free and overall survival (PFS and OS) compared to endocrine therapy (ET) alone. Despite durable responses to CDK 4/6i in a large majority of patients, treatment response monitoring in this population has historically included numerous serial blood-based and imaging studies at frequent time points. There is a growing global interest in utilizing novel non-invasive biomarker-driven disease monitoring assessments to improve patient outcomes and reduce health care costs. Thymidine kinase 1 (TK1), a key cell-cycle regulated enzyme important for nucleotide metabolism during DNA synthesis, is regulated by the E2F pathway, downstream of CDK 4/6. Studies have shown that DiviTum® TK1 activity (TKa) may serve as both a prognostic and predictive biomarker of CDK 4/6i treatment response (McCartney et al, Clin Canc Res, 2020; Malorni et al, Eur J Cancer, 2022; Bagegni et al, Breast Cancer Res, 2017). Early TKa suppression within 2 weeks (wk) post CDK 4/6i therapy initiation is associated with improved PFS, suggesting a subgroup of patients who may be able to de-escalate imaging frequency. Elevated TKa at baseline and post CDK 4/6i may identify patients with CDK 4/6i-resistant disease and disease progression (PD) requiring early therapy modification. TK IMPACT is a prospective, single-arm trial designed to assess the impact of incorporation of DiviTum® TKa on a physician's decision regarding subsequent timing of routine disease monitoring modalities in patients with advanced HR+, HER2- MBC receiving ET plus CDK 4/6i (NCT04968964). Methods: Blood sample collections will be analyzed using DiviTum® TKa at baseline (bl), wk 2, 4, 6, 8, and Q 4 wks thereafter beginning at wk 8 during the first 24-wk time period of study enrollment (+/- 3 days); followed by Q 12 wks thereafter, until PD or 36 months, whichever occurs first. Optional repeat TKa within 2-4 wks (+/-3 days) is permitted in case of rising TKa. Research blood (bl, wk 2, 12, 24, 48, and PD) and optional archival tumor tissue collection at diagnosis and PD will be obtained for correlatives. The investigator will record intended imaging modalities and timing prior to receipt of TKa, followed by documentation of any changes in imaging testing interval after receipt of TKa. Key eligibility criteria include postmenopausal women age ≥18 years with HR+, HER2- MBC, to initiate (Cohort 1) or are currently receiving (≤24 months, Cohort 2) any FDA approved first line ET plus CDK 4/6i with a life expectancy > 6 months. The primary endpoint is any physician-reported intended change in imaging testing interval post TKa by study cohort, within the first 48-wk period of study participation. Key secondary endpoints are concordance rate between TKa values and progression status at first on-study imaging and longitudinal TKa dynamics. Key exploratory endpoints include plasma and tumor tissue-based biomarkers of CDK 4/6i response and resistance. A total of 40 patients will be enrolled (n=20/Cohort). The expected change rate is 20% with a 95% Wilson confidence interval of 0.105~0.248 across all patients and if within each cohort, with a 95% Wilson confidence interval of 0.081~0.416 for N=20. N=40 allows the lower limit of the 95% CI > 10% and that of the N=20 in Cohort 1 to be ~10%, indicating some clinically meaningful influence of

TKa progression on patient management. The study is open to accrual and has presently enrolled 5 patients.

Disclosure(s):

Nusayba A. Bagegni, MD: Ambrx Inc: Contracted Research (Ongoing), Institutional research funding, no personal payments (Ongoing); AstraZeneca Pharmaceuticals LP: Contracted Research (Ongoing), Institutional research funding, no personal payments (Ongoing); Biovica International AB: Contracted Research (Ongoing), Institutional trial funding, no personal payments (Ongoing); Daiichi Sankyo: Contracted Research (Ongoing), Institutional research funding, no personal payments (Ongoing); Novartis Pharmaceuticals Corporation: Contracted Research (Ongoing), Institutional research funding, no personal payments (Ongoing); Pfizer Inc: Contracted Research (Ongoing), Institutional research funding, no personal payments (Ongoing); Sarah Cannon Development Innovations LLC: Contracted Research (Ongoing), Institutional research funding, no personal payments (Ongoing); Seattle Genetics Inc: Contracted Research (Ongoing), Institutional research funding, no personal payments (Ongoing); Sermonix Pharmaceuticals: Contracted Research (Ongoing), Institutional research funding, no personal payments (Ongoing); Xcovery Holding Company, LLC: Contracted Research (Terminated, March 31, 2022), Institutional trial funding, no direct personal payments (Terminated, March 31, 2022)

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Amy Williams, n/a: Biovica: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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12/8/2022

5:00 PM - 6:15 PM

OT3-11-02

SOLTI-1910: Predicting olaparib sensitivity in patients with unresectable locally advanced/metastatic HER2-negative breast cancer with BRCA1/2, PALB2, RAD51C/D mutations or HRD by the RAD51 test: RADIOLA TRIAL

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Background The OlympiAD trial evaluated the PARP inhibitor (PARPi) olaparib versus a non-platinum standard chemotherapy in HER2-negative metastatic breast cancer (MBC) patients with a germline BRCA1/2 (gBRCA) mutation. Olaparib resulted in improved progression-free survival (PFS) and doubled the response rate vs chemotherapy. Nevertheless, the response rate to PARPi is ~60% in the gBRCA1/2 population with MBC (current approval), suggesting a limited positive predictive value of gBRCA1/2 status. Moreover, patients with other relevant Homologous Recombination Repair defects (HRD) such as PALB2 or RAD51C/D mutation carriers, or HRD epigenetic silencing, are not captured with a gBRCA analysis. We have previously shown that the functional HRD biomarker RAD51, tested in FFPE tumor samples using an optimized immunofluorescence-based assay, is associated with platinum response in early TNBC and PARPi response in preclinical BC models. We hypothesize that the RAD51 test would help to expand the clinical benefit of PARPi by predicting response to olaparib in MBC with germline/somatic BRCA1/2, PALB2 or RAD51C/D mutation and beyond. Study design RADIOLA is an open-label, single-arm, multicentre phase II study evaluating treatment with olaparib in male or female ≥18 years patients with HER2-negative MBC with ≤ two prior chemotherapy lines in two cohorts: cohort 1 (N=41) with known germline/somatic BRCA1/2, PALB2 or RAD51C/D mutation; cohort 2 (N=25) with functional HRD, namely RAD51-low score (≤10%), in wild-type/unknown mutation status at study entry. All patients will receive olaparib 300mg po BID until progression or unacceptable toxicity. Primary objective will assess, in terms of overall response rate (ORR), the capacity of the RAD51 score to predict olaparib efficacy in cohort 1. Secondary objectives include PFS, clinical benefit rate, duration of response, safety in both cohorts and ORR in cohort 2. Recruitment Recruitment (11 sites) started in March 2022. As of July 2022, 7 patients have been enrolled in Spain. Funding This study is financially supported by AstraZeneca.

Disclosure(s):

Judith Balmaña, MD: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Travel assistance (Ongoing); Pfizer: Conferences (Terminated, April 15, 2022)

Tomás Pascual, MD: Astra Zeneca: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Terminated, June 28, 2022); Pfizer: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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5:00 PM - 6:15 PM

OT3-11-03

The PREDICT Registry Australia: A prospective registry to evaluate the clinical utility of a 7-gene predictive biosignature on treatment decisions in patients with ductal carcinoma in situ

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Background: For women with ductal carcinoma in situ (DCIS) treated with breast conserving surgery (BCS), the benefit of adjuvant radiation therapy (RT) remains controversial. Since there is level 1 evidence supporting the role of RT in reducing the risk of local recurrence, current guidelines generally recommend RT for all women having BCS even though the absolute benefit is variable. In response to the need for prognostic and predictive tools to better assess risk and RT benefit, a 7-gene predictive biosignature (DCISionRT, PreludeDx, Laguna Hills, CA) was developed. The test provides a validated score (DS) for assessing 10-year risk of recurrence and RT benefit using individual tumor biology, as assessed by clinical and pathologic biomarkers. The primary objective of the PREDICT registries is to understand the decision impact such a tool has on treatment decisions. Prospective Clinical Trial Design: This is a multicenter, prospective, observational registry for women diagnosed with DCIS in Australia. After DCIS diagnosis, sites will send the most representative tissue block or sections mounted on charged slides to the PreludeDx lab for biosignature testing. Treating physicians will complete a treatment recommendation survey before and after receiving the biosignature test results. Test results, treatment recommendations, patient preferences and clinicopathologic features will be stored in a de-identified registry for participating institutions from a variety of geographic regions across Australia. Women will then be followed for up to 10 years with completion of a follow-up form. The study has been approved by the North Shore Local Health District Human Research Ethics Committee, St Leonards, NSW, Australia. Universal Trial Number (UTN): U1111-1266-0439; ANZCTR: ACTRN12621000695808; ClinicalTrials.gov: NCT04916808. Eligibility Criteria: The study includes females age 26 or older who are candidates for BCS and eligible for RT and/or systemic treatment. Subjects must not have been previously treated for DCIS or have previous or current invasive or micro-invasive breast cancer. Specific Aims: The primary endpoints are changes in treatment recommendations for surgical, radiation and hormonal therapy. Secondary endpoints are identification of key drivers for treatment recommendations, including age, size, grade, necrosis, hormone receptor status, patient preference and biosignature status. Statistical Methods: Changes in pre- and post-DCISionRT treatment recommendations will be analyzed using McNemar's test (alpha level = 0.05). Multivariate logistic regression will be used to determine odds ratios of clinicopathologic factors leading to pre- and post-test treatment recommendations. Pre-test covariates include patient age, tumor size, palpability, margin status, hormone receptor status, nuclear grade, tumor necrosis, family history of breast cancer, race, ethnicity and patient preference, as well as physician specialty (surgeons vs. radiation oncologists) and post-test covariates will also include the DCISionRT Decision Score (DS). Differences in recurrence-free and overall survival will be assessed by Kaplan-Meier survival analysis using the log-rank test and/or the Cox Proportional Hazards model. Statistical analyses will be carried out using R (<https://www.r-project.org>) or SAS. An early interim analysis based on the first 200 enrolled patients is currently underway. Present and Planned Accrual: We are planning to enroll up to 1,500 women from up to 100 sites across Australia. A similar registry has recently completed enrollment of 2,500 women from 68 sites in the US.

Disclosure(s):

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OT3-12-01

Immunological predictors of nodal response in breast cancer patients undergoing neoadjuvant therapy

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Immunological predictors of nodal response in breast cancer patients undergoing neoadjuvant therapy Maria Luisa Gasparri¹, Ilary Ruscito², Filippo Bellati², Fabio Corsi³, Rosa Di Micco⁴, Oreste D. Gentilini⁴, Thorsten Kuehn⁵, Andrea Papadia¹, Donatella Caserta², Lorenzo Rossi⁶, Arianna Calcinotto⁷ ¹ Department of Gynecology and Obstetrics, Ente Ospedaliero Cantonale, Ospedale Regionale di Lugano, Lugano, Switzerland ² Department of Medical and Surgical Science and Translational Medicine, Sapienza University of Rome, Azienda Ospedaliera

Sant'Andrea, Rome, Italy 3 Breast Unit, Department of Surgery, Istituti Clinici Scientifici Maugeri IRCCS, Pavia, Italy; Department of Biomedical and Clinical Sciences "Luigi Sacco", Università di Milano, Milan, Italy 4 Breast Surgery Unit, San Raffaele University Hospital, Milan, Italy 5 Interdisciplinary Breast Center, Department of Gynecology and Obstetrics, Klinikum Esslingen, Esslingen, Germany 6 Oncology Institute of Southern Switzerland, Bellinzona, Switzerland 7 Cancer Immunotherapy lab, IOR Institute of Oncology Research, Bellinzona, Switzerland Background: Almost 20% of breast cancer patients present at diagnosis with clinically positive nodes. Most of these patients undergo neoadjuvant therapy in order to de-escalate the axillary surgery in case of response (sentinel lymph node biopsy, targeted axillary dissection or targeted axillary dissection, instead of an axillary lymphadenectomy). The conversion from positive to negative nodes after neoadjuvant therapy is expected in approximately the 60% of the cases, depending by tumor subtypes. Several models have been proposed with the goal of identifying predictors of nodal response prior to neoadjuvant treatment. The immune system plays a pivotal role in cancer invasion and progression. Its role in treatment response is currently under investigation in several settings. Primary endpoint: to identify a preoperative immune profiling of breast cancer patients with nodal involvement at diagnosis and to correlate the immune changes after neoadjuvant therapy with the nodal response (macrometastases, micrometastasis, isolated tumor cells, complete response). Trial design: It is an international prospective cohort study including breast cancer patients undergoing standard neoadjuvant therapy, who present initially with biopsy-proven axillary lymph node metastasis. Ten immune markers will be analyzed using immunohistochemistry and tissue microarray in primary tumor and nodal tissue samples (tumor associated neutrophils, CD4 lymphocytes, CD8 lymphocytes, T regulatory cells, Macrophages, Follicular dendritic cells(DC), plasmacytoid DC, interdigitant DC, mature DC, Lysosomal associated membrane protein 3). The tissue analysis will be performed on the biopsy collected at diagnosis (prior to neoadjuvant therapy) and during the axillary surgery (after neoadjuvant therapy). Target accrual/sample size: 210 patients Statistical analysis: To compare the distribution of immune cells according to the state of lymph node metastasis, Student's t test will be performed. Pearson's chi-square test will be used to evaluate the correlation between immune profile and nodal response, based on clinic-pathological features. Odds ratios (ORs) and 95% confidence intervals (CIs) will be calculated using logistic regression analysis. Multivariable analysis will be performed using the multivariable logistic regression model. Logistic regression models will be used to identify the clinical, pathologic and immunological variables associated with the nodal response. P-values less than 0.05 will be considered significant. Analyses will be performed using Microsoft IBM SPSS® version 20.0 for Mac. Current status: Recruitment has not started yet. Contact information: marialuisa.gasparri@eoc.ch

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OT3-13-01

First in Human Study of AG01 a chimerized monoclonal antibody to Progranulin/Glycoprotein 88 (GP88)

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Progranulin (PGRN/GP88) is an 88 kDa glycoprotein characterized by seven and a half double cysteine rich repeats in the granulin-epithelin family. PGRN/GP88 is an autocrine biological driver of tumorigenesis, survival & drug resistance in several cancers including breast, ovarian, multiple myeloma, prostate cancers, non-small cell lung carcinoma (NSCLCA) & digestive cancers. PGRN/GP88 tissue expression is an independent prognostic factor of recurrence while elevated serum PGRN/GP88 level in metastatic breast, lung & prostate cancer patients is associated with poor outcomes such as progression & shortened survival. An anti-human PGRN/GP88 monoclonal antibody inhibiting PGRN/GP88 action has been developed & expressed as recombinant antibody in CHO cells. Activities including pharmacology, manufacturing, formulation & GLP toxicology studies have been carried out. The IND application has been cleared by the Food and Drug Administration to proceed with the first-in-human AG01 clinical study in adult patients (pts) with advanced solid tumors. We present an ongoing First in Human Phase 1A (dose escalation, 1+(3+3) & 1B (expansion cohorts) study of AG01 in pts advanced solid tumor malignancies (1A) with 4 expansion cohorts (1B) in pts with advanced Triple Negative Breast Cancer (TNBC), Hormone Resistant ER+/Her2- BC, advanced NSCLC & mesothelioma. Study Design: This is an open-label, dose escalation study of AG01 antibody administered intravenously (IV) over 90 minutes every 14 days +/- 1 day (1A), followed by 4 predefined expansion cohorts, which will be treated at the RP2D determined in the phase 1A of this study. In the 1A part, initially accelerated titration design will be utilized to guide dose progression & estimation of the maximum tolerated dose (MTD and/or maximum administered dose (MAD). In the 1A portion of the study pts with advanced relapsed/refractory solid tumor malignancies who failed 1 or more standard of care (SOC) therapies (tx) or for whom no SOC tx exists will be accrued. The primary objective of the 1A part is to determine the MTD and/or MAD of AG01. Secondary objectives are to determine the RP2D, assess the safety/tolerability, the pharmacokinetics (PKs) & immunogenicity of AG01 & the preliminary anti-tumor activity of AG01 via RECIST 1.1. The exploratory objectives are to determine PGRN/GP88 expression in tumor tissue and PGRN/ GP88 blood levels using A&G's ELISA test. In the 1B Cohort Expansion phase, 4 separate cohorts of pts with PGRN/GP88 tissue expression of 1+, 2+, 3+ by IHC will be enrolled. Cohort 1- TNBC: ER and/or PR < 1% by IHC, HER2 < 3+ by IHC and/or FISH negative, pts must have failed 1 or more SOC tx for metastatic BC. Cohort 2- Hormone-resistant BC: ER and/or PR >1%, HER2 < 3+ by IHC and/or FISH negative, failed 1 or more prior hormonal tx (HT) or HT/CD4/6 kinase inhibitor tx or other targeted tx. Cohort 3- NSCLCA: metastatic/recurrent NSCLCA failed 2 or more SOC tx. Cohort 4 -Mesothelioma- failed 1 or more SOC tx for metastatic/recurrent mesothelioma or not a candidate for SOC tx. The primary objective of 1B part is to evaluate the antitumor efficacy of AG01 by overall response rate (ORR) defined as completed response (CR), partial response (PR), stable disease \geq 24 weeks (SD) (CR+PR+ SD) based on RECIST v1.1 in the 4 cohorts with each cohort assessed separately for response. Secondary objectives are to evaluate progression free survival (PFS), duration of response (DOR) & overall survival (OS) of pts in cohorts 1-4, & to evaluate the ORR, DOR & PFS based on GP88 tissue expression, to further characterize the PKs & the safety/tolerability of AG01. Exploratory objectives in 1B part will assess AG01 effect on circulating PGRN/GP88 levels in plasma or other potential biomarkers in the 4 cohorts. The estimated study sample is approximately 77 pts; 17 pts for the 1A part & 60 pts for 1B part. The study is open to accrual at the UMGCCC. Supported by NCI grants R44CA224718 and R44CA162629

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OT3-14-01

A longitudinal investigation of sociocultural and behavioral influences on symptom management, biological response, and functioning among Chinese American and White female breast cancer survivors

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Background: Socioeconomically disadvantaged and immigrant cancer survivors account for a significant and growing proportion of the breast cancer population in the US. Research on symptom burden and control among Chinese American (CA) breast cancer survivors (BCS) is scarce. Among all BCS, over 55% report treatment-related symptoms (e.g., fatigue and pain) and psychological stress (e.g., fear of recurrence). In our preliminary cross-sectional study, we found similar rates (~58%) but showed that CA (especially low-acculturated) BCS were particularly likely to report fatigue, pain, and poorer physical functioning relative to non-Hispanic White (NHW) BCS. We understand very little about whether CA and NHW BCS have different ways of managing symptoms, improving quality of life and decreasing risk for functional decline. We therefore propose a study to examine how CA and NHW BCS, two culturally distinct groups with divergent social resources, adapt to breast cancer. Study design: This longitudinal, prospective study will investigate sociocultural influences on individual coping behaviors and how they in turn affect racial differences in inflammation markers, symptom severity, and functional outcomes in breast cancer. This study will enroll 260 CA and 260 NHW female BCS to examine multifactorial pathways to breast cancer survivorship outcomes. The CA cases will be age- and stage-matched to the NHW cases. Utilizing a multilevel biobehavioral framework, we will investigate the dynamics of biological, sociocultural, and behavioral (diet and exercise) influences on symptom severity, physiologic status, and functional outcomes. Participants will complete telephone survey interviews and provide blood samples at baseline and 6- and 12-month follow-up. Pro-inflammatory cytokines (e.g., IL-1 β , IL-1a, IL-6, IL8, IL10, TNF α , TNF β , and CRP) and cortisol will be analyzed. In-depth individual interviews with a subset of participants will be conducted to investigate causal factors in order to develop individually and culturally appropriate interventions to improve future clinical care for targeted breast cancer survivor populations. This study is supported by NIH R01CA248413. Eligibility criteria: Eligible participants are CA and NWH women (age \geq 18) who are diagnosed with invasive breast cancer (stage I, II, or III), are 1-5 years post diagnosis, and have completed primary treatment (e.g., surgery, radiation, chemotherapy, and/or targeted therapy). Patients currently on adjuvant endocrine therapy are allowed. Specific aims: Aim 1: Examine whether CA BCS' symptom, functional, and physiologic outcomes (e.g., cytokines and cortisol), and trajectory of these outcomes differ from NHW BCS at baseline, 6- and 12-month follow-up, controlling for covariates. Aim 2: Examine to what extent social resources mediate BCS' individual behavior (e.g., medical communication, diet, and physical activity) and to what extent such pathways explain outcome differences (Aim1) among BCS. Aim 3: Examine whether race and acculturation moderate the mediational pathways. Statistical methods: Multiple general linear mixed models will be performed to examine racial differences in the trajectory of symptom and biobehavioral outcomes across time, controlling for covariates (Aim 1). To examine mediation and moderation effects (Aims 2 and 3), we will use a cross-lagged path analysis model to simultaneously describe reciprocal relationships, or directional influences, between variables over time. Present accrual and target accrual: A total of 520 participants (260 CA and 260 NHW) will be enrolled at NYU Perlmutter Cancer Center, Columbia University Irving Medical Center, Georgetown University Medical Center, and Texas A&M University community networks. Contact information: Judy Huei-yu Wang, PhD: jw235@gunet.georgetown.edu or 202-687-6306 Maryann Kwa, MD: maryann.kwa@nyulangone.org or 212-731-6364

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TBCRC-053: P-RAD: A Randomized Study of Preoperative Chemotherapy, Pembrolizumab and No, Low or High Dose RADIation in Node-Positive, HER2-Negative Breast Cancer

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Background: The introduction of immune checkpoint inhibitors (ICI) to standard neoadjuvant chemotherapy regimens has been shown to significantly improve outcomes in patients with triple negative breast cancer and is being investigated for high-risk hormone receptor-positive (HR+)/human epidermal growth factor-2 negative (HER2-) breast cancer. Preclinical evidence suggests radiation therapy (RT) can stimulate intra-tumoral T cell infiltration and enhance the expression and immune detection of tumor-specific neoantigens. This phase II pilot randomized study (NCT04443348) aims to evaluate the safety and efficacy of two different doses of preoperative primary tumor RT boost when combined with neoadjuvant pembrolizumab, then followed by standard neoadjuvant chemotherapy. Dual co-primary endpoints include determining the pathologic complete response (pCR) rate in the non-irradiated and pathologically confirmed metastatic axillary lymph node(s) in each treatment arm and quantifying tumor-infiltrating T lymphocytes in on-treatment (C1D14) tumor biopsies. We hypothesize that high-dose RT will increase the proportion of tumors with high T cell infiltration (i.e., top quartile) from 25% to 55%. Secondary endpoints include measuring residual cancer burden, evaluating tolerability of the regimen, and assessing quality of life. Exploratory endpoints include evaluation of treatment-associated changes in the tumor immune microenvironment, circulating immune cell analyses, and circulating tumor DNA kinetics.

Methods: The study plans to enroll 128 participants with either triple negative (n=80) or high-risk HR-/HER2- (n=48) breast cancer who will be randomized to receive no, low (9 Gy), or high (24 Gy) dose of preoperative RT boost, after which 24 participants of either breast cancer subtype will be enrolled to an exploratory high dose proton therapy boost cohort. The eligibility criteria include patients who have biopsy-proven, axillary lymph node-positive breast cancer that is either triple negative (defined as ER< 10%, PR< 10%, and HER2-negative) or high-risk HR+/HER2- (grade III or having a high-risk genomic assay score). Study treatment is given in 6-week cycles, with 400 mg Pembrolizumab given on day 1 of each cycle. For those participants randomized to receive a preoperative RT boost, treatment is delivered in 3 fractions (3x3 Gy or 3x8 Gy) over consecutive business days, where one of the fractions is given on the same day as C1D1 Pembrolizumab. Standard neoadjuvant chemotherapy begins on C1D15 with paclitaxel (plus carboplatin for triple negative) administered weekly for 12 weeks, and then starting on C3D15, dose-dense doxorubicin/cyclophosphamide is administered every 2 weeks for 8 weeks. Following neoadjuvant treatment, participants will receive standard breast surgery (including removal of the pathologically confirmed metastatic lymph node) followed by adjuvant pembrolizumab, radiation therapy, and standard-of-care systemic therapy as clinically indicated. Tissue samples from the primary tumor and biopsy-proven lymph node are taken at baseline, C1D14, and at the time of surgery. There are eleven blood collection timepoints throughout the neoadjuvant and adjuvant settings. Participants will be followed for 2 years after surgery to assess safety and durability of responses.

Results: This study has accrued 12 participants to date, including 10 with triple negative breast cancer and 2 with high-risk HR+/HER2- breast cancer. Formal results for this study are forthcoming, as the trial is actively accruing at 6 institutions, with plans to open at 3 more within the year. For persons with a specific interest in this trial, please contact Joseph Connolly, Multi-Center Coordinator, at jconnolly28@mgh.harvard.edu.

Disclosure(s):

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12/8/2022

5:00 PM - 6:15 PM

OT3-15-02

A Phase II Study Evaluating the Combination of Radiotherapy with Chemotherapy and Pembrolizumab in Patients with PD-L1-Positive Metastatic Triple-Negative Breast Cancer

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Background: Metastatic triple-negative breast cancer (TNBC) is aggressive and lacks targeted therapies. The KEYNOTE-355 trial demonstrated that immunotherapy could bring efficacy to the TNBC population. In this trial, the addition of pembrolizumab (PD-1 inhibitor) to chemotherapy (nab-paclitaxel, paclitaxel, or carboplatin/gemcitabine) prolonged median 1-year progression free survival (PFS) (12.0% to 39.0%) when compared to chemotherapy (CT) alone in patients with PD-L1-positive (combined positive score (CPS) ≥ 10) metastatic TNBC. Despite these encouraging results, patients with metastatic TNBC treated with the KEYNOTE-355 regimen developed delay in disease progression only for months. Studies have demonstrated that the addition of radiotherapy (RT) to immunotherapy and / or CT can result in a more robust immune response by releasing tumor antigens and promoting a local T cell response. Importantly, localized RT with immunotherapy has been shown to cause abscopal effect, a robust immune activation and tumor shrinkage at distant sites of metastasis. Based on these findings, RT in combination with immunotherapy and CT represents a potential avenue to prolong immune response in metastatic TNBC. The purpose of this study is to test this hypothesis and investigate the benefit of combining RT with pembrolizumab/chemotherapy in patients with metastatic PD-L1-positive TNBC. Methods: This two-stage, single-arm phase II study will assess the efficacy of RT in combination with CT plus pembrolizumab in PD-L1-positive unresectable or metastatic TNBC patients aged ≥ 18 years. Patients must have received < 1 prior lines of systemic therapy in the metastatic setting or adjuvant/neoadjuvant setting if metastatic recurrence was within 12 months of treatment. Patients must have a PD-L1 positive CPS ≥ 10 and must not have had a prior PD-1/PD-L1 inhibitor within 6 months. Patients will receive ablative RT 8 Gy per fraction for a total of 3 fractions (24 Gy) completed within 2 weeks prior to systemic therapy. RT will be directed at 1-4 sites of metastatic disease at the discretion of the treating radiation oncologist. Systemic therapy will then be given within seven days with either a taxane [nab-paclitaxel 100 mg/m² or paclitaxel 90 mg/m² intravenous weekly for 4 - 6 cycles] or carboplatin at area under the curve (AUC) 2 and gemcitabine 1000 mg/m³ weekly every 21 days if not taxane eligible. Pembrolizumab will be given at 200 mg every 3 weeks. Imaging will be repeated every 8-9 weeks to assess response based on RECIST 1.1. The primary endpoint of the study will be 1-year PFS which will be determined by comparing the 1-year PFS rate to historical controls. The study is powered to reject a 1-year PFS rate of 39% when the true value is 60%. Seventeen subjects will be enrolled in the first stage followed by an additional twelve subjects in the second stage if the trial is not stopped due to futility. Baseline tumor tissue will be collected for all patient and serial tumor biopsies will be performed at cycle 2 day 1 and at the end of study in patients with accessible disease (8 patients in Stage I and 5 patients in Stage II). Serial blood draws for immune assays and ctDNA will be performed in all patients.

Disclosure(s):

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12/8/2022

5:00 PM - 6:15 PM

OT3-15-03

The ARETTA Trial Experience: Radiotherapy Quality Assurance in an International Breast Cancer Trial

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Background The ARETTA trial is a Phase II feasibility study that tests the efficacy of Taxotere + Herceptin subcutaneous (SC) X 4 cycles in the neoadjuvant setting and one year of Herceptin SC as adjuvant therapy for HER2 positive breast cancer among Nigerian women. This study is being used to test an emerging platform for future biomarker based multi-institutional oncology clinical trials in Nigeria and across Sub-Saharan Africa. Radiotherapy is an integral part of multimodality breast cancer care. However, there are fewer than ten radiotherapy centers in Nigeria and limited experience in delivering radiotherapy within the context of a clinical trial. We describe the processes incorporated within the ARETTA trial to ensure protocol compliance and radiotherapy quality and to enhance patient safety. **Methods** To centralize treatment, patients from the five participating sites throughout Nigeria were all referred to the Department of Radiotherapy, Lagos University Teaching Hospital (LUTH) to receive radiotherapy. A Radiation Therapy Quality Assurance (RTQA) program was also implemented to ensure protocol compliance and enhance patient safety. This consisted of preparatory educational lectures on breast radiotherapy contours, treatment planning and plan assessment. Subsequently, pre-treatment review of contours was conducted by two radiation oncologists with expertise in breast cancer. Feedback on contours was provided via Zoom conference and email correspondence and weekly ARETTA trial meetings were used to track patient progress and adverse effects. An audit was conducted after treating 24 patients (half of the target enrollment). Patients were registered after lumpectomy or mastectomy and treated as follows: Hypofractionated radiation to the breast alone, breast and regional nodes, chest wall alone, or chest wall and regional nodes. The regional nodes will consist of the supraclavicular fossa, axilla and internal mammary nodal basin. The prescribed dose is 42.56 Gy in 16 daily 2.66 Gy fractions. Boost dose for the lumpectomy cavity or close/positive margins post-mastectomy is 10 Gy in 5 fractions of 2 Gy for cumulative total doses of 52.56 Gy. If there is suspected gross disease, these regions are treated with a boost dose of 18 Gy in 9 fractions of 2 Gy for a total dose of 60.56 Gy in 25 fractions. Treatment is given 5 days a week for 3-4 weeks. In the case

of a departmental holiday, RT may be given 4 days a week. In case of medical illness or RT side effect(s), treatment breaks are allowed as needed per standard practice. Results The average surgery to RT start interval was 82 days (range 73 – 161 days). The average duration of RT was 23.1 days (range 18-35 days) and all patients who began RT completed their course of treatment. Radiation oncologists were able to independently and accurately contour targets after attending preparatory lectures and intensive review of the first ten patients. While breast and chestwall target coverage met protocol stipulations, deviations of mean heart dose and internal mammary chain target goals were noted. No Grade 3 or 4 side effects were noted. Conclusion The implementation of RTQA procedures enhanced protocol compliance. Additional educational efforts focused on dosimetric planning and plan assessment are needed to enhance adherence to organ constraints and target goals as stipulated in the protocol.

Disclosure(s):

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5:00 PM - 6:15 PM

OT3-16-01

On-going prospective study to measure serum progranulin/GP88 levels in metastatic breast cancer patients in association with disease status

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The ability to monitor response to therapy and disease progression in metastatic breast cancer (MBC) patients is a major step in patient management. Imaging is the method of choice for the assessment of disease status and the monitoring of disease progression. However, this approach remains expensive, expose patients to radiation and thus is mainly performed every 2-3 months. During this time interval, the disease may progress significantly on ineffective treatment and the patient may present treatment related toxicities due to the inability to detect progression at earlier times. Circulating levels of tumor associated biomarkers such as CA15-3 and CEA are often determined to track disease status of MBC. However, even though they can provide information about disease progression, they do not always provide a reliable measure of response to therapy. The monitoring of disease status and progression through the measurement of drivers of disease should provide an alternative and complementary approach

to existing strategies in order to better to monitor the disease status and enable proactive management of MBC patients. Progranulin also called Glycoprotein 88kDa (PGRN/GP88) is an autocrine growth factor overexpressed in breast cancer. Biological studies have established GP88 as a critical player in breast tumorigenesis. GP88 overexpression is associated with the malignant phenotype, estrogen independence, increased proliferation, survival, and drug resistance. High PGRN/GP88 tumor expression measured by immunohistochemistry in invasive ductal carcinoma is an independent prognostic marker associated with increased risk of recurrence and mortality. Clinical studies have demonstrated that GP88 circulating levels as measured by enzyme immunoassay are elevated in breast cancer patients, compared to healthy individuals. In MBC patients, circulating GP88 levels correlate with overall survival. These facts are supportive of the hypothesis that the measurement of circulating GP88 levels in MBC patients can serve as an additional biomarker to monitor MBC disease status and be predictive to outcome. A prospective study was established is to identify whether there is a statistically significant change in serum GP88 levels associated with time to progression of breast cancer as measured by RECIST 1.1 criteria in MBC patients. With the assumptions that patients will provide a baseline and four follow up visits and that 20% of the visits record a disease progression, time to progression. Taking the plausible and clinically relevant performance to be 75% sensitivity and 46% false positive, a sample of ninety patients would give 85% power. Under IRB approved protocols at the University of Maryland Greenebaum Comprehensive Cancer Center and at two Baltimore Medstar Health Facilities, a total of 103 female breast cancer patients with measurable or evaluable metastatic disease will be consented and enrolled. The patients have been re-staged within 4 weeks and will continue or begin new therapy. Currently, we have enrolled sixty-five subjects at the three facilities. In addition to standard laboratory assessment and radiographic imaging/staging every 2-3 months on study, blood samples will be collected from each patient. The samples are stored at -70C until evaluated for GP88 using a GP88 enzyme linked immunoassay. We will analyze the GP88 serum level in correlation with survival and with disease status determined as responder, stable or progressing based on the RECIST criteria. This study is supported by grant R44CA210817 from the National Cancer Institute to Ginette Serrero Principal Investigator.

Disclosure(s):

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OT3-18-01

Electronic Health Record Patient Portal (MyChart) Research Study Recruiting Methods and Results: the WISDOM Study

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BACKGROUND: The WISDOM (Women Informed to Screen Depending on Measures of risk) Study is a population-based, pragmatic trial comparing annual mammogram screening to risk-based breast cancer screening in women ages 40-74 with no history of breast cancer or DCIS. WISDOM's enrollment process includes registration, consent, and completion of study surveys over a secure, cloud-based electronic patient reported information platform. One of the most valuable methods of study recruitment has been invitations through institutional electronic medical record (EMR) patient portals. Patient portals are used broadly today and allow patients to communicate with their care teams, pay medical bills, and access their full electronic health record. Over the last 4 years, EMR patient portals have been more widely used for research recruitment. Here we examine the recruitment results and methods used by five WISDOM sites. **METHODS:** UCLA, UCSF, UCI, UCSD, and Sanford Health medical centers have employed patient portal study recruitment via MyChart for the WISDOM study. Each site sent WISDOM recruitment messages to patient MyChart inboxes who met study criteria (females between ages 40-74). Although research messaging receipt is defaulted to opt-in, all sites provide patients with a method to opt-out. Except for at Sanford and UCSF, recruiting messages included all necessary information for study registration, including a direct link to the study website for registration. The following highlights differences in recruitment processes used by each site through June 2022. Study recruitment via MyChart is ongoing at some of the sites. • UCLA sent institution-wide messages in 3 rounds. For rounds 2 and 3, new MyChart patients and those who did not previously open a recruiting message were re-invited. • Sanford and UCSF sent institution-wide messages that allowed patients to either choose to learn more about the study or opt out. Contact information for interested patients was provided to WISDOM Study coordinators (WSCs), who emailed each patient the study website and registration steps. Sanford re-invited those who did not initially respond whereas UCSF did not track and re-invite those who did not respond. • UCSD partnered with study physicians to send research recruitment messages from their Chiefs of Medicine and Family Medicine. These messages were sent to patients in 3 rounds. For rounds 2 and 3, only patients who had not registered for WISDOM were re-invited. • UCI piloted MyChart recruitment with individual messages sent to study-eligible patients of 3 primary care physicians from the WSC. The recruiting messages included the ability for patients to opt out of further contact from the study. Patients who did not respond were contacted by phone by the WSC. **RESULTS :** For each site, the following registration and consent rates were observed: • UCLA: 2.3% registration rate; 1.9% consent rate (7,257) • Sanford: 4.1% registration rate; 3.5% consent rate (5,844) • UCSF: 3.2% registration rate; 2.6% consent rate (2,501) • UCSD: 6.6% registration rate; 4.6% consent rate (1,789) • UCI: 6.1% registration rate; 1.7% consent rate (11) **CONCLUSION:** Using EMR patient portals like MyChart for research recruitment has proven successful for WISDOM. UCSF and Sanford MyChart workflows resulted in better consent conversion rates compared to direct in-basket messages at UCLA without personal follow-up. However, accessing UCLA's large patient population size has led them to have the highest number of MyChart enrolled study participants. Having medical practices send research recruitment messages using MyChart to their patients, as UCSD piloted, showed the highest rate of enrollment. MyChart is

quickly becoming a popular method to recruit for research, but there are still variations in medical center policies around the use of MyChart for researchers, which can create challenges for certain research institutions to effectively use this platform for research outreach.

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OT3-18-02

Clinical validation of “TriNetra™-Breast” test for breast cancer screening in a prospective, observational, case-cohort study

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Introduction The Standard of Care for early detection of breast cancer in asymptomatic women is screening mammography, which has limitations such as radiation exposure and lower sensitivity to detect cancer in women with high breast density or invasive carcinomas. TriNetra™-Breast is a blood test for the detection of breast cancer associated circulating tumor cells in blood. Previously, this test has been used in a study for breast cancer detection in India, where it has shown a sensitivity of 92.5%. It has since been granted the United States Food and Drug Administration (USFDA) Breakthrough Device Designation, attesting its potential to provide for improved detection of breast cancer. This prospective, observational, case-cohort study will confirm the clinical performance characteristics of the technology in the US population. **Patients and Methods** The primary endpoint of this study will be to determine the sensitivity and specificity of the test for breast cancer screening, using mammography and histopathology confirmed diagnosis (when relevant) as the reference methods. Women ≥40 years, with no prior diagnosis of any cancer and undergoing screening mammography for breast cancer will be eligible for participation in this study. 700 women, representing the diverse ethnic US population, will be enrolled. Cohort A will have 500 women with BI-RADS score of 1, 2, or 3. Among these 500 participants, the age categories of 40-49 years, 50-74 years and >74 years will have 100, 300 and 100 women respectively. Cohort B will have 100 women with suspicion of DCIS (without a suspicion of simultaneous invasive carcinoma) and 50 women each with BI-RADS score of 4 or 5. These study population numbers will ensure optimal representation of in-situ carcinoma, malignant and benign cases. Blood samples will be collected from the enrolled women for TriNetra™-Breast, within sixty (60) days of the screening mammogram. If biopsy is indicated, sample collection will be required prior to the procedure. The lab investigators will be blinded to the clinical information of all participants, including mammography and histopathology results, while the participants and clinical investigators will be blinded to the TriNetra™-Breast test results. The results of TriNetra™-Breast will be compared with the results of mammography and/or histopathology for performance estimation

of the test. Study participants will be followed for clinical outcomes for maximum duration of 2 years.

Disclosure(s):

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OT3-18-03

The PRAIM study: A prospective multicenter observational study of an integrated Artificial Intelligence system with live monitoring

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Background. Several retrospective studies have illustrated the potential clinical benefit of artificial intelligence (AI) systems for breast cancer screening. Some systems optimize normal mammography examination triaging, while others aim to improve cancer detection. However, no AI system has shown specificity high enough to replace human radiologists, suggesting that AI should play a different role in the breast screening pathway. The decision-referral approach is a promising alternative that has demonstrated the most potential to improve radiologist screening sensitivity and specificity while reducing workload. This collaborative human-AI approach combines AI pre-screening to triage normal examinations and post-screening to prevent missed cancers. The actual performance of decision-referral, including the interaction with human radiologists, can ideally be evaluated in a prospective real-world setting. Trial design. The PRAIM (PRospective, multicenter observational study of an integrated AI system with live monitoring to support breast cancer screening) study (German Trial Register: DRKS00027322) is a prospective controlled observational non-inferiority study to compare the use of CE-marked screening software including AI support (Vara) via the decision-referral approach, with standard screening for women participating in the German breast cancer screening program. Ethics approval was obtained from the University of Lübeck Research Ethics Committee (22-043). Examinations assessed by readers using Vara are compared to examinations without Vara (control). Eligibility criteria and target accrual. Women ages 50 to 69 years old undergoing biennial breast cancer screening within the national screening program are eligible for inclusion. We expect the inclusion of approximately 400,000 women within the inclusion period of 1.5 years. Statistical methods. The primary outcome is the screen-detected

cancer rate, defined as biopsy-confirmed cancer diagnoses per 1000 screening examinations. For each screening site, rates over the prospective observation period are calculated for examinations read with AI and without. To control for systematically different screen-detected cancer rates across screening sites, a historical 5-year rate is computed for each site and subtracted from the corresponding prospective rates. Non-inferiority of the screen-detected cancer rate for the AI group compared to the control group is evaluated with a weighted, mixed-effects linear regression model. AI is considered as non-inferior if the lower bound of the two-sided 95 % confidence interval for the estimated difference in screen-detected cancer rates of AI and non-AI group is not below -10 %, which corresponds to a deviation of -0.6 screen-detected cancers per 1000 examinations.

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OT3-18-04

Personalized Breast Cancer Screening in a Population-based Study: Women Informed to Screen Depending On Measures of risk (WISDOM)

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Background: Women Informed to Screen Depending on Measures of risk (WISDOM) is a preference-tolerant, pragmatic study comparing annual mammography to risk-based breast screening. WISDOM aims to assess if risk-based screening, compared to annual screening, is as safe, less morbid, enables prevention, and is more accepted by women. Though open nationally, by 2018 recruitment of Black/African American women was low, therefore we developed a strategy to correct this disparity. Methods: Women 40-74 years old living in the US with no history of breast cancer or DCIS, and no previous double mastectomy are eligible. Participants can either elect randomization or self-select a study arm (annual vs. risk-based). Consent is obtained through an online electronic-signature platform. Participants in the risk-based arm undergo panel-based mutation testing (BRCA1, BRCA2, TP53, PTEN, STK11, CDH1, ATM, PALB2, and CHEK2). Their 5-year risk is calculated using the Breast Cancer Screening Consortium (BCSC) score combined with a Polygenic Risk Score (220 single nucleotide polymorphisms (SNPs)). The SNPs and mutations are assessed by saliva-based genetic testing. Five-year risk thresholds are used to determine starting age, stopping age, and frequency of screening, as well as modality. To strengthen generalizability, in 2020 WISDOM opened new recruitment sites and spearheaded new partnerships and an education and engagement campaign to enroll more women of color. Results: Of the 64,095 participants registered for WISDOM, over 49,611 (77%) provided consent and 41,910 (84%) have fully enrolled. 61% of fully enrolled participants selected to be randomized and 39% selected their study arm. To date, 83% of enrolled participants have received a WISDOM screening recommendation. Of the 21,572 participants in the risk-based arm, over 17,392 (80.6%) completed a saliva kit and received a genetic testing report. Median participant age is 56 years. WISDOM has improved its racial and ethnic diversity through intentional recruitment methods including expansion of enrollment centers, Veterans Affairs (VA) email outreach, and partnerships with community organizations. Prior to these efforts (from 2016-2019), the WISDOM study population was over 80% White non-Hispanic and has now decreased to 74% in 2020 and 73% in 2021. Rates of Black/African American (AA) participants increased from 1.7% prior to 2020 to 4.2% in 2020, 8.1% in 2021, and 11.3% in Q2 2022, a 10-fold increase. Across all time, 76.9% of participants identified as White, 4.6% African American, 4.6% Asian, and 3.1% identified as multiracial. 9.2% self-reported Hispanic ethnicity. Through 13 eligible VA facilities, 2,875 veterans enrolled in WISDOM and 23% identify as Black/African American. At our expansion sites, 23% UChicago, 21% University of Alabama Birmingham, and 14% Louisiana State University participants identify as Black/African American across all-time. 17% of participants enrolled at our Florida site (Femwell/ToplineMD) identify as Hispanic. At our newest site, DHR Health (Rio Grande Valley Texas), 48% of study participants identify as Hispanic. Conclusions: Engagement of VA centers, community partnerships, and opening new expansion sites in diverse communities have increased racial and ethnic diversity in WISDOM, thereby strengthening our scientific knowledge of breast cancer risk for all women. Passive recruitment efforts with VA facilities have contributed to valuable improvements to the diversity of our research studies. Results of the WISDOM Study will enable us to evaluate whether personalized screening improves healthcare value by identifying those at highest risk and offering more frequent screening and prevention options, while safely reducing screening for those a lower cost, increasing healthcare value and improving outcomes.

Disclosure(s):

Patricia Choy, MPH: No financial relationships to disclose
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OT3-19-01

Phase II Study of Screening Brain MRIs in Stage IV Breast Cancer

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Background: As systemic therapy improves, there has been an increasing number of breast cancer patients who develop brain metastasis. Screening of asymptomatic stage IV breast cancer patients with brain MRIs is not currently recommended by the National Comprehensive

Cancer Network (NCCN) Guidelines. Retrospective reports suggest breast cancer patients are more likely to present with more advanced central nervous system disease at the time of brain metastasis diagnosis compared to melanoma and non-small cell lung cancer (NSCLC) patients. This may be in part due to routine screening recommendations in melanoma and NSCLC. Early detection and treatment of brain metastases may improve outcomes for breast cancer patients. Trial Design: The study is designed as a single arm, nonrandomized phase II study, with the goal of investigating the role of screening brain MRIs in neurologically asymptomatic patients with metastatic breast cancer. Breast cancer patients will be allocated based on receptor subtypes into triple negative (TN), HER2+, and hormone receptor (HR)+/HER2- breast cancer. Following study enrollment, patients will undergo a screening brain MRI. Patients will undergo a second brain MRI at first systemic progression or at 6 months whichever event occurs sooner. Eligibility: Asymptomatic, stage IV breast cancer patients that have progressed past first line therapy in the metastatic setting with an ECOG \leq 6 months are eligible. Specific Aims: The primary objective is to determine the incidence of asymptomatic brain metastasis in metastatic breast cancer by subtype. Secondary objectives include determining the incidence of asymptomatic leptomeningeal disease, the number and size of brain metastases at diagnosis, the number of patients requiring whole brain radiation therapy vs. stereotactic radiation following diagnosis and overall survival and brain metastasis specific survival following brain metastasis diagnosis in metastatic breast cancer by subtype. Statistical Methods: A total of 30, 30, and 40 TN, HER2+, and HR+/HER2-, breast cancer patients will be enrolled, respectively. Using an incidence rate of 17%, the 95% CI by subtype will be (0.06,0.351), (0.06,0.351), and (0.07,0.322). Patient Accrual: This study is open with 30 patients enrolled at the time of submission. A total of 100 patients will be enrolled. Contact Information: Kamran A. Ahmed MD, Moffitt Cancer Center, email: kamran.ahmed@moffitt.org, Clinical trial information: NCT05115474. Funding: Florida Breast Cancer Foundation.

Disclosure(s):

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12/8/2022

5:00 PM - 6:15 PM

OT3-20-01

Ketamine Analgesia for Long Lasting Pain Relief after Surgery (KALPAS) Study

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Background: Post-mastectomy pain syndrome (PMPS) affects up to 60% of women undergoing mastectomy. Standard perioperative multimodal analgesia remains only moderately effective in preventing PMPS, and many patients continue to rely on opioids for their chronic pain. In the context of the opioid overdose crisis, alternative interventions are urgently needed. Ketamine targets risks factors for PMPS including acute pain and negative mood, making it an ideal candidate for the prevention of PMPS. Trial Design: This is a multisite, three-arm, double-blind,

RCT to test the effectiveness of ketamine in reducing PMPS in women undergoing mastectomy for oncologic indication. Arm 1 consists of continuous perioperative ketamine infusion that begins during surgery and continues for 2 hours in the post-anesthesia care unit (PACU). Arm 2 consists of a single-dose of ketamine in the PACU given over 50-60 minutes. Arm 3 consists of placebo. Standard surgical and postsurgical care remain unchanged across all arms. Eligibility Criteria: Inclusion criteria are: women ≥ 18 years of age undergoing total mastectomy for oncologic indication +/- lymph node dissection and +/- immediate or delayed reconstruction with no distant metastases. Exclusion criteria include: (1) history of cognitive impairment (2) past ketamine or phencyclidine misuse or abuse, (3) schizophrenia or history of psychosis, (4) history of post-traumatic stress disorder, (5) known sensitivity or allergy to ketamine, (6) liver or renal sufficiency, (7) uncontrolled hypertension, chest pain, cardiac arrhythmia, stroke, head trauma, intracranial mass or hemorrhage, glaucoma, porphyria, uncontrolled thyroid disease, or other contraindication to ketamine, (8) lamotrigine, alifentanil, physostigmine, or 4-aminopyridine use, (9) currently pregnant, (10) body mass index greater than 35, (11) non-English or non-Spanish speaker, (12) currently participating in another pain interventional trial, (13) patient has started or undergone hormone therapy for gender transition into male, or (14) patient is scheduled for bilateral (or greater) flap reconstruction. Specific Aims: The primary outcome is pain intensity on the Brief Pain Inventory short form scale at the surgical site three months after mastectomy. Secondary outcomes include pain severity and interference at the surgical site, incidence of PMPS, anxiety, and depression over 12 months after surgery. Tertiary outcomes include neuropathic symptoms, fatigue, sleep, physical function, and opioid use. Statistical Methods: We will test the differences in the primary outcome between 1) the continuous ketamine infusion and the control; and 2) the single-dose ketamine and the control, each at 0.025 significance level (adjusted for multiple comparisons using the Bonferroni correction), based on the two-sample t-tests (allowing unequal variances) if outcome variables are approximately normal, or Wilcoxon's rank-sum tests otherwise. Accrual: The target accrual for this study is ~750. Recruitment began January 2022. Recruitment is expected to be complete by October 2025. As of July 14, 2022, 43 participants have been enrolled across all sites. If interested in the KALPAS Study, please contact kalpas@nyulangone.org, jing.wang@nyulangone.org, or lisa.doan@nyulangone.org. This research is supported by the National Institutes of Health through the NIH HEAL Initiative under UH3CA261067. It is also supported by the NCATS Trial Innovation Network under award numbers U24TR001608 (CCC), U24TR001597 (DCC), U24TR001609 (SSC), U24TR001579 (RIC)

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OT3-20-02

SMALL: Open Surgery versus Minimally invasive vacuum-Assisted excision for small screen-detected breast cancer – a UK phase III randomised multi-centre trial

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Background: Mammographic screening programmes reduce breast cancer mortality, but detect many small tumours with favourable biological features which may not progress during a woman's lifetime. Screen-detected cancers are treated with standard surgery and adjuvant therapies, with associated morbidities. There is a need to reduce overtreatment of good prognosis tumours and numerous studies have evaluated the omission of radiotherapy in this context. However, there is little evidence to support surgical de-escalation, although percutaneous minimally invasive treatment approaches have been described. Vacuum-assisted excision (VAE) is in widespread use for management of benign lesions and lesions of uncertain malignant potential. SMALL (ISRCTN 12240119) is designed to determine the feasibility of using this approach for treatment of small invasive tumours detected within the UK NHS Breast Screening Programme (BSP). Methods: SMALL is a phase III multicentre randomised trial comparing standard surgery with VAE for screen-detected good prognosis cancers. The main eligibility criteria are age ≥ 47 years, unifocal grade 1 tumours with maximum diameter 15mm, which are strongly ER/PR+ve and HER2-ve, with negative clinical/radiological axillary staging. Patients are randomised 2:1 in favour of VAE or surgery; with no axillary surgery in the VAE arm. Completeness of excision is assessed radiologically, and if excision is incomplete, patients undergo open surgery. Adjuvant radiotherapy and endocrine therapy are mandated in the VAE arm but may be omitted following surgery. Co-primary end-points are: 1. Non-inferiority comparison of the requirement for a second procedure following excision 2. Single arm analysis of local recurrence (LR) at 5 years following VAE Recruitment of 800 patients will permit demonstration of 10% non-inferiority of VAE for requirement of a second procedure. This ensures sufficient patients for single arm analysis of LR rates, where expected LR free survival is 99% at 5 years, with an undesirable survival probability after VAE of 97%. To ensure that the trial as a whole only has 5% alpha, the significance level for each co-primary outcome is set at 2.5% with 90% power. The Data Monitoring Committee will monitor LR events to ensure these do not exceed 3% per year. Secondary outcome measures include time to ipsilateral recurrence, overall survival, complications, quality of life and health economic analysis. A novel feature of SMALL is the integration of a QuinteT Recruitment Intervention (QRI), which aims to optimise recruitment to the study. Recruitment challenges are identified by analysing recruiter/patient interviews and audio-recordings of trial discussions, and by review of trial screening logs, eligibility and recruitment data and study documentation. Solutions to address these are developed collaboratively, including individual/group recruiter feedback and recruitment tips documents. Results: SMALL opened in December 2019, but recruitment halted in 2020 for 5 months due to COVID-19. At 7st July 2022, 142 patients had been randomised from 26 centres, with a randomisation rate of approximately 45%, and a per site recruitment rate of 0.4-0.5 patients/month, approaching the feasibility recruitment target of 144 patients. Drawing from preliminary QRI findings and insights from patient representatives, a recruitment tips document has been circulated (on providing balanced information about treatments, encouraging recruiters to engage with patient preferences, and explaining randomisation). Individual recruiter feedback has commenced, with wider feedback delivered across sites via recruitment training workshops. Conclusion: Despite pandemic-related challenges, SMALL has an excellent recruitment rate to date and is expected to have a global impact on treatment of

breast cancer within mammographic screening programmes. SMALL is funded by the UK NIHR HTA programme, award 17/42/32

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5:00 PM - 6:15 PM

OT3-20-03

Refusal of Breast Surgery in Breast Cancer Patients With cCR After Neoadjuvant Systemic Therapy and Vacuum-assisted Biopsy (VAB) and SLNB Confirmed pCR. An interim report of the prospective non-randomized trial. NCT04293796.

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Introduction The aim of the study was to prove efficacy and safety of de-escalation of traditional breast surgery in BC patients who develop cCR after neoadjuvant systemic therapy. Refusal of surgery was offered to exceptional responders after vacuum-assisted tumor bed biopsy and sentinel lymph node biopsy confirmed absence of residual disease (pCR). Materials and methods A single-center prospective study was run in the NMRC n.a. N.N. Petrov. Starting from August of 2020, 35 patients with early cT1-2N0-1M0 (stage Ia-IIb) triple-negative and HER2-positive (both ER+ and ER-) unifocal tumours without DCIS in core-biopsy specimen enrolled in

the study. Primary lesions were marked with a single clip in the centre. In cases with nodal involvement (cN1) the affected lymph nodes were also clipped. Patients with triple-negative breast cancer received 4 cycles of AC q21d followed by 12 cycles of weekly paclitaxel and carboplatin AUC 2.0. HER2-positive patients received 4 cycles of AC followed by 4 cycles of docetaxel combined with trastuzumab and pertuzumab q21d. Breast US, mammography and SPECT were used at baseline and at response evaluation. Vacuum-assisted biopsy was performed with 7G needle and US-guidance in the OR simultaneously with the SLNB. VAB protocol included retrieval of the tumor clip as first stage. Subsequently surrounding tissues were sampled, and markers were placed to guide radiotherapy. In case residual tumor was found patients received standard breast-conserving surgery. In case the sentinel lymph nodes were found to be positive, standard level II axillary clearance was performed. HER2-positive patients with pCR confirmed by VAB and SLNB received adjuvant trastuzumab up to one year. HER2-positive patients with residual breast or nodal involvement received trastuzumab emtansine up to one year. In case ER+, all patients received appropriate endocrine-therapy. In case of residual in-breast or nodal involvement patients with triple-negative breast cancer received standard capecitabine. Results The interim analysis included 25 patients in both groups. The median follow-up of disease-free survival for patients is 12 months. In the triple-negative group 12 patients achieved cCR. All patients went on to receive VAB and SLNB. After VAB and SLNB pCR was confirmed 11 patients (91.7%). 1 patient had invasive residual tumor with less than 5% cellularity. FNR in this group was 8.3% (1/12). Patient with invasive residual tumor received standard breast-conserving surgery. All the patients in the TNBC group were also found to be (sn)ypN0. In the HER2-positive group cCR was achieved 13 patients. All patients went on to receive VAB and SLNB. After VAB and SLNB pCR was confirmed 10 patients (77%). 3 patients had invasive residual tumor with less than 5% cellularity. FNR in this group was 23% (3/13). Patients with invasive residual tumor received standard breast-conserving surgery. All HER2-positive patients were found to be (sn)ypN0. One patient with HER2-positive subtype experienced a local recurrence in the postoperative zone 16 months after surgery. Initially, this patient achieved cCR and undergone VAB with SLNB. On final pathomorphologic examination isolated focuses of DCIS were found (ypTisN0). Standard breast-conserving surgery was performed and histologically only DCIS was found. This patient received 1-year of Trastuzumab and standard radiotherapy with boost. After the histologic confirmation of local recurrence patient underwent nipple-sparing mastectomy with reconstruction and nowadays she is receiving therapy with trastuzumab emtansine (T-DM1). Conclusion All visualization modalities fail to provide reliable information on the true rate of pCR. Contemporary systemic therapy regimens after accurate selection of patients, following the inclusion criteria, allows to achieve pCR in 75-90%, thereby reducing the risk of FNR after VAB. The trial continues to enroll patients and further follow-up is needed.

Disclosure(s):

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12/8/2022

5:00 PM - 6:15 PM

OT3-20-04

SerMa – Seroma formations of the Mammary gland in breast cancer patients after mastectomy and implant-based reconstruction (EUBREAST 5)

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Background Postoperative seroma formations are one of the most common and serious complications after implant-based breast reconstruction and can lead to implant and thus breast loss. The cause hasn't yet been clarified. Hypothesis generating and thus as a basis for this multicenter study is the suspicion of a connection between immunological-inflammatory processes that promote the development of a seroma. First promising results of the pilot phase (SerMa pilot) have been published and gave the first impulse for this study. Trial design The SerMa (EUBREAST 5) study is a prospective, multicenter, interventional, international study including patients with primary breast cancer and a skin-/nipple-sparing mastectomy combined with an implant-based reconstruction method. Control groups were chosen to work out common group-specific differences. Intra- or directly preoperatively collected blood as well as intraoperatively collected local smear using swabs are preserved specimens. Follow-up includes visits after 2 and 6 weeks as well as after 6 months. In case of a seroma formation fluid aspirations are preserved for laboratory analyses. Eligibility criteria: The study population contains patients with primary diagnosis of breast cancer scheduled for skin-/nipple-sparing mastectomy and implant-based breast reconstruction. The three control groups are: one with simple mastectomy without breast reconstruction as well as healthy persons with implant insert but without breast cancer after bilateral risk reducing mastectomy or last in case of purely cosmetic implant placement. Specific aims: The main objective of the study is to identify a

patient subgroup with an increased risk of seroma development for future precision elucidation regarding the prevention of postoperative complications such as implant and thus breast loss. FACS-/Bioplex and microbiome analyses will be applied for the detection of certain immune markers, microbes and microbiome diversity using preoperative blood samples, intraoperative local smear collection and in case of later seroma formations also postoperative seroma aspirations. Secondary endpoints include the comparison of these factors and elaborate differences between study and control groups. Furthermore clinico-pathological factors as well as different surgical methods are compared. Statistical methods: A statistical plan for this analysis was specifically developed (Power analyses with Wilcoxon-Mann-Whitney test) and leads to a number of 300 participants per group. Target accrual: Planned start: Q1/2023 Contact: EUBREAST e.V.

Disclosure(s):

Nina Ditsch, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi-Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Lukon: Consulting Fees (e.g., advisory boards) (Ongoing); Molekular Health: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Onkowissen: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing)

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5:00 PM - 6:15 PM

OT3-21-01

A pilot study of robot-assisted nipple-sparing mastectomy followed by immediate breast reconstruction using da Vinci SP® single-port system

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Introduction- Robotic mastectomy is a novel breast surgery approach accessed from a concealable anterior axillary incision showing better cosmetic outcomes with a scarless front view. The oncological safety awaits further follow-up from clinical trials or registered studies to mature. Compared to older da Vinci systems with multiple arms, the new SP system is single-armed, equipped with flexible instruments and a camera that may avoid instrument collision and dead spots in the surgical field. This trial (NCT05448963) is not only the leading SP mastectomy trial in Asia but also the first one that incorporates autologous flap reconstruction.

Methods- -Objectives: To determine the performance, technical algorithm, safety data, and patient-reported outcomes in single-port-accessed nipple-sparing mastectomy using da Vinci SP® system. -Study design: This study is a pilot clinical study conducted in a single-arm, non-randomized design with a goal to recruit 30 participants. The da Vinci SP® surgical robot is applied in the nipple-sparing mastectomy and axillary lymph node dissection (if indicated) of each enrolled patient in Chang Gung Memorial Hospital Linkou Medical Center. The post-mastectomy reconstructive method may use autologous flaps or implants depending on the type of build, technical feasibility, and flap site availability of the patient. The eligibility criteria include: I. Meet at least one of the following indications of NSM for breast cancer: 1. Preoperative clinical tumor sizes less than 5 cm, with an adequate tumor-skin distance of at least 3mm and above, and without nipple-areolar involvement in at least 1cm around the nipple by image 2. Breast cancer up to stage IIIa (T3, N1-2) as the initial clinical stage showing adequate response to neoadjuvant therapy and meeting criteria 1. 3. Germline pathogenic/likely pathogenic BRCA1 or 2 mutation carriers (actionable mutations including pathogenic and likely pathogenic mutations) with a breast cancer diagnosis or requiring unilateral or bilateral prophylactic mastectomy as a risk reduction procedure II. Age equal to or above 20 years III. ECOG (Eastern Cooperative Oncology Group) performance score 0-1 IV. ASA anesthesia risk class 1~2, and with adequate organ functions Endpoint measures: -Primary endpoint: Ability to complete nipple-sparing mastectomy with da Vinci SP system in the per-protocol population. -Secondary endpoints: Safety measured by adverse events through 30-day post-operative follow up -Exploratory endpoints: Surgical time, blood loss, hospital stay, breast specimen weight, cancer resection margin, nipple-preservation rate morbidity and mortality rate within 30 days of operation, and reoperation within 30 days post-surgery -Statistical analysis: Point estimation with a 95% confidence interval will be used to analyze the mean or proportion of key performance parameters. No interim analysis will be performed due to the limited number intended to recruit. -Trial status: Active recruitment Conclusion: The single-port robotic system features single port access with multi-jointed instruments which is particularly designed for narrow surgical spaces such as mastectomy. The feasibility of applying da Vinci SP systems to

robotic nipple-sparing mastectomy and robotic axillary lymph node dissection will be demonstrated in this study.

Disclosure(s):

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5:00 PM - 6:15 PM

OT3-22-01

First-in-human global multi-center study of RLY-2608, a pan mutant and isoform selective PI3K α inhibitor, as a single agent in advanced solid tumor patients and in combination with fulvestrant in patients with advanced breast cancer

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Background: Targeting constitutively active mutant kinases with selective small molecule inhibitors is a key therapeutic pillar of precision oncology. Phosphatidylinositol-4,5biphosphate-3 kinase, catalytic subunit alpha (PIK3CA) mutations leading to oncogenic

activation of PI3K α represent the largest opportunity for this approach in solid tumors. However, there is no selective inhibitor that targets mutant PI3K α in the clinic. Toxicity related to non-selective inhibition of WT PI3K α (hyperglycemia) and other PI3K isoforms limits the tolerability, dosing and efficacy of the orthosteric inhibitor, alpelisib, the only approved solid tumor PI3K inhibitor. RLY-2608, a novel oral allosteric PI3K α inhibitor, is uniquely designed to overcome these limitations via mutant- and isoform-selective PI3K α inhibition for greater target coverage, improved tolerability and antitumor activity. We initiated a first-in-human (FIH), study to evaluate the clinical activity of RLY-2608 as a single agent in advanced solid tumor patients (pts) with PI3KCA mutations and in combination with fulvestrant in pts with PIK3CA mutant, HR+, HER2-metastatic breast cancer (MBC). Methods: This is a global, multi-center, dose escalation/expansion study (NCT05216432) of RLY2608 as a single agent in adults who have advanced solid tumors and are refractory, intolerant, or declined standard therapy and RLY-2608 in combination with fulvestrant in previously treated pts with HR+/HER2- MBC. Eligibility criteria include presence of PI3KCA mutation (blood or tumor) per local assessment, ECOG performance status 0-1, measurable or evaluable disease per RECIST 1.1 and no prior PI3K inhibitor (except combination group 2). RLY-2608 is administered on a continuous schedule with 4-week cycles. Adverse events (AEs) per CTCAE v5, PK, biomarkers (mutant ctDNAs and insulin pathway markers) and anti-tumor activity are assessed serially. Dose escalation employs a Bayesian Optimal Interval design to identify MTD and RP2D. Following dose escalation, pts will be treated with RLY-2608 at the MTD/RP2D in a monotherapy dose expansion with 5 groups (N=75, 15 each): 1. Clear cell ovarian carcinoma 2. Head and neck squamous cell carcinoma 3. Cervical cancer 4. Other solid tumors 5. PI3KCA double mutations. In addition, two expansion cohorts will enroll patients with HR+/HER2- MBC treated with RLY-2608 and fulvestrant combination (N = 30, 15 each): 1. No prior PI3K therapy 2. Intolerant to PI3K inhibitors. The primary endpoints are MTD/RP2D and AE profile for single agent and combination; key secondary endpoints are PI3KCA genotype in blood and tumor, PK, biomarkers, and overall response rate. US enrollment began December 2021 and ex-USA startup is under way.

Disclosure(s):

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OT3-23-01

VELA: A first-in-human phase 1/2 study of BLU-222, a potent, selective cyclin-dependent kinase (CDK) 2 inhibitor in patients with cyclin E1 gene (CCNE1)-amplified or CDK4/6 inhibitor-resistant advanced solid tumors

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Background The regulation of cell growth and proliferation is dependent on cyclins and CDKs. The formation of the cyclin D-CDK4/6 complex increases the expression of cyclin E1 and E2. Cyclin E1 and E2 bind to and activate CDK2; this results in a cyclin E/CDK2 complex that assists with downstream expression of DNA synthesis machinery. The use of CDK4/6 inhibitors such as palbociclib or ribociclib is an effective treatment in patients with hormone receptor-positive (HR+), human epithelial growth factor receptor-2 negative (HER2-) breast cancer; however, resistance to treatment eventually occurs. Aberrant cyclin E/CDK2 activity has been identified as a potential resistance mechanism by which tumors can evade CDK4/6 inhibitors. BLU-222 is an oral, investigational, potent, and selective CDK2 inhibitor. In preclinical studies, BLU-222 treatment in combination with ribociclib led to durable tumor regression in both CDK4/6-resistant and sensitive models of HR+HER2- breast cancer. Trial design VELA (NCT05252416) is an international, open-label, first-in-human phase 1/2 study evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of BLU-222 in adult patients with CCNE1-amplified tumors or with HR+HER2- breast cancer with disease progression on CDK4/6 inhibitors. In phase 1 and 2, patients aged ≥ 18 years with an Eastern Cooperative Oncology Group performance status 0–2 are eligible. In phase 2, all patients must have ≥ 1 measurable target lesion per Response Evaluation Criteria in Solid Tumors version 1.1. Primary endpoints include assessing the safety of BLU-222 as a single agent or BLU-222 in combination with either carboplatin or ribociclib and/or fulvestrant (phase 1 and 2), identifying the maximum tolerated dose and/or recommended phase 2 dose (phase 1), and determining the objective response rate (phase 2). In the phase 1 dose-escalation part, patients with any advanced solid tumor with progression on standard of care (SOC) will receive BLU-222; patients with gastric or endometrial cancer (EC) with progression on ≥ 2 prior therapies (including ≥ 1 platinum-based therapy) or with CCNE1-amplified platinum-resistant/refractory ovarian cancer (OC) will receive BLU-222 and carboplatin; patients with HR+HER- breast cancer with progression on CDK4/6 inhibitors will receive BLU-222, ribociclib, and fulvestrant. In the phase 2 dose-expansion part, patients with CCNE1-amplified tumors including EC (progression on ≥ 2 prior therapies), platinum-resistant/refractory OC, or other advanced solid tumors (progression after SOC) will receive BLU-222 monotherapy; patients with CCNE1-amplified platinum-resistant/refractory OC will receive BLU-222 and carboplatin; and patients with CDK4/6 inhibitor-resistant HR+HER2- breast cancer will receive BLU-222 and fulvestrant with/without ribociclib. Pharmacokinetic parameters will be calculated using standard non-compartmental methods from the plasma concentration–time data. Tissue biopsies will be collected during cycle 1 to assess the phosphorylation of retinoblastoma 1 (Rb1) protein which will be used as a pharmacodynamic marker to assess target inhibition. Dose escalation is ongoing and approximately 50 sites are anticipated to enroll patients across North America, Europe, and the Asia/Pacific region.

Disclosure(s):

Manish R Patel, MD: Accutar Biotech: Research Funding (Ongoing); Acerta Pharma: Research Funding (Ongoing); Adagene: Research Funding (Ongoing); Adaptive Biotechnologies: Honoraria (Ongoing); ADC Therapeutics: Research Funding (Ongoing); Agenus: Research Funding (Ongoing); Aileron Therapeutics: Research Funding (Ongoing); Artios: Research Funding (Ongoing), Research Funding (Ongoing); Astellas: Research Funding (Ongoing); AstraZeneca: Research Funding (Ongoing); Bayer: Honoraria (Ongoing); BioNTech AG: Research Funding (Ongoing); BioTheryX: Research Funding (Ongoing); Black Diamond Therapeutics: Research Funding (Ongoing); Blueprint Medicines Corporation: Research Funding (Ongoing); Boehringer Ingelheim: Research Funding (Ongoing); Celgene: Research Funding (Ongoing), Speakers Bureau (Ongoing); Checkpoint Therapeutics: Research Funding (Ongoing); CicloMed: Research Funding (Ongoing); Clovis Oncology: Research Funding (Ongoing); Cytair Therapeutics: Research Funding (Ongoing); Daiichi Sankyo: Research Funding (Ongoing); EMD Serono: Research Funding (Ongoing); Evelo Therapeutics: Research Funding (Ongoing); Exelixis: Speakers Bureau (Ongoing); FORMA Therapeutics: Research Funding (Ongoing); Genentech: Honoraria (Ongoing); Genentech/Roche: Research Funding (Ongoing), Speakers Bureau (Ongoing); Gilead Sciences: Research Funding (Ongoing); GlaxoSmithKline: Research Funding (Ongoing); H3 Biomedicine: Research Funding (Ongoing); Hengrui Therapeutics: Research Funding (Ongoing); Hutchison MediPharma: Research Funding (Ongoing); IgM Biosciences: Research Funding (Ongoing); Ignyta: Research Funding (Ongoing); Immunogen: Research Funding (Ongoing); Incyte: Research Funding (Ongoing); ION Pharma: Leadership Role (Ongoing); Jacobio: Research Funding (Ongoing); Janssen: Research Funding (Ongoing); Janssen Oncology: Honoraria (Ongoing); Klus Pharma: Research Funding (Ongoing); Kymab: Research Funding (Ongoing); Lilly: Research Funding (Ongoing); Loxo: Research Funding (Ongoing); LSK Biopartners: Research Funding (Ongoing); Lycera: Research Funding (Ongoing); Mabspace: Research Funding (Ongoing); MabSpace Biosciences: Research Funding (Ongoing); MacroGenics: Research Funding (Ongoing); Merck: Research Funding (Ongoing); Millennium: Research Funding (Ongoing); Mirati Therapeutics: Research Funding (Ongoing); Moderna Therapeutics: Research Funding (Ongoing); NGM Biopharmaceuticals: Research Funding (Ongoing); Novartis: Research Funding (Ongoing); Nurix: Research Funding (Ongoing), Research Funding (Ongoing); Olema: Research Funding (Ongoing); ORIC: Research Funding (Ongoing); Pfizer: Honoraria (Ongoing), Research Funding (Ongoing); Pfizer/EMD Serono: Consulting Fees (e.g., advisory boards) (Ongoing); Pharmacyclics: Honoraria (Ongoing); Pharmacyclics/Janssen: Consulting Fees (e.g., advisory boards) (Ongoing); Placon: Research Funding (Ongoing); Portola Pharmaceuticals: Research Funding (Ongoing); Prelude Therapeutics: Research Funding (Ongoing); PureTech: Research Funding (Ongoing), Research Funding (Ongoing); Relay Therapeutics: Research Funding (Ongoing); Ribon Therapeutics: Research Funding (Ongoing); Samumed: Research Funding (Ongoing); Seven and Eight Biopharmaceuticals: Research Funding (Ongoing); Silicon Therapeutics: Research Funding (Ongoing); Syndax: Research Funding (Ongoing); Taiho Pharmaceutical: Research Funding (Ongoing), Speakers Bureau (Ongoing); Takeda: Research Funding (Ongoing); TeneoBio: Research Funding (Ongoing), Research Funding (Ongoing); Tesaro: Research Funding (Ongoing); TopAlliance BioSciences Inc: Research Funding (Ongoing); Treadwell: Research Funding (Ongoing); Treadwell Therapeutics: Research Funding (Ongoing); Vigeo: Research Funding (Ongoing); Zymeworks: Research Funding (Ongoing)

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ReFocus: A Phase 1/2 Study of the Highly Selective FGFR2 Inhibitor, RLY-4008, in Patients with Advanced Solid Tumors Including Breast Cancer

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Background: Oncogenic alterations (gene amplification, mutation, and fusion/rearrangements) of fibroblast growth factor receptor 2 (FGFR2) are rare and occur at varying frequencies across solid tumor types and have become critical therapeutic targets in drug development. First generation FGFR pan-kinase inhibitors non-selectively inhibit FGFR1-4 and are associated with dose limiting toxicities and narrow therapeutic windows. Off-isoform toxicity (FGFR1-hyperphosphatemia; FGFR4-diarrhea) and on-target acquired resistance have led to limited efficacy, which is primarily seen in FGFR2-fusion+ intrahepatic cholangiocarcinoma. Therapies that selectively target FGFR2 remain an unmet need in advanced breast cancer as well as other solid tumor types. RLY-4008 is a novel, oral FGFR2 inhibitor designed to overcome the limitations of pan-FGFR inhibitors (FGFRi) by potently and selectively targeting primary oncogenic FGFR2 alterations and acquired resistance mutations. RLY-4008 is > 200-fold selective over FGFR1, > 80- and > 5000-fold selective over FGFR3 and FGFR4 respectively. Here we describe a phase 1/2 study to investigate the safety and antitumor activity in advanced FGFR2 altered cancers, including breast cancer. Methods: ReFocus is a phase 1/2 open label global study evaluating the safety and efficacy of RLY-4008 (NCT04526106) in adult patients with advanced unresectable and/or metastatic cancers harboring an FGFR2 alteration. Key eligibility criteria include: documented FGFR2 alteration in blood or tissue per local assessment, ECOG performance status of 0-1, disease that is refractory or not adequately responding to standard therapy, has no available standard therapy, or patient is intolerant of, or declined standard therapy (including pan-FGFRi), and measurable or evaluable disease per RECIST 1.1. FGFR2 alteration will be confirmed retrospectively by central laboratory assessment. Part 1 dose escalation employed the Bayesian Optimal Interval (BOIN) design to determine the MTD/RP2D of RLY-4008. Part 2 dose expansion is presently enrolling patients at the RP2D of RLY-4008 and includes 5 cohorts comprised of patients with: 1. FGFR2 fusion+ cholangiocarcinoma previously treated with an FGFRi; 2. FGFR2 fusion+ cholangiocarcinoma not previously treated with an FGFRi; 3. FGFR2 fusion+ solid tumors; 4. FGFR2 mutation+ solid tumors and 5. FGFR2 amplified solid tumors. Solid tumors in cohorts 3, 4 and 5 will have a focus in breast cancer. The primary endpoint is objective response rate (ORR); key secondary endpoints include: duration of response, safety and tolerability, correlation of FGFR2 genotype by central tissue assessment with antitumor response, characterization of PK profile, and quality of life. US enrollment began September 2020 and has expanded into Europe and Asia. Clinical trial information: NCT04526106.

Disclosure(s):

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5:00 PM - 6:15 PM

OT3-25-01

**Neoadjuvant HER2-targeted Therapy +/- Immunotherapy with Pembrolizumab (neoHIP):
An Open Label Randomized Phase II Trial**

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Background: Immune checkpoint inhibition (ICI) is synergistic with HER2-directed therapy in pre-clinical models. Clinically, pembrolizumab (K)-mediated ICI plus HER2-directed therapy with trastuzumab (H) was safe and demonstrated modest activity in H-resistant HER2-positive (HER2+) metastatic breast cancer. Because ICI may confer more robust activity when administered earlier in the course of disease, H and K administered in the curative-intent, treatment-naïve setting may allow for de-escalation of cytotoxic chemotherapy; confer life-long, tumor-specific immunity; and ultimately, improve cure rates. Moreover, the synergy of H and K with paclitaxel (T) may overcome the need for dual HER2-blockade with H plus pertuzumab (P). In this randomized, multicenter, phase II, open-label, multi-center trial the efficacy and safety of neoadjuvant THP vs THP-K vs TH-K are explored. Methods: 174 patients (pts) ≥18y with previously untreated, stage II-III, HER2+ breast cancer will be randomized and stratified by clinical nodal status (positive vs. negative) and hormone receptor status (positive vs. negative). In arm A, pts receive T at 80mg/m² weekly for 12 weeks, H at 8mg/Kg (loading dose) and then 6mg/Kg every 3 weeks x 3 doses, P at 840 mg (loading dose) and then 420mg/Kg every 3 weeks x 3 doses (THP). In arm B, pts receive THP plus K at 200mg every 3 weeks x 4 doses (THP-K). In arm C, pts receive TH-K; however, in a preplanned interim analysis, arm C did not meet the pre-defined efficacy threshold and this arm was subsequently closed. Enrollment to arms A and B continue. Definitive surgery is 3-6 weeks after the last dose. After surgery, pts are treated per the treating physician's discretion including radiotherapy per local clinical standard. Pts whose tumors are hormone-receptor positive will receive hormone therapy per local standard-of-care. The primary end point is pathologic complete response (pCR) rate in the breast and axilla (ypT0/Tis ypN0). Secondary end points include pCR rate by ypT0ypN0 and ypT0/Tis, residual cancer burden index, event free survival, breast conserving surgery rate, safety and overall survival. Exploratory correlative studies will characterize potential immune biomarkers predictive of efficacy and/or toxicity. Funding sources: BCRF, Merck NCT03747120

Disclosure(s):

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Inetetamab combined with pyrotinib and Chemotherapy in Pretreated Patients with HER2-positive metastatic breast cancer , a single arm , multicenter phase II clinical trial

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Background: The HER2-targeted drugs selection after trastuzumab failure has become a challenging issue for HER2-positive metastatic breast cancer (MBC) patients. Inetetamab is a neotype of HER2-targeted monoclonal antibody with an engineered Fc segment that optimizes the antibody-dependent cell-mediated cytotoxicity (ADCC) effect, which was important for disease control. Moreover, HER2-targeted tyrosine kinase inhibitors, as pyrotinib, were found to further improve the ADCC effect of monoclonal antibodies in pre-clinical researches, indicating that the combination of pyrotinib and inetetamab could achieve complementarity and synergy effects in terms of short-term tumor killing effect and long-term immunotherapy benefits. Therefore, the combined treatment pattern of the two drugs has potential clinical benefits.

Methods: This is a prospective, multi-center, single-arm clinical study designed to evaluate the efficacy and safety of pretreated patients with HER2-positive MBC. We recruited patients with

pathologically confirmed HER2-positive MBC who had received 1-3 prior regimens for metastatic disease, which must include trastuzumab. The enrolled patients received 6 cycles of Inetetamab combined with pyrotinib and chemotherapy, subsequent maintenance therapy should be considered according to tolerability. The chemotherapy drugs were decided by physicians' choice, and could be microtubules, anthracyclines, or antimetabolites. The primary endpoint was objective response rate (ORR) after 6 cycles of treatment, secondary endpoints included progression-free survival (PFS), overall survival (OS), and clinical benefit rate (CBR) and adverse events (AEs). Results: 57 patients were enrolled from October 2020 to July 2022. And 45 patients were available for response evaluation. The ORR and DCR were 53.5 % (24 / 45) and 86.7 % (39 / 45), respectively after 6 cycles treatment. The median PFS was 7.3 months. The incidence of grade III-IV AEs was 15.8 %. The most common treatment-related AEs were diarrhea, anemia, neutropenia, leukopenia, hand and foot syndrome. No patient's left ventricle ejection fraction (LVEF) decreased to < 50% or decreased by >15%. And no significant decline in quality of life score was reported. Conclusion: Inetetamab combined with pyrotinib and chemotherapy showed a promising efficacy and a good tolerance in patients with HER2-positive metastatic breast cancer, confirming the synergistic effect between the ADCC optimized monoclonal antibodies and TKIs, which brings more treatment options for HER2-positive metastatic breast cancer.

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CCTG MA40: DOUBLE-BLIND PLACEBO CONTROLLED PHASE III TRIAL OF FULVESTRANT AND IPATASERTIB FOR ADVANCED HER-2 NEGATIVE AND ESTROGEN RECEPTOR POSITIVE (ER+) BREAST CANCER POST FIRST LINE CDK 4/6 AND AROMATASE INHIBITOR THERAPY (FINER)

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Background: The PI3K/AKT/mTOR pathway is a rational target in the metastatic disease setting for hormone receptor positive breast cancer based on preclinical and clinical data demonstrating that pathway inhibition improves outcome (Baselga 2012, Andre 2019, Jones

2019). Combining fulvestrant and AKT inhibition demonstrated efficacy in pts with HR+abc (Howell 2022). Ipatasertib is a potent, highly selective, small-molecule inhibitor of three isoforms of serine/threonine kinase AKT. We hypothesize that Ipatasertib plus fulvestrant will improve PFS compared to fulvestrant in the second line setting post disease progression on aromatase inhibitor (AI) + CDK 4/6 inhibitor therapy. Methods: MA40 is a double blind, placebo-controlled trial in patients with hormone receptor positive, HER2-negative breast cancer with prior progression on AI plus CDK4/6 inhibitor therapy. Patients are randomized to fulvestrant/ipatasertib 400 mg po days 1-21 every 28 day or fulvestrant/placebo. The primary objective is to compare Progression Free Survival (PFS) between arms (RECIST 1.1, investigator assessed). Secondary objectives include comparisons between arms: PIK3CA/AKT1/PTEN altered cohort and non-altered cohorts; PFS by Blinded Central Radiology Review (all enrolled patients, PIK3CA/AKT1/PTEN altered and non-altered cohorts), Response rate; Duration of Response; Clinical Benefit Rate; Overall Survival; Time to Commencement of Subsequent Line of Systemic Therapy or Death; Safety and Tolerability (CTCAE version 5.0); QOL (EORTC QLQ-C30, NCI PRO-CTCAE); Economic Evaluation, (healthcare utilization and health utilities(EQ-5D-5L)). Statistical Design: Allocation 1:1 balanced for: PIK3CA/PTEN/AKT1 mutation status (ctDNA analysis using FoundationOne@Liquid Platform) (altered vs wildtype/unknown); prior treatment duration with CDK4/6 inhibitor (< 6 months vs > 6 months) and centre. Sample size is 250 to detect a benefit in PFS with the addition of ipatasertib. Eligibility Criteria: Histologically and/or cytologically confirmed ER positive and HER-2 negative breast cancer by local assessment that is advanced; postmenopausal status; clinical and/or radiographic progression during treatment with or within 28 days after discontinuation of first line of treatment with a CDK 4/6 inhibitor and an AI; only one prior line of chemotherapy in the advanced setting. Conduct to Date: Enrollment is ongoing. Supported by Hoffmann-La Roche Limited, CCS

Disclosure(s):

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A Phase 3 study of gedatolisib plus fulvestrant with and without palbociclib in patients with HR+/HER2- advanced breast cancer previously treated with a CDK4/6 inhibitor plus a non-steroidal aromatase inhibitor (VIKTORIA-1)

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Background: Gedatolisib is a potent reversible dual inhibitor that selectively targets all Class I isoforms of phosphoinositide 3-kinase (PI3K) and mechanistic target of rapamycin (mTOR). Two separate pivotal clinical trials demonstrated that PI3K and mTOR inhibitors are active in combination with endocrine therapy and prolong progression-free survival (PFS) among patients with hormone receptor positive (HR+)/HER2-negative (HER2-) advanced breast cancer (ABC) who had previously received endocrine therapy (SOLAR-1, BOLERO-2). CDK4/6 inhibitor (CDK4/6i) therapy has been approved in the front-line setting. However, patients eventually experience disease progression on CDK4/6i based therapy. Available data indicates that resistance to CDK4/6i is a transient adaptive mechanism that may be reversed by adding inhibitors of the PI3K/mTOR pathway (PI3K/mTORi). Thus, combination of PI3K/mTORi and CDK4/6i in patients whose disease progressed on prior CDK4/6i could potentially both restore sensitivity to CDK4/6i and prevent adaptive activation of the PI3K/mTOR pathway. This hypothesis was evaluated in a Phase 1b study (Layman SABCS 2021). Subjects with HR+/HER2- ABC who were CDK4/6i pretreated received gedatolisib (180 mg IV weekly for 3 weeks, then one week off) in combination with standard doses of palbociclib and fulvestrant. Median PFS was 12.9 months, and overall response rate was 63%. Grade 3-4 adverse events (AE) were observed at a low rate, and toxicity was overall easily managed with available standards of care, and few patients discontinued treatment due to treatment-related adverse events (4%). The most common AE was stomatitis; hyperglycemia of any grade occurred in 26% of patients. This preliminary data, dosing schedule, and study population characteristics form the basis for the Phase 3 trial, VIKTORIA-1. Trial design: This Phase 3, open-label, randomized, multinational two-part clinical trial will evaluate the efficacy and safety of gedatolisib and fulvestrant with or without palbociclib in patients with HR+/HER2- ABC previously treated with any CDK4/6i in combination with non-steroidal aromatase inhibitor therapy. Those without tumor PIK3CA mutations will be assigned to Study 1 and those with PIK3CA mutations will be assigned to Study 2. Study 1 will include up to 351 subjects randomized in a 1:1:1 ratio to Arm A (gedatolisib, palbociclib, and fulvestrant), Arm B (gedatolisib plus fulvestrant), or Arm C (fulvestrant). For subjects in Arm C whose disease progresses, crossover to Arm A or B is allowed. Study 2 will include up to 350 subjects randomized in a 3:3:1 ratio to Arm D (gedatolisib, palbociclib, and fulvestrant), Arm E (alpelisib plus fulvestrant), or Arm F (gedatolisib plus fulvestrant). Key eligibility criteria include adults with confirmed metastatic or locally advanced breast cancer, any menopausal status for females, radiologically evaluable disease, and prior CDK4/6i treatment with non-steroidal AI. Prior therapy with SERD, including fulvestrant is allowed. Key exclusion criteria include prior treatment with a PI3K, protein kinase B (Akt), or mTOR inhibitor, prior treatment with chemotherapy for advanced disease, more than two lines of prior endocrine therapy, bone only disease with no soft tissue components, active CNS metastases, and type 1 diabetes or uncontrolled type 2 diabetes. The primary endpoint is PFS assessed by blinded independent central review (BICR) per RECIST v1.1. Secondary endpoints included overall survival (OS), safety and tolerability, ORR, duration of response, time to response, CBR, quality of life, and pharmacokinetics. This trial is open for enrollment.

Disclosure(s):

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Subtyping-based platform guides precision medicine for heavily pretreated metastatic triple-negative breast cancer: a multicenter, phase 2, umbrella, FUTURE trial

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Background: Triple-negative breast cancer (TNBC) is a heterogeneous disease and lacks effective treatment. Our previous study classified TNBCs into four subtypes (luminal androgen receptor [LAR], immunomodulatory [IM], basal-like immune-suppressed [BLIS], mesenchymal-like [MES]) with distinct molecular features. We aimed to assess the efficacy and safety of molecular subtype-derived precision treatment in patients with heavily pretreated metastatic TNBC.

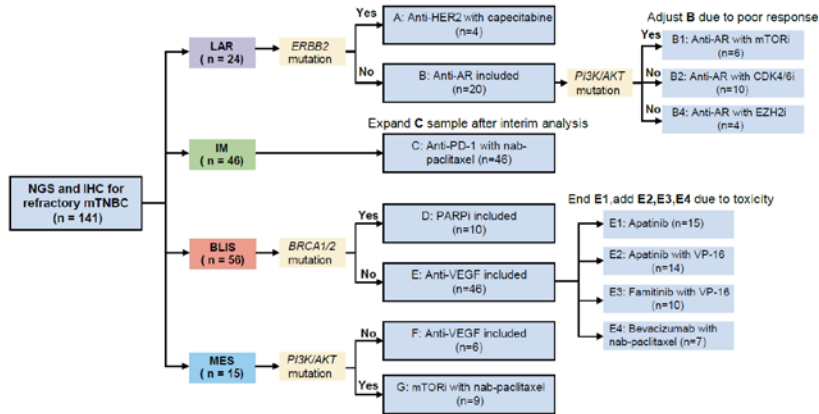
Methods: This open-label, phase 2, umbrella trial included patients from four centers in China. Participants were women (aged ≥ 18 years) with histologically confirmed metastatic TNBC with disease progression after multiple lines of standard chemotherapy. Patients were enrolled into seven parallel arms according to their molecular subtypes: LAR with or without ERBB2 somatic mutation/amplification assigned to arm A (pyrotinib with capecitabine) and arm B (androgen inhibitor included therapy); IM assigned to arm C (anti-PD-1 antibody with nab-paclitaxel); BLIS with or without BRCA1/2 germline mutation assigned to arms D (PARP inhibitor included therapy) and E (anti-VEGFR included therapy); MES without or with PI3K-AKT mutation assigned to arms F (anti-VEGFR included therapy) and G (everolimus with nab-paclitaxel). Bayesian predictive probability was adopted to monitor each arm, which can be terminated independently according to a prespecified futility or efficacy boundary. This trial is registered with ClinicalTrials.gov, NCT03805399.

Findings: Between October 18, 2018, and February 11, 2022, we enrolled 141 patients. All patients were heavily pretreated and resistant to six categories of the most common chemotherapeutic agents used in breast cancer treatment, with a median of 3 previous lines of therapies in the metastatic setting (Table 1 and 2). The median follow-up was 18.3 months (IQR 11.7-27.7). A confirmed objective response was achieved in 42 (29.8%, 95% CI 22.4-38.1) of the 141 patients. The median PFS was 3.4 months (95% CI 2.7-4.2), and the median OS was 10.7 months (95% CI 9.0-12.3) (Table 3). Arms A, C, E and G achieved efficacy boundaries, with 3 (75.0%) out of 4 patients in arm A, 20 (43.5%) out of 46 patients in arm C, 13 (28.3%) out of 46 patients in arm E, and 3 (33.3%) out of 9 patients in arm G achieving objective responses. Potential predictive biomarkers of efficacy in each arm were explored. Safety data were consistent with the known safety profiles of relevant drugs.

Interpretation: We demonstrate the feasibility and clinical utility of a subtyping-based, genomic sequencing-guided strategy which allows the majority of heavily pretreated metastatic TNBCs to benefit from precision treatment. Most arms exhibit promising efficacy and manageable

toxicities, providing subtyping schema to optimize personalized treatment.

Table 1. The FUTURE trial schema.



Patients are stratified into seven arms using the FUSCC 484-gene NGS panel testing and IHC subtyping. Abbreviations: mTNBC, metastatic triple-negative breast cancer; NGS, next-generation sequencing; IHC, immunohistochemistry; FUSCC, Fudan University Shanghai Cancer Center; LAR, luminal androgen receptor; IM, immunomodulatory; BLIS, basal-like immune-suppressed; MES, mesenchymal-like; n, number; AR, androgen receptor; PD-1, programmed cell death-1; PARPi, poly ADP-ribose polymerase inhibitor; VEGF, vascular endothelial growth factor; mTORi, mammalian target of rapamycin inhibitors.

Table 2. Patient characteristics in the FUTURE trial.

Characteristic	ITT (n = 141)	A (n=4)	B (n=20)	C (n=40)	D (n=30)	E (n=40)	F (n=9)	G (n=9)
Median age at enrollment (range) - year	62 (23 - 74)	58 (54-68)	64 (53-74)	60 (529-71)	60 (29-91)	60 (28-60)	67 (34-68)	61 (23-65)
ECOG								
0	5 (3.5%)	0	0	4 (10%)	3	1 (2.5%)	0	0
1	105 (86.1%)	4 (100%)	16 (80%)	36 (90%)	27	38 (95%)	9 (100%)	9 (100%)
2	10 (11.3%)	0	1 (5%)	3 (8%)	2 (7%)	7 (17.5%)	0	0
Previous lines of treatment median no. (range)	1 (1 - 0)	4 (3-4)	3 (1-7)	3 (1-8)	3 (2-5)	3 (1-5)	2 (2-4)	3 (2-5)
Previous chemotherapy (drug - no. (%))								
Taxanes	140 (99.3%)	4 (100%)	20 (100%)	40 (100%)	30 (100%)	40 (100%)	9 (100%)	9 (100%)
Antirrhodines	131 (92.9%)	4 (100%)	19 (95%)	40 (100%)	30 (100%)	40 (100%)	9 (100%)	9 (100%)
Platinum agents	132 (93.6%)	4 (100%)	19 (95%)	40 (100%)	30 (100%)	40 (100%)	9 (100%)	9 (100%)
Genitotoxic	10 (7.1%)	0	1 (5%)	3 (8%)	2 (7%)	7 (17.5%)	0	0
Cyclophosphamide	10 (7.1%)	0	1 (5%)	3 (8%)	2 (7%)	7 (17.5%)	0	0
Topotecan	114 (80.8%)	3 (75%)	16 (80%)	36 (90%)	27	38 (95%)	9 (100%)	9 (100%)
Other	114 (80.8%)	3 (75%)	16 (80%)	36 (90%)	27	38 (95%)	9 (100%)	9 (100%)
No. of metastatic organ								
1	21 (14.9%)	0	7 (35%)	5 (13%)	1 (3%)	5 (13%)	2 (22%)	1 (11%)
2	40 (28.4%)	0	12 (60%)	10 (25%)	10 (30%)	10 (25%)	3 (33%)	3 (33%)
≥ 3	71 (50.4%)	4 (100%)	13 (65%)	25 (63%)	19 (57%)	25 (63%)	4 (44%)	5 (56%)
Metastatic site								
Lymph nodes	68 (48.2%)	2 (50%)	6 (30%)	20 (50%)	10 (30%)	20 (50%)	5 (56%)	5 (56%)
Lung	49 (34.8%)	2 (50%)	8 (40%)	10 (25%)	10 (30%)	10 (25%)	3 (33%)	3 (33%)
Liver	43 (30.5%)	2 (50%)	12 (60%)	11 (28%)	10 (30%)	10 (25%)	4 (44%)	4 (44%)
Bone	69 (49.0%)	3 (75%)	8 (40%)	21 (53%)	10 (30%)	10 (25%)	3 (33%)	3 (33%)
Chest wall	51 (36.2%)	1 (25%)	7 (35%)	10 (25%)	10 (30%)	10 (25%)	3 (33%)	3 (33%)
Brain	22 (15.6%)	0	1 (5%)	3 (8%)	4 (12%)	4 (10%)	1 (11%)	1 (11%)
Other	30 (21.3%)	0	5 (25%)	11 (28%)	4 (12%)	4 (10%)	3 (33%)	3 (33%)
Duration of the first line therapy (months)								
< 3	40 (28.4%)	1 (25%)	6 (30%)	14 (35%)	2 (6%)	10 (25%)	4 (44%)	4 (44%)
3-6	42 (29.8%)	2 (50%)	6 (30%)	10 (25%)	10 (30%)	10 (25%)	3 (33%)	3 (33%)
> 6	35 (24.8%)	1 (25%)	8 (40%)	16 (40%)	18 (54%)	10 (25%)	2 (22%)	2 (22%)
Unknown	10 (7.1%)	0	5 (25%)	10 (25%)	10 (30%)	10 (25%)	3 (33%)	3 (33%)
Disease-free interval* (months)								
< 6	33 (23.4%)	2 (50%)	5 (25%)	10 (25%)	3 (9%)	10 (25%)	3 (33%)	3 (33%)
6-12	17 (12.1%)	1 (25%)	3 (15%)	5 (13%)	5 (15%)	5 (13%)	1 (11%)	1 (11%)
> 12	47 (33.3%)	1 (25%)	12 (60%)	25 (63%)	22 (66%)	25 (63%)	6 (67%)	6 (67%)
NA due to initial stage IV	24 (17.0%)	0	3 (15%)	10 (25%)	10 (30%)	10 (25%)	0	0

* Interval between the time of metastasis or relapse and the last dose of adjuvant chemotherapy or surgery (or neoadjuvant chemotherapy cases without adjuvant chemotherapy).
Abbreviations: ITT, intention to treat; n, number; NA, not available.

Table 3. Summary of treatment efficacy of TNBC in the FUTURE trial

	Total (n=141)	A (n=4)	B (n=20)	C (n=46)	D (n=10)	E (n=46)	F (n=6)	G (n=9)
CR-no. of patients (%)	4 (2.8)	0	0	2 (4.3)	1 (10.0)	1 (2.2)	0	0
PR-no. of patients (%)	30 (27.0)	3 (75.0)	0	18 (39.1)	1 (10.0)	12 (26.1)	1 (16.7)	3 (33.3)
SD-no. of patients (%)	26 (18.4)	0	2 (10.0)	10 (21.7)	1 (10.0)	11 (23.9)	1 (16.7)	1 (11.1)
PD-no. of patients (%)	44 (31.2)	1 (25.0)	10 (50.0)	9 (19.6)	4 (40.0)	15 (32.6)	2 (33.3)	2 (22.2)
NE-no. of patients (%)	29 (20.6)	0	8 (40.0)	7 (14.3)	3 (30.0)	7 (15.2)	2 (33.3)	2 (22.2)
ORR								
no. of patients	42	3	0	20	2	13	1	3
% of patients (95%CI)	29.8 (22.4-38.1)	75.0 (19.4-99.4)	0	43.5 (28.9-58.9)	20 (2.5-55.6)	28.3 (16.0-43.5)	16.7 (0.4-64.1)	33.3 (7.5-70.1)
DCR								
no. of patients	68	3	2	30	3	24	2	4
% of patients (95%CI)	48.2 (39.7-56.8)	75 (19.4-99.4)	10 (1.2-31.7)	65.2 (49.8-78.6)	30 (6.7-65.3)	52.2 (36.9-67.1)	33.3 (0.4-77.7)	44.4 (13.7-79.8)
median PFS (95%CI)-mo	3.4 (2.7-4.2)	3.4 (0-7.3)	1.9 (1.7-2.1)	4.6 (3.4-5.9)	2.0 (1.7-2.3)	3.4 (1.7-5.0)	1.2 (0-2.5)	3.0 (2.4-3.8)
median OS (95%CI)-mo	10.7 (9.1-12.3)	16.7 (0-35.3)	6.1 (2.8-9.4)	16.1 (11.7-20.5)	6.2 (1.9-10.5)	10.1 (3.8-16.3)	2.7 (0-17.0)	4.5 (2.4-6.6)

TNBC, triple-negative breast cancer; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; NE, not evaluated; ORR, objective response rate; DCR, disease control rate; CI, credible intervals; PFS, progression free survival; OS, overall survival.

Disclosure(s):

Zhi-Ming Shao, M.D. Ph.D: No financial relationships to disclose

Zhong-Hua Wang, n/a: No financial relationships to disclose

Yi-Zhou Jiang, M.D.: No financial relationships to disclose

Yin Liu, n/a: No financial relationships to disclose

Xiu-Zhi Zhu, n/a: No financial relationships to disclose

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Qiang Yu, n/a: No financial relationships to disclose

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Tao Sun, n/a: No financial relationships to disclose

Jiuwei Cui, MD: Adlai Nortye Biopharma Co., Ltd: Contracted Research (Ongoing)

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(Ongoing)

12/8/2022

5:00 PM - 6:15 PM

OT3-28-01

A Dose-escalation Study of the Safety and Pharmacology of DAN-222 in Subjects with Metastatic Breast Cancer NCT05261269

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Clinical Study:

This clinical study is designed to evaluate DAN-222 as a monotherapy and in combination with a PARP inhibitor which is expected to increase efficacy without significant increase in toxicity. DAN-222 is a novel therapeutic nanoparticle with a complimentary mechanism for combination with a PARP inhibitor anticipated for patients with HRD+ and HRD- tumors, and not restricted to BRCAm.

This is an ongoing phase 1/2 study to evaluate the safety and pharmacology of DAN-222 in patients with metastatic breast cancer and initial evaluation of efficacy. Here we report on the initial pharmacology. The results in the patients show the expected characteristics of the designed product, including consistency with preclinical models (e.g. T1/2= 28 hours), which is a feature of this platform given the non-enzymatic release mechanism of the payload that allows for improved translation from preclinical species to clinical patients as well low variability between patients (e.g. CV%=16.5).

Study Rationale:

DAN-222 is a topoisomerase-1 inhibitor (Camptothecin) nanoparticle therapeutic that has been optimized for tumor biodistribution and pharmacokinetics. DAN-222 has a broad therapeutic index in preclinical evaluation and the complementary mechanism of action with PARP inhibitors provides significantly enhanced efficacy while also sparing bone marrow. Importantly, the complementary enhanced efficacy is independent of tumor homologous repair deficiency (HRD) status, including BRCA status.

The efficacy of DAN-222 was evaluated alone and in combination with a PARP inhibitor (niraparib) in HRD+ breast cancer (MDA-MB-436) and HRD- ovarian cancer (OVCAR-3) xenograft models. Table 1 highlights the endpoints of the study as measured by partial response, complete response, tumor free survival and median tumor volume at end of study (Day 60). DAN-222 alone had PR effects and reduced median tumor volume compared to niraparib alone. The combination demonstrated enhancement of response as evidenced by an increase in partial response, a shift from partial to complete response, an increase in tumor-free survivors, and significant further reduction in median tumor volume.

Conclusion:

The clinical pharmacology will be presented and demonstrates the designed behavior of the

nanoparticle. A design feature of the nanoparticle is that the payload and linker are sequestered in the core, protecting them from circulatory components. Moreover, the covalent attachment of the payload allows for tunable release kinetics via a hydrolytic linker, preventing burst release and associated toxicities common to physical encapsulation-based nanoparticle systems (e.g., liposomes, micelles). The preliminary PK profile in patients supports the translatability across species and consistency of exposure across patients.

Treatment	Dose (mg/kg)	HRD+				BRCAwt			
		PR	CR	TFS	MTV Day 60 (mm ³)	PR	CR	TFS	MTV Day 60 (mm ³)
Niraparib	50/40	0	0	0	1372	0	0	0	726
DAN-222	1	6	0	0	321	4	0	0	405
DAN-222 + Niraparib	1, 50/40	5	3	2	18	1	6	4	4

HRD = homologous recombination deficiency, PR = partial response, CR = complete response, TFS = tumor-free survivor, MTV = median tumor volume

Disclosure(s):

Ashley P. Wright, n/a: Dantari, Inc.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

Emily A. Wyatt, n/a: Dantari, Inc.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Salary (Ongoing)

Timothy Hagerty, n/a: Dantari, Inc.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

12/8/2022

5:00 PM - 6:15 PM

OT3-29-01

A Phase Ib/II Study of anlotinib combined with pyrotinib and capecitabine for HER2-Positive Metastatic Breast Cancer

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Background: Preclinical data showed that high levels of vascular endothelial growth factor (VEGF) may lead to aggressive behavior in breast tumors that overexpress HER2. AVEREL study demonstrated that bevacizumab in combination with trastuzumab and docetaxel as first-line treatment increased progression-free survival (PFS) in HER2 positive metastatic breast cancer (BC) patients (BTH vs TH : 16.5m vs 13.7m · HR=0.82 · P=0.0775). It is necessary to exploring new effective and tolerable strategy of targeting both HER2 signaling and angiogenesis. PHENIX and PHOEBE studies proved pyrotinib (an irreversible pan-ErbB receptor tyrosine kinase inhibitor) plus capecitabine improved prognosis for patients with advanced HER2 positive BC. Anlotinib is a novel multi-target tyrosine kinase inhibitor that effectively inhibits VEGFR, FGFR, c-KIT, c-MET and RET. This study is aimed to evaluate safety, tolerability and efficacy of anlotinib combined with pyrotinib and capecitabine for HER2-Positive metastatic BC. Methods: This open-label study is designed to include patients with pathologically confirmed HER2-positive metastatic breast cancer that have progressed or relapsed after treatment with trastuzumab or inability to receive trastuzumab in West China Hospital, Sichuan University. Eligible patients have at least one measurable lesion according to RECIST v1.1; previously received taxanes regimen and had ≤2 line of chemotherapy for advanced disease; an ECOG performance status of 0-1; adequate organ function. In the “3+3” dose-exploring phase, pyrotinib and capecitabine are given at a fixed dose of 400mg qd and 1000 mg/m² bid respectively. Anlotinib is initially given at a dose of 10mg/d (Level I). If the initial dose level could be tolerated, subsequent patients are assigned to the higher level (Level H) with anlotinib 12mg/d; otherwise, to Level L with anlotinib 8 mg/d. Primary endpoints of phase Ib are dose-limiting toxicities (DLTs), maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), safety and efficacy. Phase II is an expansion cohort at the recommended phase II dose (RP2D). The primary endpoint for phase II is one-year PFS rate by investigator-assessed, and secondary endpoints include PFS, overall response rate (ORR), clinical benefit rate (CBR), duration of response (DoR), overall survival (OS) and quality of life. A sample size of 23 provided 80% power at 2-sided alpha = 0.20 to detect a minimum of 20% improvement (45% vs. 65%) in one-year PFS. The phase Ib portion of the trial is currently enrolling in China. Clinical trial information: ChiCTR2100045962. Funding: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

Disclosure(s):

Ting Luo, n/a: No financial relationships to disclose

Xiaorong Zhong, n/a: No financial relationships to disclose

Jie Chen, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

OT3-30-01

A randomized double-blind placebo controlled phase 3 trial on the effect of Salovum™ and SPC-Flakes™ on abemaciclib-induced gastrointestinal toxicity in early breast cancer – the ASF-BC study

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Background: In patients with high-risk luminal breast cancer, the addition of CDK 4/6-inhibitor abemaciclib to adjuvant endocrine therapy for two years has been associated with improved disease-free survival and is now recommended as the preferred treatment strategy for this patient group. However, patients treated with abemaciclib frequently (82%) experience diarrhea which primarily occurs during the first three months from treatment initiation and seems to impact patients' quality of life. No proactive strategy to reduce the occurrence of abemaciclib-induced diarrhea is proposed but patients are recommended to start with loperamide upon the occurrence of diarrhea to be combined with treatment interruption and dose adjustment as needed. Cholera induced diarrhea, as well as other forms of diarrhea-inducing agents, has been shown to elicit a stimulated, endogenous production of a protein, named "antisecretory factor", ASF, which acts by modulating secretion of water and ions but also counteracts inflammatory processes. ASF is commercialized as Salovum® and registered by the EU authorities as "Food for specific medical purposes". Another way to increase ASF and, thus, to achieve benefit, is to induce its production /conversion by ingestion of malted oat flakes (SPC-flakes®) which has been recommended or considered for several secretory pathological conditions. Salovum has been shown to rapidly, ie within hours to a few days, antagonize diarrheal diseases of various etiologies. It has also been used against high fluid passages and inflammation in Crohn disease, Colitis ulcerosa and carcinoids in adults. SPC-flakes have similar effects but need weeks of administration to emerge. Importantly, to raise body ASF, by Salovum or SPC-flakes, for the above indications has not been associated with adverse effects. Methods: This is a randomized double-blind multicenter phase III study aiming to investigate a proactive strategy including Salovum and SPC-flakes to prevent the occurrence of abemaciclib-induced diarrhea in patients with early breast cancer treated with abemaciclib. A total of 100 patients will be randomized, in a 1:1 manner, between 13 weeks with Salovum / SPC flakes (A) or placebo (B). The study will be conducted in up to ten different oncology departments in Sweden starting in Q3 2022. Primary objective: Occurrence of any-grade (mild, moderate, severe) diarrhea according to the Systemic Treatment-Induced Diarrhea Assessment Tool (STIDAT; patient-reported outcome). Secondary objectives: Occurrence of any-grade diarrhea according to CTCAE v. 5.0, health-related quality of life (QoL), other adverse events related to abemaciclib, adherence to planned abemaciclib treatment, adherence to and pharmacodynamic effect from study products, safety of investigational products, sick leave

duration, breast cancer recurrence. Investigational product, dosage and mode of administration: Salovum/placebo egg powder high in antisecretory factor, 4 g. Four sachets, ie 16 g q 8 h for 5 - 7 days before start of abemaciclib. The appropriate amount of Salovum is mixed with 100 – 200 ml of suitable liquid, e.g., fruit juice, and ingested orally. SPC-flakes/placebo flat dose of 75 g/d divided in 2 – 4 doses started in parallel with Salovum/placebo to be continued during the first 12 weeks of treatment with abemaciclib. End of study: All included patients will be followed using questionnaires up to 12 weeks from initiation of abemaciclib. After 12 weeks, all the patients will be followed through electronic medical records until the end of abemaciclib treatment (up to two years) for collecting potential adverse events and information on sick leave. Data from electronic medical records regarding recurrence and subsequent therapy will be collected until breast cancer recurrence or up to 5 years from initiation of abemaciclib.

Disclosure(s):

Henrik Lindman, n/a: Astra-Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Daiichi: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Terminated, May 14, 2022); MSD: Consulting Fees (e.g., advisory boards) (Ongoing); Pierre-Fabre: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing)

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Antonis Valachis, n/a: No financial relationships to disclose

12/8/2022

5:00 PM - 6:15 PM

OT3-31-01

The Amelia-1 Study: A phase 1b/2 trial of evexomostat (SDX-7320) plus fulvestrant (Faslodex®) and alpelisib (Piqray®) in patients with advanced breast cancer at risk for alpelisib (Piqray)-induced hyperglycemia

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Background: Breast cancer patients with mutation(s) in the PIK3CA gene have more aggressive disease and worse outcomes relative to patients without PIK3CA mutations. Alpelisib (Piqray), an inhibitor of PIK3CA, was approved for breast cancer patients with PIK3CA mutations. An on-target toxicity of alpelisib is hyperglycemia leading to hyperinsulinemia which may limit effectiveness of this drug. Patients with baseline metabolic dysfunction, insulin resistance, and/or elevated HbA1c are at greater risk of developing grade 3,4 hyperglycemia after receiving alpelisib (Piqray) than patients without metabolic dysfunction. Restoring insulin sensitivity and reducing systemic insulin levels improved the efficacy of alpelisib in preclinical models of breast cancer. Evexomostat is a polymer-drug conjugate of a novel small molecule methionine aminopeptidase 2 (MetAP2) inhibitor that in normal mice reduced alpelisib-induced hyperglycemia/hyperinsulinemia and in the MCF-7 model of HR+/PIK3CA-mutant breast cancer showed synergistic anti-tumor activity with alpelisib (Piqray). Evexomostat was well-tolerated in a phase 1 monotherapy safety study in late-stage cancer patients and improved insulin resistance in patients with elevated insulin at baseline, among other metabolic and angiogenic markers. Methods: This is a phase 1b/2, open-label, single-arm pilot study (NCT05455619) in postmenopausal women with PIK3CA-mutated, HR+, HER2- metastatic breast cancer with disease progression following treatment with endocrine therapy plus a CDK4/6 inhibitor who are at risk for hyperglycemia, with risk factors defined as HbA1c between 5.7 and 6.4% and/or

HOMA-IR ≥ 1.8 . The primary objective is to determine the safety of evexomostat plus standard of care treatment alpelisib (Piqray) and fulvestrant (combined, the 'triplet therapy'), to measure the severity and number of hyperglycemic events, and to assess clinical, anti-tumor benefit of the triplet therapy. The trial will begin with a dose-escalation cohort (n=6) at an evexomostat dose of 36 mg/m² (one dose below the monotherapy MTD of 49 mg/m²) in combination with alpelisib and fulvestrant given in accordance with their respective labels. Based on safety data from the first 6 patients (two cycles), the safety review committee may increase the evexomostat dose for the next cohort of six patients to 49 mg/m² or may decrease the evexomostat dose to 27 mg/m² and may adjust the dose of alpelisib if warranted. Once the MTD of the triplet therapy has been defined, additional enrollment will occur until a total of up to 20 patients have completed at least two cycles of triplet therapy at that dose. If warranted, an additional 20 patients may be enrolled to further characterize the safety profile and/or anti-tumor effect of the triplet therapy (total of up to 52 patients). This trial will open to accrual in August, 2022. Primary safety analysis consists of the type, frequency, and severity of treatment-emergent adverse events (TEAEs) per the NCI CTCAE, v5.0, the number of patients with grade 3 or 4 hyperglycemia during the first 2 cycles of therapy plus an estimate of the proportion and its exact upper one-sided 97.5% confidence bound will be analyzed. Efficacy analyses include calculation of the ORR, consisting of complete response (CR) and partial response (PR). The number of patients alive without disease progression six months from the start of the triplet therapy will be assessed. The CBR of CRs, PRs plus stable disease ≥ 24 weeks from C1D1 will be calculated. Overall survival data will be summarized as available or appropriate. QoL will be analyzed according to functional scores and recommendations in the EORTC scoring manual. ECOG performance status and change from baseline will be summarized.

Disclosure(s):

Peter Cornelius, PhD: SynDevRx, Inc: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Salary (Ongoing)

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OPTIMA, a prospective randomized trial to validate the clinical utility and cost-effectiveness of gene expression test-directed chemotherapy decisions in high clinical risk early breast cancer.

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Background: Multi-parameter tumor gene expression assays (MPAs) are used to estimate individual patient risk and guide chemotherapy use in hormone-sensitive, HER2-negative early breast cancer. The TAILORx trial supports MPA use in a node-negative population. Evidence for MPA use in postmenopausal node-positive breast cancer has been provided by the RxPONDER trial interim analysis but this relies on the absence of superiority in an analysis where >50% of events were unrelated to breast cancer. There is much uncertainty about MPA use for premenopausal patients. OPTIMA (Optimal Personalised Treatment of early breast cancer using Multi-parameter Analysis) (ISRCTN42400492) is a prospective international randomized controlled trial designed to validate MPAs as predictors of chemotherapy sensitivity in a largely node-positive breast cancer population.

Methods: OPTIMA is a partially blinded study with an adaptive two-stage design. The trial recruits women and men age 40 or older with resected ER-positive, HER2-negative invasive breast cancer and up to 9 involved axillary lymph nodes. Randomization is to standard management (chemotherapy and endocrine therapy) or to MPA-directed treatment using the Prosigna (PAM50) test. Those with a Prosigna tumor Score (ROR_PT) >60 receive standard management whilst those with a low score (≤ 60) tumor are treated with endocrine therapy alone. Endocrine therapy for pre-menopausal women includes ovarian suppression for all participants unless they experience a chemotherapy-induced menopause. Adjuvant abemaciclib is permitted. The trial will be analyzed for (1) non-inferiority of recurrence according to randomization and (2) cost-effectiveness. The key secondary outcome is non-inferiority of recurrence for patients with low ROR_PT score tumors. The efficacy analyses will be performed Per Protocol using Invasive Breast Cancer Free Survival (IBCFS) as the primary outcome measure to limit the risk of a false non-inferiority conclusion. Recruitment of 4500 patients over 8 years will permit demonstration of up to 3% non-inferiority of test-directed treatment with at least 83% power, assuming 5-year IBCFS is 87% with standard management. An integrated qualitative recruitment study addresses challenges to consent and recruitment, building on experience from the feasibility study which found that a multidisciplinary approach is important for recruitment success. OPTIMA is strongly supported by a patient group which has helped design all patient documents and which is represented on the TMG.

Results: The OPTIMA main trial opened in January 2017 and has continued to recruit throughout the COVID-19 pandemic. Overall recruitment as of 1 July 2022 was 2814 (2593 from UK, 221 from Norway). Patient characteristics are well balanced between the trial arms. Currently 95% of randomized participants are eligible for inclusion in the PP analysis. 66% of the MPA-directed arm participants have been allocated to endocrine therapy only. The test failure rate is < 1%.

Conclusion: OPTIMA will provide robust unbiased evidence on test-directed chemotherapy safety for both postmenopausal and premenopausal women with 1-3 involved nodes as well as for patients with 4-9 involved nodes and for patients treated with abemaciclib.

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Characteristic		%
Median age in years (range)	56 (40-83)	
Menopause status	Pre	36
	Post	63
	Male	1
Tumour size	<30mm	55
	≥30mm	45
Node status	pN0	3
	pN1mi(sn)	4
	pN1(sn)	27
	pN1	48
	pN2	18
Histologic grade	1	5
	2	63
	3	32

Patient characteristics

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Prospective, Multi-Center, Artificial Intelligence Study for Early Prediction of Serious Events under Treatment Is Now Open for Recruitment in Breast Cancer - OMCAT Trial in Progress

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Background: Aim of the OMCAT trial ('One Million CAncer Treatment months', NCT04531995) is improvement of cancer patient care and safety by developing artificial intelligence (AI)-based, incident prediction algorithms. Incident detection allows early notification of treatment teams, enabling timely management changes or interventions. Ultimately the algorithms can also support improved health resource allocation. This trial in progress aims to provide learning databases in breast cancer comprising both electronic patient reported outcome (ePRO) data using the mobile medical device 'CANKADO PRO-React' and ground truth outcome data, which provide disease-specific events of interest ("incidents") verified by the physician (e.g., during patient examinations). Methods: Incident prediction is posed as an application of stochastic time series analysis using AI and knowledge engineering technology. The learning process begins by fitting individualized and disease-specific stochastic process models to "incident-free" intervals extracted from the ePRO data series. Incidents produce detectable deviations from "ordinary" ePRO fluctuations. The algorithms are trained on CANKADO PRO-React data to produce real-time risk functions for predicting incidents on a clinically specified time horizon.

Results: Considering the heterogeneity and combinatorics of diseases, stages, therapies, and types of events considered in this study, ultimately the AI algorithms aim to discover about 360 distinct predictive relationships. The estimate of one million treatment months is derived from statistical power analysis of this target, considering estimated median documentation time of six months per patient and estimated 400-500 patients per predictive relationship. To date, 45 centers in Germany have expressed interest in participating. This participation level will enable proof of principle. Ethics votes are already available in most regions. Other centers are invited to participate in this trial. Conclusions: OMCAT opens a whole new path towards evidence-trained AI and a novel combination of patient observation and predictive care. The goals of OMCAT are ambitious and will therefore require many more supporters.

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P5-01-01

Multiscale Deep Learning framework to capture systemic immune features in lymph nodes predictive of triple negative breast cancer outcome

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Systemic immune responses in lymph nodes (LN) convey significant prognostic value for breast cancer patients, which can inform disease progression and optimal treatment management. However, have, so far, not been assessed in large patient cohorts. We have previously shown that morphological alterations in axillary LNs, namely the formation of germinal centres (GCs) in cancer-free LNs, add prognostic value to tumour infiltrating lymphocytes (TILs) in triple-negative breast cancer patients (TNBC) for the development of distant metastasis. Extending manual assessment of LNs beyond the detection of cancer requires the integration of robust deep learning pipelines into the digital pathology workflow. Here, we propose a supervised multiscale deep learning framework named smuLymphNet to capture and quantify GCs and sinuses within LNs from digitised Haematoxylin and Eosin-stained (H&E) whole slide images (WSIs) and show good concordance compared with an inter-pathologist Dice coefficient of manual annotations from four pathologists. The smuLymphNet framework consists of (i) a detection algorithm to determine the boundaries of each LN section on the WSI, using an Otsu-based thresholding method and contouring algorithm; (ii) a supervised multiscale deep learning module for the segmentation of GCs and sinuses; and (iii) quantification of the number, size, and shape of the predicted features. We applied smuLymphNet to a total of 1,800 H&E-stained WSI of >4,000 cancer-free and involved LNs from a retrospectively collected breast cancer cohort collected at Guy's Hospital (London, UK) from 177 patients (122 N+) enriched for the triple-negative phenotype. A subset of 114 WSI and five breast cancer LN WSIs from each Barts Hospital (London, UK) and Tianjin University Hospital (Tianjin, China) were used to train and evaluate the supervised deep learning module. For training Fully Convolutional Networks (FCNs), WSIs manually annotated for both GCs and sinuses formed a ground-truth set and three FCNs were implemented: (i) a standard U-Net architecture; (ii) a U-Net model with an attention gate mechanism; and (iii) a multiscale-U-Net network (MS U-Net) that encodes, in parallel, a feature representation of the image at multiple resolutions. The MS U-Net achieved the best performance with an average dice score of 0.86 for GCs and 0.74 for sinuses. In comparison, the average dice score amongst four pathologists assessing 24 LN WSI for GCs and sinuses was 0.67 and 0.61, respectively, demonstrating the robustness of the smuLymphNet framework. To establish associations between morphometric immune features and patients' outcomes, we assessed smuLymphNet captured GCs and sinuses from 686 WSIs from 96 TNBC patients with extensive longitudinal outcome data. We found significant morphological differences in involved and cancer-free LNs between N0 and N+ patients, with the latter displaying larger GCs with more irregular shapes, especially in their involved LNs. Moreover, in alignment with our previously published studies, our multiscale smuLymphNet framework recapitulated and extended the prognostic value of the assessment of GC formation in TNBC N0 patients. We further revealed, for the first time, the prognostic significance of the intranodal lymphatic sinuses when measured in their totality in involved LNs, and the association of alterations in subcapsular sinus areas with superior distant metastasis-free survival in cancer-

free and involved LNs in TNBC N+ patients. In summary, smuLymphNet presents a robust multiscale deep learning framework to automatically detect, localise and quantify histopathological immune features in WSI of LNs. By applying smuLymphNet to LNs of TNBC patients from clinical trials, and thereby further evaluating its clinical utility, smuLymphNet could be implemented into the diagnostic digital pathology workflow and, as such, aid in informing on a patient's disease trajectory.

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Diagnostic Accuracy of 18F-FDG PET/CT plus Contrast-Enhanced MRI for Axillary Lymph Node Metastasis Involved in Invasive Ductal Carcinoma

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Background: Positron emission tomography/computed tomography (PET/CT) and magnetic resonance imaging (MRI) are useful imaging modalities for the preoperative nodal staging in breast cancer; however, clinical evidence demonstrating the diagnostic accuracy of the combination of PET/CT and MRI is limited. The purpose of this study is to establish a clinical prediction model based on PET/CT plus contrast-enhanced MRI for ALN metastasis, and explore the possibility of non-invasive patients' risk stratification using the PET/CT plus MRI model preoperatively. Methods: A total of 361 women (370 axillae; mean age, 56 years \pm 12 [standard deviation]) who underwent surgery for primary invasive ductal carcinoma at a single institution between April 2017 and March 2020 were evaluated. Subjects were divided into two cohorts: a derivation cohort (n = 333) and a validation cohort (n = 37). In the derivation cohort, we constructed a prediction model with logistic regression to estimate the potential explanatory variables obtained by PET/CT, MRI, and preoperative core-needle biopsy. Using a simple integer risk score, patients were divided into low-risk and high-risk groups. We assessed the predictive ability of the PET/CT plus MRI model using the area under the curve (AUC), and internal validation was achieved by risk scoring system in the validation cohort. Results: The PET/CT plus MRI model included five predictor variables: maximum standardized uptake value of primary tumor and ALN, primary tumor size, ALN cortical thickness, and histological grade. The PET/CT plus MRI model had significantly improved AUC of 0.867 ($p < 0.05$) as compared to those of the PET/CT model (AUC = 0.821) and MRI model (AUC = 0.815). We assigned the

weighted scores to each retained variables in the PET/CT plus MRI model, and determined the optimal cut-off value of 7 (range, 0–17). In the derivation and validation cohorts, 55% and 65% of the patients were classified as low-risk by the risk scoring system, with negative predictive values of 97% and 100%, respectively. Conclusions: Our findings demonstrated a better diagnostic accuracy of the clinical prediction model utilizing both PET/CT and MRI than previous models based on either PET/CT or MRI, and the negative predictive value of 97% was not inferior to that of sentinel lymph node biopsy. Thus, the preoperative risk evaluation of axillary lymph node macrometastasis using our integrated model could be useful while considering individualized therapy for patients with invasive ductal breast cancer. Further validation should be performed for clinical applications.

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Evaluation of novel diagnostic kits using the semi-dry dot-blot method combined with an automatic reader for detecting metastases in sentinel lymph nodes of patients with breast cancer: a multi-center prospective study

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Background: The semi-dry dot-blot (SDB) method, a diagnostic procedure for detecting lymph node (LN) metastases using an anti-cytokeratin (CK) antibody, is based on the theory that epithelial components, such as CK, are not found in normal LNs. Thus, metastases are diagnosed according to the presence of CK in the lavage fluid of sectioned LNs. We prospectively evaluated novel SDB kits that use a newly developed anti-CK19 antibody and an automatic reader for diagnosing sentinel LN metastases in patients with breast cancer as a multi-center study. **Methods:** We obtained 924 sentinel LNs dissected from 405 patients with breast cancer between January 2021 and December 2021 at six institutes in Japan. We excluded patients who underwent neoadjuvant chemotherapy and neoadjuvant endocrine therapy. LNs were sectioned at 2-mm intervals and washed with phosphate-buffered saline. Cells suspended in the lavage fluid of sectioned LNs were centrifuged and lysed to extract protein. The extracted protein was applied to the SDB kit to diagnose LN metastasis using an automatic absorbance reader. Hematoxylin and eosin (H&E) stained and washed LNs were blindly examined by pathologists using intraoperative and permanent histological examination. Diagnoses based on SDB kit and automatic reader findings were compared with diagnoses made by permanent histological examination of paraffin-embedded H&E-stained sections of LNs. Primary endpoints were the sensitivity, specificity, and overall agreement of the SDB kit for distinguishing macrometastases from non-macrometastases. **Results:** Ninety-four of the 924 LNs were assessed as macrometastases, 40 as micrometastases, and 790 as isolated tumor cells by histological examination. Compared with patients with non-macrometastases, those with macrometastases had significantly younger age ($p < 0.01$), larger primary tumor ($p < 0.01$), higher nuclear grade ($p = 0.04$), increased lymphatic invasion ($p < 0.01$), and increased venous invasion ($p = 0.01$). Using a borderline CK19 absorbance of 11.9 milli-absorbance for detecting macrometastases with an area under the curve of 0.989, the sensitivity, specificity, and overall agreement of the SDB kit were 94.7%, 98.3%, and 97.9%, respectively. Moreover, the sensitivity, specificity, and overall agreement of the intraoperative histological examination compared with permanent histological examination for distinguishing macrometastases from non-macrometastases were 91.4%, 99.1%, and 98.3%, respectively. Furthermore, the kits and automatic reader yielded diagnoses within approximately 20 min at a cost of < 30 USD for the SDB kit and < 3,000 USD for the automatic reader. **Conclusions:** The kits with an automatic reader used in our study were accurate, quick, and cost-effective in diagnosing LN metastases without the loss of LN tissue and were particularly useful for distinguishing macrometastases. We plan to make the SDB kit and automatic reader commercially available worldwide soon.

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Contralateral Axillary Lymph Node Metastasis after Ipsilateral Breast Tumor Recurrence: Is it distant metastasis or locoregional progression?

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Background: Contralateral axillary lymph node metastasis (CAM) in breast cancer is currently classified as a stage IV disease but its prognosis is still controversial. Purpose: To determine outcomes in overall survival (OS) and disease-free survival (DFS) in patients with and without locoregional tumor recurrence who present with contralateral axillary lymph node metastasis (CAM). Methods: Patients with pathologically confirmed invasive breast cancer with metachronous CAM who received treatment between 1988 and 2017 were retrospectively reviewed. Patients with other distant metastases at the time of CAM diagnosis were excluded. The outcome of CAM in cases of IBTR and regional recurrence (RR) were compared to CAM not accompanied by locoregional tumor recurrence. Results: Thirty-eight patients with metachronous CAM were included in the study. Metachronous CAM occurred 55 months (interquartile range, 17-77 months) after surgical treatment of the primary tumor and median follow-up was 95 months (interquartile range, 49-117 months) from the initial operation date and 40 months (interquartile range, 15-54 months) from the diagnosis of CAM. At the time of initial CAM diagnosis, 11 patients had IBTR, 12 patients had RR, and 15 patients had no

locoregional recurrence. The estimated 5-year OS was 49.1% and 5-year DFS was 45.3%. Although statistically insignificant due to small sample size, when stratified by loco regional recurrence, the prognosis of CAM patients with IBTR appeared to be better than those without locoregional recurrence (5-year OS: 88.9% vs. 41.4%, HR 5.88, $p = 0.09$) whereas the prognosis of CAM patients with RR was worse than those without locoregional recurrence (5-year OS: 35.4% vs. 41.4%, HR 0.44, $p = 0.20$). Axillary lymph node dissection (ALND) improved median OS (83 vs. 36 months, $p = 0.069$) in all patients. When stratified, improvement in median OS was 13 vs 27 months ($p = 0.094$) in patients with RR, and 36 vs. 65 months ($p = 0.061$) in patients without locoregional recurrence. For patients accompanied by IBTR, ALND was performed in 8 out of 11 and only one patient died during the follow-up period. Conclusion: Our study indicates that the patients with CAM have superior survival outcome when compared to other stage IV patients, especially when CAM was accompanied by other loco regional recurrences. These data suggest that the CAM patients may benefit from active loco regional treatment.

Disclosure(s):

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5:00 PM - 6:15 PM

P5-01-05

A Predictive Model for Axillary Pathologic Response after Neoadjuvant Chemotherapy for Clinically Node-Positive Breast Cancer

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Purpose: Neoadjuvant chemotherapy (NAC) has resulted in the eradication of axillary lymph node metastasis in approximately 40% of patients. Sentinel lymph node biopsy (SLNB) could be an alternative surgical procedure for these patients to avoid complications from axillary lymph node dissection (ALND). However, high false-negative rates of SLNB for clinically node-positive patients were reported in previous prospective trials. The aim of the present study was to evaluate clinicopathological factors and imaging characteristics by MRI and ultrasound (US) as predictors of axillary pathologic complete response (ypN0) after NAC, which enables to identify candidates for SLNB in patients with clinically node-positive disease. Patients and methods: We identified 177 patients with clinically node-positive breast cancer who received NAC from May 2009 to May 2021. All patients underwent MRI and US before and after NAC. Patients were judged to be node-positive when they have the cytologically-proven nodal disease by fine-needle aspiration (FNA) or suspicious lymph nodes by diagnostic imaging. Lymph nodes with the cortical thickness ($>3.5\text{mm}$), loss of fatty hilum, or round shape (short-axis/long-axis ratio >0.5) were defined as suspicious lymph nodes. To develop a predictive model for ypN0, the association between ypN0 status and clinicopathological and imaging characteristics was assessed by multivariate logistic regression analysis. The area under the

receiver operating characteristic (ROC) curve was used to evaluate discrimination by the model. The model was further evaluated in the validation cohort with 20 patients who received NAC from March 2021 to December 2021. Results: The median age was 54.0 (range: 22-79) years and the mean tumor size was 3.97 ±2.29cm. Of 177 patients, 90 (50.8%) patients had luminal, 47 (26.6%) had HER2-positive, and 40 (22.6%) had triple-negative disease. Sequential anthracycline and taxane were administered for 157 (88.7%) patients, and 45 (95.7%) patients with HER2-positive-disease received concomitant anti-HER2 agents preoperatively. Overall, 77 (43.5%) patients achieved ypN0. Independent predictors of ypN0 status were clinical stage N1 (odds ratio [OR]: 9.17 vs. cN2-3, p=0.002), absence of lymphadenopathy after NAC (OR: 8.54, p< 0.001), breast complete response (CR) by MRI (OR: 5.96, p< 0.001), HER2 positivity (OR: 3.80, p=0.008), nuclear grade (NG) 3 (OR: 2.77 vs. NG1-2, P=0.020) and hormone receptor negativity (OR: 2.52, p=0.048). In a model using these predictors, the area under the ROC curve was 0.887 (95% confidence interval: 0.839-0.935, p< 0.001). The sensitivity, specificity, positive predictive value and negative predictive value of the model were 80.0%, 82.8%, 77.9% and 84.5%, respectively. In the validation cohort, the sensitivity, specificity, positive predictive value and negative predictive value were 66.7%, 90.9%, 85.7% and 76.9%, respectively. Among 84 patients who were predicted ypN0 by the model, SLNB was performed in 42 (50.0%) patients, and the identification rate of SLN was 95.2% (40/42). Overall, ALND was omitted in 38 (45.2%) patients and irradiation to regional lymph nodes was performed in 23 (60.5%) out of 38 patients. After a median follow-up of 53.9 months, 5-year recurrence-free survival was comparable between patients with or without ALND (78.0% vs. 94.4%, p=0.259). Conclusions: Our predictive model based on clinicopathological factors and imaging characteristics by MRI and US could help to identify good candidates for the omission of ALND after NAC in patients with clinically node-positive breast cancer.

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P5-01-06

Single cell profile of tumor and immune cells in primary triple-negative breast cancer and different sites in the axillary lymph nodes

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Purpose: Little is known about the host-tumor interaction in the lymph node basin at a single cell level. This study examines single cell sequences in breast cancer nodal metastasis of a patient with triple negative breast cancer. Methods: The primary breast tumor, sentinel lymph node, an adjacent lymph node with metastatic involvement and a clinically normal-appearing lymph node were collected during operation. Single-cell sequencing was performed on all specimens. Results: 14,016 cells were clustered as 6 cell populations. Cancer cells demonstrated the molecular characteristics of TNBC basal B subtype and highly expressed genes in the MAPK signaling cascade. Tumor associated macrophages regulated antigen processing and presentation and other immune-related pathways to promote tumor invasion. CD8+ and CD4+ T lymphocytes concentrated more in sentinel lymph node and mainly stratified as two transcriptional states. The immune cell amount variation among primary tumor, sentinel and normal lymph nodes showed the similar tendency between the scRNA-seq profile of TNBC samples and a previous reported bulk RNA-seq profile of a breast cancer cohort including all four breast cancer subtype samples. Discussion: Single-cell sequencing analysis suggested that the sentinel lymph node was the initial meeting site of tumor infiltration and immune response, where partial T lymphocytes perform anti-tumor activity while other T cells exhibit an exhaustion state. We proposed a molecular explanation to the well-established clinical principle that the 5-year and 10-year survival outcomes were noninferior between SLND and ALND.

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P5-01-07

Recruitment, clinical equipoise, patient acceptance and compliance in the UK-ANZ POSNOC trial

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Background: POSNOC is a UK-ANZ multicentre, non-inferiority, randomised trial comparing systemic therapy alone with systemic therapy plus Axillary Treatment (Axillary radiotherapy or ALND) for women with ≤ 2 macrometastases at SNB. The primary outcome is axillary recurrence within 5 years. This paper describes screening, recruitment and compliance data. Methods: Sites were requested on a monthly basis to upload screening data and provide reasons for non-recruitment of eligible patients into the trial. Sites entered in the online database whether the patients were compliant with their randomisation allocation. Results: The study opened in July 2014 and completed target recruitment of 1900 women (24% of those screened) in July 2021, at 95 sites in the UK and 20 sites in Australia and New Zealand. The reason for non-enrolment was unknown in 1300 women. Of the remaining 4774 women with known reasons, who were screened but not randomised, the most common reasons for non-recruitment were due to either patients (n=2219, 46.5%) or their clinicians (n=782, 16.4%) favouring axillary treatment, or patients (n=490, 10.3%) or their clinicians (n=170, 3.6%) not wishing to have axillary treatment. Over the course of the study, there was an increase in the proportion of patients wanting axillary treatment and declining the trial (Mean % patients declined 2015 – 17.9%, 2021 – 39.1%). Mean number of participants recruited per site per month was 0.24 (SD 0.18) overall, 0.25 (SD 0.19) in the UK, and 0.19(SD 0.15) in ANZ. The mean was < 0.3 in 79 sites and >0.9 in only one site. Recruitment rate remained consistent throughout the study (mean 25.3 per month) except for during the first 6 months of recruitment (5.7) and during the COVID pandemic Apr-Sep 2020 (7.5). Of 89 (4.8%) participants non-compliant with allocation, n=45 (50.6%) received systemic therapy alone and n=44 (49.4%) received systemic therapy plus axillary treatment. There was no fluctuation in the direction of non-compliance during the study duration. There was increasing uptake of axillary radiotherapy to treat the axilla instead of ALND over the course of the study in patients receiving axillary treatment (Number who had ART of all who had axilla treatment 2014-2017 - 248/454 (54.6 %); 2018-2021 – 315/449 (70.2%)). Conclusion: Recruitment and compliance with randomised allocation remained consistent over a seven-year period. POSNOC with in-built radiotherapy QA will provide definitive data on axillary management in patients undergoing mastectomy or BCS with ≤ 2 macrometastases on SNB.

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Steps toward noninvasive lymph node staging (NILS) in clinically node negative patients: Artificial neural network model to preoperatively predict lymphovascular invasion

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Background: Lymphovascular invasion (LVI) is one of the most important predictors for nodal status in breast cancer patients [1]. Multiple models have been published for prediction of preoperatively disease-free axillary using i.a. LVI [1-2]. However, LVI detection in preoperative core needle biopsy has been reported with a failure rate of 30% [3] and the analysis is not routinely performed in Sweden. Thus, a preoperative model of LVI status would be useful in prediction models for noninvasive lymph node staging (NILS). The purpose of this study was to develop an artificial neural network (ANN) model for LVI prediction using only clinicopathological variables that are routinely available in the preoperative setting. Methods: Data gathered prospectively during 2009-2012 in Lund, Sweden from 761 clinically node negative breast cancer patients were retrospectively extracted. Inclusion criteria were female sex, primary breast cancer and that each patient was scheduled for primary surgery. Patients with metastatic disease, bilateral cancer, tumor size greater than 50 mm, previous ipsilateral breast or axillary surgery, patients omitted of standard axillary staging procedure by SLNB or ALND, and those who had neoadjuvant treatment were excluded. LVI was assessed on surgical breast specimens and was defined as the presence of tumor cells within endothelium-lined vascular channels. Out of the 761 patients in the cohort, 613 patients were documented with LVI status. The LVI full case dataset was split 80/20 for training and validation. The remaining 148 patients were set aside for model testing. Since the test dataset did not contain information on LVI status, it was used to compare the predicted fraction of LVI positive patients to that of the development dataset. Only variables possible to obtain in the preoperative setting were included in the prediction models, comprising age, menopausal status, mode of detection (mammography screening or symptomatic representation), tumor size, multifocality (yes/no), histopathological type, histological grade, ki-67 percentage, estrogen receptor status, progesterone receptor status, and human epidermal growth factor receptor 2 status. An ensemble approach was used, where each ensemble constituted 30 ANNs that were trained and validated using 5-fold cross validation. For every ensemble model, different model parameters, such as L2-regularization and the number of hidden nodes, were tested. Model selection was based on validation AUC. Results: The study cohort included female clinically node negative breast cancer patients scheduled for primary surgery. Data from 613 patients (lymph node stages N0: 67.4%, N1: 26.9%, N2+: 5.7%) were used to develop the model, and

148 patients (N0: 56.8%, N1: 35.8%, N2+: 7.4%) constituted the internal test cohort. Fifteen percentage of the patients in the development dataset were LVI positive. The selected ensemble model achieved a validation AUC of 0.80 (CI 0.75-0.85). This model predicted an LVI positive rate of 16.2% in the test dataset. Conclusion: LVI was predicted with high accuracy using an ANN model based on routine preoperative clinicopathological variables. The result of validation AUC 0.80 (CI 0.75-0.85) indicates a potential for preoperative prediction of LVI, and the model can putatively be useful when applying preoperative nodal prediction models in patients without known LVI status. To confirm these results, verification in an external dataset is needed. Validation of the LVI-model in an independent dataset from the National Breast Cancer Registry will be performed, as well as an evaluation of the usefulness of the LVI-model as an imputation in a nodal prediction model. [1] Dihge, L. et al. BMC Cancer (2019). PMID: 31226956 [2] Bevilacqua, J. L. et al. J Clin Oncol. (2007). PMID: 17664461 [3] Harris, G. C. et al. Am J Surg Pathol. (2003). PMID: 12502923

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Evaluation of the efficacy of using fluorescence-associated indocyanine green in sentinel lymph node biopsies from breast cancer patients

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Introduction: Sentinel lymph node biopsy is the technique of choice for axillary staging in patients with breast cancer. Although it is already a widespread technique, its history is relatively recent. Three techniques are globally used to detect sentinel lymph nodes: the patent blue, described by Giuliano et al. (1994); the technetium-99 radiopharmaceutical with gamma probe, published by Krag et al. (1993); and the combination of these two techniques. Objective: This study aims to evaluate sentinel lymph node detection rate using the innovative fluorescence-associated indocyanine green technique in breast cancer patients, and to compare it with that of patent blue and with a combination of the two dyes. Method: A randomized trial was conducted on 99 patients who were equally divided into three arms, each one undergoing sentinel lymph node detection using either patent blue, indocyanine green, or a combination of the two dyes. The study was conducted at Hospital de Esperança, Presidente Prudente, SP, Brazil, in partnership with the Breast Department of Paulista School of Medicine, Federal University of São Paulo. Results: The accuracy rate in identifying sentinel lymph nodes was 78.8% with patent blue, 93.9% with indocyanine green, and 100% with patent blue + indocyanine green. Two sentinel nodes (48.5%) were mostly identified in the combined group; however, only one sentinel node was identified in the other groups. The mean time for sentinel lymph node identification was 20.6 minutes with the traditional dye, 8.6 minutes with indocyanine green, and 10 minutes with the combination of the two methods ($p < 0.001$). The mean surgical time was 69.4 minutes with patent blue, 55.1 minutes with indocyanine green, and 69.4 minutes with their combination ($p < 0.001$). Conclusion: Sentinel lymph node detection rate by fluorescence-associated indocyanine green was considered effective. The comparison

of sentinel lymph node detection rates between patent blue, indocyanine green, and a combination of patent blue + indocyanine green revealed statistically significant differences ($p = 0.030$), with the combined method being the most effective. Keywords: breast neoplasm, sentinel lymph node biopsy, fluorescence, indocyanine green

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Utility of 18F-FDG PET/CT for the prediction of pathologic complete response in axilla to neoadjuvant chemotherapy in breast cancer

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Purpose: To evaluate the value of early FDG-PET (18F-Fluorodeoxyglucose-Positron Emission Tomography) metabolic criteria for prediction of pathologic complete response in axilla (pCR_{ax}) after neoadjuvant chemotherapy (NAC) in breast cancer. Methods: Inclusion criteria were all T-stage breast cancers, non-metastatic, with initial lymph node involvement estimated by PET +/- lymph node biopsy, treated with NAC followed by surgery with axillary lymph node dissection (ALND), managed at the George-François Leclerc Cancer Center in Dijon, France, between 2009 and 2019. A PET was performed before and after the first course of chemotherapy (PET1 and PET2). pCR_{ax} was defined as the absence of invasive cells in the nodes at the time of ALND (i.e. ypN0). The Sataloff classification was used as reference on each pathological report. Patients with a Sataloff NA classification (i.e. evidence of therapeutic effect, and no residual disease) and, if axillary involvement was proven at diagnosis, NB (i.e. no metastasis, no therapeutic effect) were considered as pCR_{ax}. The PET metabolic criteria studied in the axilla were: - SUV_{max} (Standard Uptake Value) on PET1 and PET2 = fixation in the axillary voxel with the highest activity (kBq/mL) / (injected dose (kBq)/weight (g)) - Δ SUV_{max} (%) = metabolic response after the first course of NAC = $100 \times (\text{SUV}_{\text{max}1} - \text{SUV}_{\text{max}2}) / (\text{SUV}_{\text{max}1})$. Univariate and multivariate analysis were performed to identify factors (clinical, pathologic, metabolic) that may be associated with pCR_{ax}. Relationships between baseline TEP uptake and prognostic parameters were assessed using Receiver Operating Characteristic (ROC) curves. Results: Among 188 patients included, the rate of pathologically proven node involvement was 63.3% (n=119). The pCR_{ax} rate was 45.7% (n=86/188) but varied according to tumor subtypes: 14.5% (n=9/62) of HR(Hormone Receptor)+/HER2-negative, 47.7% (n=21/44) of HR+/HER2-positive, 61.4% (n=27/44) of triple-negative (TN) and 76.3% (n=29/38) of HR-/HER2-positive. Factors significantly associated with pCR_{ax} were by univariate analysis:

HER2-positive (HR+ and HR-) and TN subtypes ($p < 0.001$), SBR (Scarff-Bloom-Richardson) grade ($p = 0.01$), breast pCR (ypT0/is) ($p < 0.001$), SUVmax2 ($p = 0.01$) and Δ SUVmax ($p < 0.001$). By multivariate analysis, it persisted the HR-/HER2-positive ($p = 0.02$) and TN ($p = 0.02$) subtypes and breast pCR ($p < 0.001$). In global population, a decrease in Δ SUVmax of 63% was the optimal threshold to predict pCRax (Area Under the Curve AUC = 0.73) with a sensitivity (Se) of 51% and specificity (Sp) of 83%. Δ SUVmax remains the best performing parameter in TN (AUC = 0.72; Se at 52%; Sp at 88%). In HR-/HER2-positive patients, SUVmax2 appeared to be a better predictor of pCRax than Δ SUVmax. A SUVmax2 value of 1.99 was the optimal threshold for predicting pCRax (AUC = 0.72), yielding a Se of 66% and a Sp of 78%. None of the PET criteria predicted axillary response with sufficient accuracy for HR+ subtypes. Conclusion: PET alone does not appear to be sufficient to predict pCRax. It seems necessary to use other parameters, whether clinical, biological or imaging, to discriminate responders from non-responders to NAC in order to adapt the subsequent surgical management.

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Genomic Landscape of ER+/HER2- metastatic breast cancer as a function of prior treatment with a CDK4/6 inhibitor.

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Background CDK4/6 inhibitors (CDK4/6i), like palbociclib, ribociclib, and abemaciclib, along with antiestrogens, have revolutionized treatment for ER+/HER2- metastatic breast cancer (MBC). Although most patients initially respond, almost all eventually progress, and ER+ HER2- MBC remains incurable. There is an urgent need to understand the molecular processes that drive resistance in order to improve survival. The landscape of acquired somatic alterations causal to CDK4/6i resistance remains unknown. Here we report differences in mutational landscapes between ER+ HER2- MBC patients treated with and without CDK4/6i. Methods Deidentified data from 780 and 1073 ER+ HER2- MBC patients (solid tumor or ctDNA liquid biopsy sequencing respectively) with at least 6 months between diagnosis of Stage 4 disease and biopsy were analyzed. Patients were divided into either treated or untreated with CDK4/6i prior to biopsy. Sequencing was performed using the Tempus xT tumor assay (DNA sequencing of 595-648 genes at 500x coverage) and Tempus xF liquid biopsy (ctDNA sequencing of 105-523 genes). Gene alterations (consisting of pathogenic/likely pathogenic short variants and copy number alterations) were compared between groups by Chi-squared/Fisher's Exact tests and p-values adjusted for false-discovery. Results We first analyzed sequencing data of both solid tumor and liquid ctDNA from ER+/HER2- MBC patients. ESR1 mutations were significantly more frequent in those that received CDK4/6i than those that did not (Solid tumor 33% vs 16%, $p < 0.001$, $q = 0.001$; Liquid biopsy 32% vs 16%, $p < 0.001$ and $q < 0.001$). We also saw more frequent mutations/amplifications in the following genes in

the CDK4/6i treated cohort vs. those that were not. These results trended towards significance in our solid tumor, but not in our liquid biopsy cohort: CCND1 (18% vs 11% $p = 0.028$ $q = 0.3$); FGF3 (17% vs 9.5% $p = 0.010$ $q = 0.2$); FGF4 (17% vs 11% $p = 0.035$ $q = 0.3$), GATA3 (17% vs 8.9% $p = 0.008$ $q = 0.2$), PTEN (12% vs 6.1% $p = 0.030$ $q = 0.3$) and FGF19 (8.2% vs 1.7% $p = 0.002$ $q = 0.12$). Interestingly, 96-98% of CCND1, FGF3, FGF4 and FGF19 alterations were copy number amplifications. Conversely, we saw a trend towards significance for more mutations in TP53 (37% vs 27% $p=0.008$ and $q=0.2$) in those that had not received a CDK4/6i than those that did. Conclusions Here we present the landscape of somatic alterations in ER+/HER2- MBC patients with and without prior CDK4/6i therapy from our large real world de-identified data set. Patients with prior CDK4/6i therapy harbored significantly more ESR1 somatic alterations, demonstrated in both solid tissue and liquid biopsies. In solid tissue biopsies, patients with prior CDK4/6i therapy harbored more CCND1, FGF3, FGF4, and GATA3 alterations and less TP53 alterations. These trends were not significant after adjustment for multiple testing. CCND1, FGF3, FGF4 and FGF19 alterations were copy number amplifications, which may be consistent with 11q13 amplification. Further studies will provide insights into how these trends translate towards our understanding of CDK4/6i related resistance mechanisms.

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Combined biomarker analysis for prediction of pathological complete response (pCR) after 12 weeks of pembrolizumab + trastuzumab + pertuzumab in HER2-enriched early breast cancer: Keyriched-1 trial

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Background In unselected HER2+ early breast cancer (EBC), de-escalated chemotherapy-free neoadjuvant therapy (NAT) with dual HER2-blockade induces pCR rates of only 20%-40%. In

order to achieve pCR rates by de-escalated therapy comparable to those achieved by chemotherapy-based regimens, patient selection and more effective chemotherapy-free regimens are thus key. KEYRICHD-1 (NCT03988036), a single-arm phase 2 study, is the first trial to investigate chemotherapy-free NAT with dual HER2 blockade and pembrolizumab in HER2-enriched HER2+ EBC. In a translational subproject, we analyzed gene signatures together with tumor cell proliferation and spatiotemporal immune cell profiling to identify predictive factors for pCR. Methods 48 pre- and postmenopausal patients with newly diagnosed HER2 2+ (ISH positive) or 3+ EBC (stage I-III) and HER2-enriched (HER2-E) subtype by PAM50 were included in the study. All patients received 4 cycles of pembrolizumab (200 mg), trastuzumab biosimilar ABP 980 (loading dose (LD) 8 mg/kg bodyweight (BW), maintenance dose (MD) 6 mg/kg BW), and pertuzumab (LD 840 mg/kg BW, MD 420 mg/kg BW) q21d. Primary objective was pCR (centrally confirmed absence of invasive tumor in breast and lymph nodes: ypT0/is, ypN0). NanoString Breast Cancer 360 panel was performed in baseline biopsies (n=42). $\geq 30\%$ Ki67 decrease, < 500 invasive tumor cells or no evidence of tumor in week 3 biopsies (on treatment) were classified as early response. sTILs were analyzed at baseline (n=42) and week 3 (n=28). Ongoing analyses include whole exome sequencing and multiplexed immunohistochemistry for expression of PD1, PDL1, CD4, CD8, CD68, and CD20 levels in tumor and stroma at baseline and at week 3. Impact of standardized expression of single genes, signatures, and sTILs on pCR was evaluated with univariable and multivariate logistic regression analyses and summarized with odds ratios (OR) and 95% confidence intervals (95%CI). Results 42 patients with BC360 and sTILs data at baseline were included in the analysis. Median age was 55 years (range: 22-83), 11 patients (31%) had node-positive EBC. At baseline, 28 patients had sTIL levels $\geq 30\%$ and 14 had sTILs $< 30\%$; the corresponding pCR rates were 57.1% (n=16) and 28.6% (n=4, p=0.108). At week 3 (on treatment), 16 patients had sTIL levels $\geq 30\%$, 50% (n=8) had a pCR vs 8.3% in those with $< 30\%$ sTILs (one patient out of 12, p=0.039). 37 patients had early response, 54.1% of them (n=20) had a pCR vs 0% in early non-responders (n=5, p=0.049). In univariate analysis, IDO1, ERBB2, IFN γ , cytotoxic cells, cytotoxicity, CD8 T-cells, TIGIT, and tumor inflammation signatures were statistically significantly associated with pCR (OR 2.3-3.6); ERBB2, IDO1, IFN γ and CD8 T-cells remained significant after adjusting for hormone receptor (HR) and central HER2 status (OR 2.2-4.3). 70 single genes were predictive for pCR; none of them remained significant after false discovery rate adjustment (25%). In multivariable analysis for baseline markers including signatures, sTILs, HR and central HER2 status, only ERBB2 (OR 8.7, 95%CI 1.9-39.0, p=0.0046) and cytotoxic cells signatures (OR 4.6, 95%CI 1.6-13.5, p=0.0059) were predictive for pCR. Results of whole exome sequencing, and multiplexed immunohistochemistry analysis of immune cell markers will be presented at the Symposium. Conclusions Biomarker analysis in the unique KEYRICHD-1 cohort revealed that early response at week 3, ERBB2 and immune related signatures as well as on-therapy sTIL levels predict pCR after a chemotherapy-free combination of immunotherapy and dual HER2 blockade in HER2-enriched EBC. These results pave the way for validation in larger de-escalation trials investigating short, chemotherapy-free regimens in selected patients with HER2+ EBC. Funding for this research was provided by MSD Sharp & Dohme GmbH.

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Immune Signatures Display Subtype-Specific Activation in Breast Cancer

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Background. The development of new anti-HER2 therapies for the treatment of HER2-positive breast cancer (BC) is changing the concept of HER2 dichotomization to select and treat this patient population. In addition, different immunotherapies tested in HER2-low BC are gaining continuous interest. However, a comprehensive characterization of HER2 BC subgroups and patients is required to identify the best treatment approach. **Materials and Methods.** Using 123 BC samples with gene expression and IHC/FISH determined HER2 status we determined cutoff values to identify HER2 positive, HER2 low, and HER2 ultralow cohorts. With the inclusion of hormone receptor (HR) status six clinically relevant cohorts were defined (HR+/HER2+, HR+/HER2-low, HR+/HER2-ultralow, and HR-/HER2+, HR-/HER2-low, HR-/HER2-low). An integrated database of 7,624 BC cases were assigned to the six subtypes. Prognosis determination was based on relapse-free survival (RFS), distant-metastasis-free survival (DMFS), and overall survival (OS). Clinical parameters evaluated include MKI67 expression, lymph node status and grade. All together 17 immune signatures resembling immune genes and related activated pathways were tested against the six molecular BC subgroups. **Results.** We defined a robust cutoff for HER2 expression levels to define six distinct HER2 BC molecular subgroups (>3034 for HER2 positivity and < 1780 for HER2 ultralow). Regardless the HR positivity, the overall distribution of HER2-low, and HER2-ultralow was 23% and 52%, respectively. In the HR+ subgroups the HER2-low showed a better prognosis as compared to the HER2-ultralow and HER2+ (RFS and DMFS P = 0.0048 and 0.0015, respectively) while there was no prognostic effect of HER2 expression in the HR- subgroups. Not surprisingly, an association with higher grade was demonstrated in all HR- as compared to the HR+ subgroups regardless of HER2 status. Overall, all HR- subgroups showed a higher involvement of immune genes as compared to the three HR+ subgroups. Of interest, HER2-low (HR+ and HR-) and HR-/HER2+ showed a significant overlap expression of immune signatures (71%). While the HR+/HER2-ultralow and HR+/HER2+ displayed minimal activation of immune pathways, the HR-/HER2-ultralow was the group most significantly associated with the activation of immune signaling including IFN signaling (67% percent of genes in the panel with altered expression), T cell active cytokines (34% of genes hit), and cytotoxic effector molecules (48% of genes hit). **Conclusions.** Our study supports a further molecular stratification of breast cancer based on HER2 status. The different tumor-immune background of these BC subgroups highlights that selected patient cohorts may derive benefit from targeted immunotherapy.

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Detection of high-risk patients resistant to CDK4/6 inhibitors with hormone receptor-positive HER2-negative breast cancer in Japan

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(Background) Cyclin-dependent kinase 4 and 6 inhibitors (CDK4/6i) improve the prognosis of hormone receptor-positive HER2-negative breast cancer (HR+/HER2- BC) by approximately 5 years. However, some patients show resistance to CDK4/6i and have poor prognosis. Thus, predicting resistance in patients is important. Although PAM50 is a strong tool for predicting late recurrence risk in HR+/HER2- BC by analyzing gene expression signatures, it is not always available. The non-luminal disease score (NOLUS), developed as an approximate formula for PAM50, is a pathology-based subtyping assay used to predict non-luminal disease using immunohistochemical analysis (Pascual et al. *Front Oncol*, 2021). (Materials & Methods) This multicenter, retrospective observational study was approved by the central ethics committee of Gifu University. From December 2017 to December 2021, real-world data of patients with metastatic HR+/HER2- BC who received CDK4/6i therapy were collected from 11 institutes in Japan. Data were obtained for patients who received CDK4/6i, such as palbociclib (PAL) or abemaciclib (ABE), as the first- or second-line endocrine therapy. The association between the efficacy of CDK4/6i and NOLUS was investigated by evaluating pathological and clinical data, including progression-free survival (PFS) and overall survival (OS). Pathological data, including the expression levels of ER, PgR, HER2, and Ki67, were evaluated according to the ASCO/CAP guidelines by experienced pathologists in each institute using either primary or metastatic tumors. PFS was defined as the period from the 1) starting date of combination therapy to progressive disease (PD); 2) the starting date of combination therapy to PD when CDK4/6i was interrupted due to adverse events or patients' preference; and 3) the starting date of endocrine monotherapy to PD when CDK4/6i was added. NOLUS was calculated using the formula: $NOLUS(0-100) = -0.45 * ER\% - 0.28 * PR\% + 0.27 * Ki67\% + 73$, and the patients were divided into two groups, NOLUS(+) [≥ 51.38 , non-luminal disease] and NOLUS(-) [< 51.38 , luminal disease]. The expression levels of ER, PgR, HER2, and Ki67 in each group were compared using Wilcoxon rank-sum and Fisher's exact tests. Next, prognosis, including survival rate, PFS, and OS, was evaluated with a 95% confidence interval (CI) using the Kaplan-Meier method with the log-rank test. Statistical significance was set at $p < 0.05$. (Results) Of the 300 patients, 28 (9.3%) were NOLUS(+) and 272 (90.7%) were NOLUS(-). The expression rates (%) in NOLUS(+) and NOLUS(-) were, respectively, 28.2 ± 19.4 and 89.0 ± 11.3 for ER ($p < 0.001$); 6.3 ± 15.9 and 44.3 ± 37.9 for PgR ($p < 0.001$); and 42.5 ± 23.8 and 26.9 ± 19.1 for Ki67 ($p < 0.001$). The expressions of HER2 (score 0, 1, 2, and ISH-negative, 3) were 42.9%, 28.6%, 28.6%, and 0% for NOLUS(+); and 30.8%, 51.7%, 17.5%, and 0.4% for NOLUS(-) ($p = 0.086$). There were apparent statistical differences in prognosis between the NOLUS(+) and NOLUS(-) groups. PFSs for 6M and 1y were 71.4% and 30.5% for NOLUS(+), and 85.2% and 66.6% for NOLUS(-) (HR, 3.15; 95%CI: 2.02-4.93; $p < 0.001$). OS for 6M and 1y were 92.6% and 92.6% for NOLUS(+), and 97.7% and 93.8% for NOLUS(-) (HR, 3.01; 95%CI: 1.48-6.09, $p = 0.001$). NOLUS(-) patients showed statistically better PFS with first-line therapy than with second-line therapy. However, NOLUS(+) patients showed no prognostic difference between the first and second therapeutic lines, suggesting CDK4/6i inefficacy. (Conclusion) CDK4/6i efficacy and prognosis were significantly different between NOLUS(+) and NOLUS(-) patients. This feasible method can predict patients with CDK4/6i-resistance and help select a better therapeutic approach to overcome resistance.

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5:00 PM - 6:15 PM

P5-02-07

Cell-free DNA detection of GATA3 mutations in metastatic hormone receptor positive breast cancer: a retrospective, observational multi-institutional analysis

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Background GATA3 mutations (GATA3mut) have been reported in 10-20% of hormone receptor positive (HR+) breast cancers. It has been shown that targeting GATA3mut HR+ breast cancer with MDM2 inhibitors invokes synthetic lethality. MDM2 is an E3 ubiquitin ligase that targets p53 for degradation, and research suggests that restoring p53 by blocking MDM2 may be effective in treating GATA3mut HR+ breast cancer. One potential mechanism of this efficacy has been shown to be through the PI3K-AKT pathway. We thus sought to characterize the GATA3mut landscape in a multi-institutional cell-free DNA (cfDNA) analysis and to determine the association between GATA3mut and TP53 mutations, as well as alterations in the PI3K-AKT pathway and the impact of GATA3 on survival. Methods We analyzed cfDNA data collected at the Massachusetts General Hospital and at Washington University in St Louis via Guardant360, a next generation sequencing assay that analyzed up to 74 genes during the study period. The association of GATA3mut and co-mutations as well as number of prior therapies was estimated using Pearson's chi-squared test for categorical variables, two-sample Wilcoxon rank-sum test for continuous variables, and multivariable logistic regression. The impact of GATA3mut and GATA3 wildtype (WT) on progression-free survival (PFS) and overall survival (OS) was analyzed using multivariable Cox regression analysis, adjusting for age, number of prior therapies, visceral metastases, and de novo metastases. PFS and OS were evaluated in the overall study population, as well as in subgroups of patients that received endocrine monotherapy and chemotherapy. Results Out of 647 patients with HR+ MBC, 10% (n = 68) had non-synonymous GATA3 mutations. Among these 68 GATA3mut patients, 37% (n = 25) were mutations in exon 5, all but two of which were in the second zinc finger, and 62% (n = 42) were in exon 6. 62% (n = 42) were frameshift mutations, 20% (n = 14) were indels, and 18% (n = 12) were point mutations. Median mutant allele fraction (MAF) of GATAmut was 0.95% (range 0.03 – 30.5%). There was no statistically significant association of GATA3mut with the number of prior therapies, PR status, or the presence of ESR1, TP53, or PI3K-AKT pathway mutations. In the GATA3mut population, TP53 co-mutations (n = 21) were found with a median MAF of 0.6%. PI3K-AKT pathway alterations occurred in 47% (n=32) of GATA3mut patients (PIK3CA n = 27; AKT n = 2; PTEN n = 3). In the combined cohort, there was no significant difference in PFS or OS after adjusting for visceral metastases, de novo disease, number of prior therapies, and age. In a cohort of 80 patients that received endocrine monotherapy (GATA3 WT n = 74, GATA3mut n = 6), GATA3mut were associated with borderline worse PFS (HR 2.6; p = 0.061) and worse OS (HR 4.5; p = 0.009). There was no statistically significant difference in PFS or OS in a subgroup that received chemotherapy. Conclusions GATA3 mutations can be identified via cfDNA in patients with HR+ MBC. Co-mutations in TP53 occurred at overall low MAF. Further research is needed to characterize the functional impact of these low level TP53 co-mutations and develop therapeutic strategies to target GATA3 mutant MBC.

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5:00 PM - 6:15 PM

P5-02-08

Biomarker associated with response to CDK4/6 inhibitors in metastatic hormone receptor positive breast cancer

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Background: In spite of widespread use and known mechanism of action, predictive biomarkers for the use of CDK4/6 inhibitors in conjunction with endocrine therapy have yet to emerge. Here a cohort of patients treated with standard-of-care combination regimens was utilized to explore features of disease and determinants of progression-free survival (PFS). Patients and Methods: In this cohort of 235 patients, >90% of patients were treated with Palbociclib in combination with either an aromatase inhibitor (AI) or fulvestrant (FUL). The PFS mirrored that observed in randomized clinical trials. A total of 151 patient tumor tissues were used for targeted gene expression analyses with the HTG-Oncology Biomarker Panel. The association of disease state and gene expression analyses were interrogated for disease evolution and association with PFS. Results: HER2 immunohistochemistry (HER20, Her21+, Her22+) was not associated with PFS in full cohort, or AI and FUL subgroup analyses. The lack of progesterone receptor (PR+, PR-), was associated with shorter PFS in the full patient cohort ($p=0.012$) and selectively in patients treated with AI ($p=0.005$), but not FUL. Gene expression-based subtyping indicated that the majority of patients, as expected, had luminal breast cancer; however, the predominant subtypes changed with treatment and disease evolution. Primary tissue from tumor resection was dominated by luminal A subtype, which diminished in the context of metastatic disease, and was rare in post-progression specimens. The luminal B, HER2, and basal subtypes exhibited shorter PFS in CDK4/6 inhibitor combinations (AI, $p=0.01$; FUL, $p=0.03$). Existing clinically developed breast cancer signatures (e.g. breast cancer index) had variable associations with PFS; however, high expression of gene signatures associated with cell cycle were broadly associated with short PFS. Concordantly, utilizing unbiased analyses, gene expression programs linked to cell cycle were associated with short PFS, while interferon response processes were associated with longer PFS. Algorithms that incorporated standard pathological and clinical variables with the gene expression data were developed that exhibited potent predictive power. Conclusions: Tumor evolution occurs on treatment with CDK4/6 inhibitors; however, analyses of pretreatment biopsies can inform the duration of PFS. These data support discrete biological processes associated with sensitivity/resistance. Predictive algorithms could be developed to inform features of treatment decision which will require prospective validation which is ongoing.

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P5-02-09

Quantitative analysis of fiber-level collagen features in H&E whole-slide images predicts neoadjuvant therapy response in patients with HER2+ breast cancer

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Background: Neoadjuvant treatment (NAT) combining chemotherapy and HER2-targeted agents is frequently administered to HER2-positive (HER2+) breast cancer (BC) patients, with some experiencing a pathological complete response (pCR) and others having residual disease measured by the residual cancer burden (RCB) score. Here, we use a physics-guided machine learning (ML)-based approach to extract fiber-level collagen features from hematoxylin and eosin (H&E)-stained whole slide images (WSIs) and identify collagen-related associations with treatment response in HER2+ patients receiving NAT.

Methods: Clinical data and specimens from stage II-III HER2+ BC patients enrolled on the De-escalation to Adjuvant Antibodies Post-pCR to Neoadjuvant THP (DAPHNe; NCT03716180) clinical trial and treated with neoadjuvant paclitaxel/trastuzumab/pertuzumab were analyzed. An ML-based model trained to identify regions of BC tissue as invasive carcinoma, ductal carcinoma in situ (DCIS), diffuse inflammatory infiltrate, stroma, necrosis, or normal tissue was deployed on WSIs of H&E-stained diagnostic core needle biopsies (N=89) to generate tissue overlays. Additional tissue areas were computed from the tissue model predictions using heatmap transformation, including tumor nests (continuous regions predicted as invasive cancer epithelium or DCIS), tumor nest borders (stromal region boundaries 10 μm from tumor nests), and bulk tumor borders (stromal region boundaries 300 μm from aggregated tumor nests). A separate ML-based model trained to identify fiber-level collagen features in WSIs of H&E-stained specimens was also deployed to generate collagen overlays. A fiber feature extraction pipeline was utilized to characterize properties of all identified collagen fibers in the WSI (on the order of hundreds of thousands per slide), including length, width, tortuosity, and angle. These fiber features were then assessed based on their position within the tumor (e.g. relative to the tumor nest border). Combinatorial features (e.g. angle of fibers with respect to tumor boundary) were then explored univariately for associations (N=609) with treatment response. Patients with pCR (RCB=0; N=53) were considered responders, while all other cases

(RCBI-III; N=36) were designated non-responders. Due to the small size of the cohort analyzed here, raw p-values are reported.

Results: Using estrogen receptor status as a clinical covariate, a logistic regression-based univariate analysis of 609 collagen-associated features revealed six features to strongly associate with pCR ($p < 0.05$, $AUC \geq 0.75$; Table 1). Notable feature themes were identified: 1) fiber tortuosity in tumor nest borders and tumor borders, 2) angle of fibers in tumor border with respect to tumor boundary, and 3) distribution patterns of fiber width in tumor nest borders. The presence of fibers perpendicular to tumor boundary tangents was negatively associated with pCR, as was higher fiber tortuosity and thickness in tumor nest borders.

Conclusions: Improved prediction of response to NAT in patients with BC is needed to determine appropriate treatment strategies for each patient. Here, using ML-based models to identify tissue features and collagen fibers, we identify collagen-associated features, measured directly from WSIs of H&E-stained diagnostic BC biopsies, that negatively correlate with pCR. Additional development of this strategy, including the addition of cell identification models and known clinical information, is underway to further refine this novel predictive model.

Theme	Feature	P-value	AUC
Tortuosity	90th percentile tortuosity of fibers in tumor nest border	0.034	0.79
Tortuosity	Standard deviation of fiber tortuosity in tumor nest borders	0.042	0.80
Tortuosity	Mean tortuosity of fibers in tumor nest borders	0.043	0.77
Tortuosity	Median fiber tortuosity in densely inflamed stroma	0.052	0.75
Angle	Standard deviation of fiber relative-angles in bulk tumor borders	0.036	0.79
Angle	Proportion of fibers with high relative-angle in bulk tumor borders	0.053	0.77
Width	Kurtosis of fiber widths in tumor nest borders	0.027	0.78
Width	Skewness of fiber widths in tumor nest borders	0.038	0.78

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5:00 PM - 6:15 PM

P5-02-10

In-silico approaches that detect immune contexture to trastuzumab response in neo-adjuvant studies

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Introduction: Computational approaches have aided in estimating cellular composition of the tumour microenvironment. The evaluation of immune composition in tumours before treatment may predict pathologic complete response (pCR). The aim of the study was to perform a meta-analysis of HER2-positive breast cancer subjects who received neoadjuvant trastuzumab to detect associations between immune cells measured by CIBERSORT and ESTIMATE and pCR. Methods: PubMed was used to identify transcriptomic data of HER2-positive breast cancer patients who received neoadjuvant trastuzumab. Baseline data from eight neoadjuvant studies (N=338) was downloaded from GEO. Data from each study was background corrected and quantile normalised using 'limma' or 'oligo' packages in R. Immune profiles per sample was generated using computational softwares CIBERSORT and ESTIMATE, and were then linked to pCR status. Correlations between immune contexture and pCR for each study were interpreted using statistical testing. Meta-analysis by a logistic regression model was conducted on studies which passed assumptions to identify CIBERSORT immune subsets robust to pCR. Results: CIBERSORT results showed that three studies had reduced T follicular helper cells (Tfh) (Brodsky p=0.38, CHER-LOB p=0.17, TransNOAH p=0.25) and two studies had reduced plasma cells (CHER-LOB p=0.15, Brodsky p=0.38) in the pCR group, but was not significant after multiple correction. ESTIMATE analysis showed that data from two studies had elevated immune infiltration in pCR (Brodsky p=0.19, CHER-LOB p=0.10) but was not significant. A meta-analysis of pooled data from four studies (TRIO-US B07, 03-311, TransNOAH, CHER-LOB) showed that low Tfh (p=0.053, OR=0.04, CI [0.0012-0.99]) and high memory B-cells (p=0.008, OR=2126.9, CI [8.12-7.65x10+5]) prior to trastuzumab treatment may be associated with a better chance of achieving pCR. Conclusion: Results from our meta-analysis proposed that memory B- and T follicular helper subsets may predict a role in achieving pCR. Incorporating studies with larger sample cohorts such as the CALGB-40601 (N=265) study can achieve statistical power of this analysis.

Disclosure(s):

Dalal AlSultan, BSc, MSc: No financial relationships to disclose

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5:00 PM - 6:15 PM

P5-02-11

Immune cell profile of tumors from patients with metastatic (met) HER2+ breast cancer (BC) with < 30 months overall survival (OS).

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Background: The “Thousand Patient HER-2 database” project at Saint Vincent’s University Hospital (SVUH) Dublin has been used to identify HER2+ BC patients with durable complete response (never relapsed) to trastuzumab-based therapy. ~10% of met HER2+ BC patients achieve a durable complete response to trastuzumab, meaning the majority of patients progress on treatment. Higher stromal tumour immune infiltrate has been associated with longer OS in met HER2+ BC. There is limited tumor immune profile and PD-1 expression data available for patients with met HER2+ BC with short OS. Using the SVUH database, we have identified a preliminary cohort of 21 met HER2+ BC patients that received trastuzumab and had an OS < 30 months. This study examines the levels of pan T cell marker CD3, cytotoxic T cell marker CD8, Natural Killer (NK) cell marker CD56 and immune checkpoint PD-1 by immunohistochemistry (IHC) in this preliminary cohort. Methods: Formalin-fixed, paraffin-embedded (FFPE) biopsy specimens (n=21 primary, n=7 matched metastatic biopsies) and associated clinico-pathological data were curated. Tumor biopsies were processed for IHC staining of CD8 (Agilent IR62361-2), CD3 (Agilent IR50361-2), CD56 (Agilent IR62861-2) and PD-1 (Roche 07099029001). PD-1 staining was available for 20/21 samples. Staining was performed using the DAKO Link 48 Autostainer as per the manufacturer’s instructions using positive (tonsil tissue) and negative controls (isotype controls). Slides were processed using the Aperio AT2 Digital Slide Scanner (Leica Biosystems), reviewed using Aperio ImageScope 12.4 software (Leica Biosystems) and analyzed in QuPath (University of Edinburgh). Images were annotated to outline tumor areas and an algorithm was trained to identify cells and classify them as either tumor or stromal. Data was expressed as number of positively stained cells/mm² breast tumor or stromal tissue. Survival studies utilized the Kaplan Meier method. The paired Student’s T test was utilized for primary vs metastatic site comparisons. Results: Designating samples with > 1 stained cell/mm² breast tumor as positive (pos) and zero stained cells as negative (neg), 19/21 (90.5%) primary samples were pos for CD3, 15/21 (71.4%) for CD56, 14/21 (66.6%) for CD8, and 10/20 (50%) for PD-1. Within the stromal compartment, 20/21 (95.2%) primary samples were pos for CD8, 18/21 (85.7%) for CD56, 16/21 (76.2%) for CD3 and 8/20 (40%) for PD-1. PD-1 expression in the primary tumor (median OS PD-1pos 7.85 mo vs PD-1neg 5.39 mo, hazard ratio (HR) 0.642 (95% CI 0.256-1.613), p=0.346) or the stroma (median OS PD-1pos 8.84 mo vs PD-1neg 5.39 mo, HR 0.495 (95% CI 0.197-1.244), p=0.135) was not significantly associated with OS. When comparing matched primary and metastatic samples (n=7), increased stromal levels of CD3 (4/7), CD8 (4/7), CD56 (5/7) and PD-1 (4/7) were observed. Increased levels of CD3 and CD8 were observed for 2/7 samples, and increased levels of CD56 and PD-1 for 4/7 samples. With the exception of tumor CD8 levels which decreased, mean values for tumor and stromal CD3, CD56, PD-1 and stromal CD8 levels were higher in metastatic sites but all differences were not found to be significant (p>0.05). Conclusions: Our results suggest that met HER2+ BC patients with < 30 months OS have significant T cell and NK cell presence in the tumor and stromal compartments in both primary and metastatic sites. Further expansion of this limited dataset is planned to gain greater insight in to the immune cell profiles and PD-1 status of met HER2+ BC patients with short OS.

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5:00 PM - 6:15 PM

P5-02-12

Prognostic relevance of PD-L1 expression on circulating tumor cells in metastatic breast cancer patients treated with anti-PD-1 immunotherapy

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Rationale: Breast cancer has become the leading cause of cancer mortality in women. Although immune checkpoint inhibitors targeting programmed death-1 (PD-1) are promising, it remains unclear whether PD-L1 expression on circulating tumor cells (CTCs) has predictive and prognostic values in predict and stratify metastatic breast cancer (MBC) patients who can benefit from anti-PD-1 immunotherapy. Methods: Twenty six MBC patients that received anti-PD-1 immunotherapy were enrolled in this study. The peptide-based Pep@MNPs method was used to isolate and enumerate CTCs from 2.0 ml of peripheral venous blood. The expression of PD-L1 on CTCs was evaluated by an established immunoscore system categorizing into four classes (negative, low, medium, and high). Results: Our data showed that 92.3% (24/26) of patients had CTCs, 83.3% (20/26) of patients had PD-L1-positive CTCs, and 65.4% (17/26) of patients had PD-L1-high CTCs. We revealed that the clinical benefit rate (CBR) of patients with a cut-off value of $\geq 35\%$ PD-L1-high CTCs (66.6%) was higher than the others (29.4%). We indicated that PD-L1 expression on CTCs from MBC patients treated with anti-PD-1 monotherapy was dynamic. We demonstrated that MBC patients with a cut-off value of $\geq 35\%$ PD-L1-high CTCs had longer PFS ($P < 0.05$) and OS ($P < 0.01$) compared with patients with a cut-off value of $< 35\%$ PD-L1-high CTCs. Conclusion: Our findings suggested that PD-L1 expression on CTCs could predict the therapeutic response and clinical outcomes, providing a valuable predictive and prognostic biomarker for patients treated with anti-PD-1 immunotherapy.

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P5-02-13

TRK inhibitor in a patient with metastatic triple negative breast cancer and NTRK fusions identified via cell-free DNA analysis.

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Introduction: Tissue-agnostic indications for targeted therapies are expanding options for patients with advanced solid tumors. The FDA approvals of the PD-1 inhibitor pembrolizumab and the TRK inhibitors larotrectinib and entrectinib provide rationale for next generation sequencing (NGS) in effectively all advanced solid tumor patients, as findings may indicate targeted therapy even in disease that may seem otherwise refractory. Here, we present the case of a post-menopausal woman with metastatic triple negative breast cancer (TNBC) who had disease progression on multiple lines of therapy prior to the identification of two actionable NTRK mutations, identified via cell-free DNA (cfDNA) and tissue-based NGS. She was subsequently started on the TRK inhibitor larotrectinib and had a marked clinical response.

Case Presentation: A 64-year-old woman presented with metastatic TNBC five years after being treated for a localized breast cancer. The cancer rapidly progressed through 4 lines of therapy in the metastatic setting, including immunotherapy [atezolizumab/nab-paclitaxel (progression after 5 months)], antibody-drug conjugate-based therapy [sacituzumab govitecan (progression after 2 months)], and chemotherapy [gemcitabine/carboplatin (progression after 3 months), eribulin (progression after 2 months)]. Her CA 15-3 had also been consistently increasing to a peak of 206 IU/mL. Germline genetic testing was negative. Ultimately, NGS evaluation of cfDNA via an 83-gene assay (Guardant Health, Inc.) identified two NTRK3 fusions: an ETV6-NTRK3 fusion [mutant allele fraction (MAF) = 10.9%] associated with the rare secretory breast carcinoma, and CRTC3-NTRK3 (MAF = 3.2%), a fusion partner previously undescribed in breast cancer. Liver biopsy was sent for whole exome sequencing and RNA-seq analysis (BostonGene, Inc), which provided orthogonal confirmation of both the ETV6-NTRK3 and CRTC3-NTRK3 fusions. Review of the tumor pathology showed invasive ductal carcinoma with secretory features; this pathology and the ETV6-NTRK3 fusion were consistent with a diagnosis of secretory breast carcinoma. She was started on the TRK inhibitor larotrectinib, and she had a significant clinical and radiographic response after only two months of therapy. Recheck of her CA 15-3 showed a decrease to 48 IU/mL, the lowest level in our records. Repeat cfDNA testing showed a decrease of the ETV6-NTRK3 fusion to MAF 0.40% and the CRTC3-NTRK3 fusion to MAF 0.07%. The patient took larotrectinib for 7 months with good disease control. Unfortunately, unrelated to her therapy, she had experienced multiple fractures secondary to her existing osseous metastases, and these led to significant morbidity. She and her family elected to transition to comfort measures, after which she passed away.

Discussion: In the presented case, the identification of NTRK fusions by plasma-based genotyping resulted in matched selection of genotype-directed therapy, and this otherwise refractory TNBC exhibited marked response to targeted therapy. While TNBC had historically been considered a subtype of breast cancer without targetable options, the expanding roles of NGS testing and targeted therapies are changing the paradigm. The actionability of rare genomic events such as NTRK fusions makes identifying them critical for individual patients, particularly in heterogeneous diseases such as TNBC. Tissue-agnostic targeted therapies now give reason for NGS testing in most solid tumors, as reflected in updated consensus guidelines. This case demonstrates the significant potential benefits of NGS testing in advanced and refractory cancers.

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P5-02-14

Identification of mechanisms of acquired resistance to ribociclib plus endocrine therapy using baseline and end-of-treatment circulating tumor DNA samples in the MONALEESA-2, -3, and -7 trials

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Background: Genetic alterations that contribute to resistance to therapy may be acquired during treatment (tx) for hormone receptor–positive/human epidermal growth factor receptor–negative (HR+/HER2–) advanced breast cancer (ABC). A previous pooled analysis of circulating tumor DNA (ctDNA) in MONALEESA (ML)-2, -3, and -7 identified potential predictive biomarkers for response and resistance to ribociclib (RIB) at baseline (BL). Here, we describe an analysis of paired BL and end of treatment (EOT) samples from ML-2, -3, and -7 to identify acquired mechanisms that may impact resistance to RIB + endocrine therapy (ET) vs placebo (PBO) + ET. Methods: ML-2 (NCT01958021), ML-3 (NCT02422615), and ML-7 (NCT02278120) evaluated efficacy and safety of RIB + ET vs PBO + ET in pre- and postmenopausal patients (pts) with HR+/HER2– ABC treated in first-line (1L) and second-line (2L) settings. Plasma samples were collected at cycle 1 day 1 (C1D1; prior to first therapy exposure) and at EOT (\pm 28 days of recorded progression). ctDNA was sequenced using a targeted next-generation sequencing panel of \approx 550 genes. Genes with an alteration frequency of $>$ 5% at EOT, regardless of their frequency at BL, were included. Tumor mutational burden (TMB) was assessed by tx arm; a TMB cutoff of 10 mutations/MB was used to categorize pts as TMB high vs low. To assess differences in the presence of alterations, a McNemar test was performed on paired samples and adjusted (adj) for multiple testing using the false discovery rate (FDR). A Bayesian mixed effects model was used to account for ctDNA fraction and trial and to test for tx-specific resistance by including a tx \times visit interaction term. Results: A total of 905 paired samples from ML-2, -3, and -7 were included in this analysis, 441 and 464 samples from pts treated with RIB + ET and PBO + ET, respectively. Overall, 17 genes had an alteration frequency of $>$ 5% at EOT. The ctDNA fraction was higher at EOT vs C1D1 in both the RIB (P=.037) and PBO (P=.033) arms. The frequency of alterations in RB1 (10.4% vs 2.0%), ATM (11.3% vs 8.4%), FAT1 (4.8% vs 3.0%), and FAT3 (5.0% vs 2.5%) was higher at EOT vs C1D1 in the RIB arm (FDR-adj P $<$.10). Alterations in ESR1 were also higher at EOT vs C1D1 in both the RIB (26.3% vs 9.1%) and PBO arms (28.9% vs 5.4%) (FDR-adj P $<$.0001). Conversely, alterations in GATA3 were higher at EOT in the PBO arm (FDR-adj P=.11). These results were consistent after adjusting for ctDNA fraction. The most common ESR1 mutations were D538G, Y537S/N/C/D, E380Q, and L536H/P/R. Tx \times visit interaction effects were observed for RB1 in the RIB arm and GATA3 in the PBO arm, suggesting tx-specific resistance. A tx \times visit interaction for ESR1 was also observed, suggesting a larger relative increase in ESR1 mutations with PBO vs RIB. The percentage of pts with high TMB ($>$ 10) at EOT increased from 1.1% to 5.7% in the RIB arm and from 1.7% to 3% in the PBO arm. After accounting for ctDNA

fraction and trial, a larger numerical increase in TMB was observed for RIB (odds ratio [OR], 9.0; 95% CI, 2.9-32.7) vs PBO (OR, 2.1; 95% CI, 0.7-6.5); however, the model did not support a differential tx effect. Conclusions: This comprehensive analysis of pooled samples from ML-2, -3, and -7 identified acquired gene alterations in pts with HR+/HER2- ABC treated with 1L or 2L RIB + ET or PBO + ET. The frequency of several genes known to contribute to resistance (ESR1, RB1, ATM, FAT1, and FAT3) was higher at EOT vs C1D1 in pts treated with RIB + ET, while ESR1 and GATA3 alterations were higher at EOT vs C1D1 in pts treated with PBO + ET. This paired dataset of BL and EOT samples from pts with HR+/HER2- ABC treated with a CDK4/6 inhibitor and ET is the largest to date and could be used to validate and confirm acquired resistance mechanisms with low alteration frequency.

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5:00 PM - 6:15 PM

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SPEN is a biomarker for CDK4/6 inhibitor resistance in patients with metastatic hormone receptor positive (HR+)/HER2- breast cancer

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Background: Despite significant improvements in the treatment of breast cancer (BC), metastatic disease remains the principal cause of BC-related death. Through analysis of rapid autopsy collected biospecimens, we have previously identified Split Ends (SPEN) alterations in patients with metastatic HR+/HER2- BC (Savas et al. 2016). The role of SPEN in BC is poorly defined. Here we aimed to further explore the function of this gene in metastatic HR+/HER2- metastatic BC (mBC). **Methods:** We explored the clinical and genomic characteristics of SPEN altered mBC in human sequencing datasets. We created a model of SPEN loss using a gene knockdown (KD) via siRNA in MCF7 cells. Flow cytometry and western blot analysis was utilized to investigate the molecular impact of SPEN loss. The KD and non-targeting control cells were then subjected to a high throughput kinase inhibitor screen (n=480 compounds) to identify sensitive and resistant therapeutics. Finally, we used an in-house metastatic HR+/HER2- BC patient cohort treated with CDK (cyclin-dependent kinase) 4/6 inhibitors to validate SPEN loss as a marker of resistance. **Results:** Using a cohort of 7519 BC samples, SPEN alterations (mutation and copy number deletions) were found to be significantly enriched in HR+ mBC vs primary HR+ disease (29% vs 7%, respectively $p < 0.0001$). SPEN altered compared with SPEN wild type (WT) HR+ mBCs were significantly associated with higher tumor mutational burden (median 4.6 vs 1.7, $p < 0.0001$), more large-scale transitions (median 20 vs 14, $p = 0.006$), increased fraction of genome altered (52% vs 35%, $p < 0.0001$), and enrichment of APOBEC-induced mutations (65% vs 42%, $p = 0.004$) respectively. Taken together, these results suggest greater genomic instability in patients with tumors with SPEN loss compared with WT. This hypothesis was further supported when SPEN KD cells showed significantly increased growth rate ($p = 0.04$), and significantly greater DNA damage by γ H2Ax staining ($p = 0.03$) compared with control cells. In a kinase inhibitor compound screen, SPEN KD cells displayed significant resistance to the CDK4/6 inhibitor palbociclib ($p < 0.0001$) compared with WT cells. We validated this finding in vitro by demonstrating SPEN KD cell resistance to other CDK4/6 inhibitors ribociclib and abemaciclib ($p = 0.02$ and 0.0004 respectively). In our in-house cohort of 56 patients with HR+ mBC treated with CDK4/6 inhibitors, we found that the HR+ mBC patients with a SPEN alteration have significantly decreased overall survival (OS) compared with WT patients, (median OS 34 months vs not reached, respectively; HR 3.18, 95%CI 0.94-10.73, $p = 0.049$). **Conclusion:** These results provide the first clinical evidence that SPEN alterations are enriched in HR+ mBC. Additionally, SPEN may be a biomarker for CDK4/6 inhibitor resistance in this subtype. These results warrant further analysis into the role of SPEN in BC and its relevance in clinical management. **Reference:** Savas P, Teo ZL, Lefevre C, et al. The subclonal architecture of metastatic breast cancer: Results from a prospective community-based rapid autopsy program "cascade". *PLoS medicine* 2016;13:e1002204.

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5:00 PM - 6:15 PM

P5-02-17

Prognostic and predictive role of RBsig and CCNE1/RB1 gene-expression signatures in patients with advanced breast cancer treated with palbociclib in combination with endocrine therapy in the PALOMA-2 and 3 trials

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Background: We have previously identified two potentially predictive signatures of palbociclib resistance: the RBsig, composed of E2F1/E2F2 dependent genes, which is correlated with genetic loss of RB1, and the ratio between the gene expression levels of CCNE1 to RB1 (CCNE1/RB1). Both signatures have been previously tested in vitro and in neoadjuvant studies with palbociclib. The present analysis aims to explore the prognostic and predictive role of RBsig and CCNE1/RB1 in the pivotal phase III randomized trials PALOMA-2 and PALOMA-3. Materials and methods: Gene expression data from the PALOMA-2 and PALOMA-3 datasets were generated using the HTG EdgeSeq Oncology BM Panel, as previously described. Of the 87 genes composing RBsig, 46 were available within the EdgeSeq dataset and were used for the analyses; CCNE1 and RB1 were both available. RBsig was calculated as the mean of the Z-score scaled gene expression (log) of the 46 genes; CCNE1/RB1 was computed as the log ratio between the mRNA expression of CCNE1 and RB1. High and low values of RBsig and CCNE1/RB1 were defined based on the third quartile (Q3) as cutoff or as continuous variables. The prognostic/predictive effect of the signatures in terms of PFS was tested using Cox proportional hazard models and the Wald test. Results: The 46-genes RBsig versus the original signature showed excellent correlation in the METABRIC dataset ($R=0.99$), confirming its reliability as a surrogate of the original RBsig using EdgeSeq data. In both PALOMA-2 and PALOMA-3, RBsig high was significantly associated with a worse outcome compared to RBsig low in the palbociclib arm but not in the control arm [PALOMA-2: HR 1.4 (95% CI 1.0, 2.0) $p=0.029$ for palbociclib arm; HR 1.1 (95% CI 0.7, 1.6) $p=0.71$ for control arm. PALOMA-3: HR 1.7 (95% CI 1.1, 2.6) $p=0.01$ for palbociclib arm; HR 1.2 (95% CI 0.7, 1.9) $p=0.49$ for control arm]. However, in both studies RBsig was not predictive of palbociclib resistance both when considered as a continuous variable and when dichotomized at Q3. Similarly to RBsig, in PALOMA-3 patients with CCNE1/RB1 high tumors treated in the palbociclib arm showed a significantly worse outcome compared to those with CCNE1/RB1 low but this effect was not observed in those treated in the control arm [HR 1.6 (95% CI 1.1- 2.5) $p=0.03$ for palbociclib arm; HR 1.2 (95% CI 0.7, 1.9) $p=0.5$ for control arm]. In addition, CCNE1/RB1 as a continuous variable was predictive of palbociclib benefit in PALOMA-3 (interaction $p=0.047$). These effects were not observed in PALOMA-2. Conclusions: RBsig is a prognostic biomarker in patients treated with palbociclib, suggesting it may help in patients' risk stratification. CCNE1/RB1 is predictive of palbociclib benefit in PALOMA-3, but not in PALOMA-2 probably due to the different patient populations and characteristics. Further studies of these biomarkers in patients treated with CDK4/6 inhibitors in the metastatic as well in the adjuvant setting are warranted.

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5:00 PM - 6:15 PM

P5-02-18

HER2 status and response to neoadjuvant anti-HER2 treatment among patients with breast cancer and Li-Fraumeni syndrome

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Background: Breast cancer (BC) is the most common tumor in women with Li-Fraumeni syndrome (LFS), with a cumulative incidence of 85% by the age of 60 years. However, LFS-related BC characteristics are still underexplored since most data derive from small

retrospective cohorts. A variable enrichment in HER2-positivity (ranging from 34 to 80%) has been reported, but information regarding the response to anti-HER2 treatments are currently lacking. Moreover, data regarding the new emerging category of HER2-low are missing. Methods: Invasive BCs diagnosed in patients (pts) with TP53 germline pathogenic/likely pathogenic variant between 2002-2022 at Institut Gustave Roussy (France), Dana-Farber Cancer Institute (USA) and Hospital Sírio-Libanês (Brazil) were included. HER2 and hormone receptor (HR) expression were retrospectively retrieved from pathology records and evaluated according to ASCO/CAP recommendations in place at the time of diagnosis. HER2-positive cases were defined by an immunohistochemistry (IHC) score of 3+ and/or HER2 gene amplification by ISH; HER2-negative cases were classified as HER2-low (IHC 1+ or 2+ with negative ISH assay) or HER2-zero (IHC score 0). Pathologic complete response (pCR) was defined as ypT0/is and ypN0. Results: Among 197 invasive BCs identified in a total of 176 pts, 50.3% (n=99) were HER-positive. Among those, median age at BC diagnosis was 33 years (range 21-61) and the most frequent TP53 variants were missense mutations (n=68), affecting the DNA-binding domain in 70.6% of cases and the tetramerization domain in 29.4% of cases. Most BCs were invasive ductal carcinoma (n=90), with histologic grade 3 in 56.6% of cases. At diagnosis, most pts had early stage disease (34.3% stage I; 32.3% stage II; 21.2% stage III), while 6 pts presented de novo stage IV disease. Most tumors were HR-positive (76.8%, n=76), while 23.2% were HR-negative. 38 patients with HER2-positive BCs were treated with neoadjuvant therapy, 32 cases had post-neoadjuvant pathology reports available for pathological response classification. Among those, 26 (81.2%) were HR-positive and 6 (18.8%) HR-negative. Among pts with neoadjuvant treatment data, 87.1% received trastuzumab, which was combined with pertuzumab in 43.3% of cases; chemotherapy regimens included taxanes in all pts, anthracycline in 43.3% and platinum in 16.7%. 71.9% (n=23) of pts reached a pCR (69.2% among HR-positive and 83.3% among HR-negative), while 9 (28.1%) had residual disease; pCR rate was 82.4% among pts treated with an anthracycline-free regimen. At a median follow-up of 36 months, only one patient relapsed. Among HER2-negative BCs with available IHC score and ISH for HER2-low classification (n=85), 28 (32.9%) were HER2-low and 57 (67.1%) HER2-zero. Conclusions: In this first report of treatment results in BC pts with LFS, enrichment of HER2-positive BCs was confirmed and a remarkable pCR rate was observed with neoadjuvant treatment. Our findings require validation in a larger cohort, which is in progress. Collaborative efforts are essential for high quality data about BC treatment in this subgroup of pts.

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P5-02-19

ctDNA as dynamic marker of response to fulvestrant and everolimus in CDK4/6 inhibitor-pretreated ER+ HER2- metastatic breast cancer patients: a prospective study

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ctDNA as dynamic marker of response to fulvestrant and everolimus in CDK4/6 inhibitor-pretreated ER+ HER2- metastatic breast cancer patients: a prospective study. Background The combination of fulvestrant with everolimus is recognized by NCCN and ESMO guidelines as a valid second line treatment option for ER+ HER2- metastatic breast cancer (mBC), upon

progression on CDK4/6 inhibitor. The underlying evidence consists in a single randomized phase 2 trial (PrE0102, JCO 2018), in which N=66 patients allocated to fulvestrant and everolimus achieved a median PFS of 10.3 months (95%CI [7.6-13.8]). However, none of PrE0102 patients were pre-treated with CDK4/6 inhibitors. We set up a prospective study to document the PFS achieved by fulvestrant and everolimus in the pre-treated patients and investigated the clinical validity of ctDNA early changes as pharmacodynamic marker. Methods Eligible patients had ER+ HER2- mBC and had to be pre-treated by CDK4/6 inhibitor. Upon the signature of informed consent, patients were enrolled in the prospective observational ALCINA study (NCT02866149) and had their blood drawn at baseline (prior to treatment start), after 1 month on treatment, at first radiological assessment (3-4 months) and at disease progression. DNA from archived tumor tissue sample (or, when missing, from plasma obtained at baseline) was subjected to a large panel next generation sequencing. ctDNA levels were then assessed on the matched serial plasma samples by targeting the identified somatic mutation(s) with droplet digital PCR (ddPCR). Associations between clinicopathological characteristics, ctDNA levels and prospectively registered patient outcomes (PFS and OS) were then analyzed. Results Fifty-seven patients have been included, with a median age of 56.8 years. N=30 (52.6%) patients had ≥ 3 metastatic sites and N=34 (59.6%) had visceral metastases. Most patients (N=48, 84.2%) had only one prior line of treatment in the metastatic setting. After a median follow-up of 17.7 months, the median PFS was 6.9 months (95%CI[5.3-10.7]) and the median OS was 38.3 months (95%CI[26.9-NA]). The ORR was 33.3% (N=19 PR, no CR) whereas N=22 (38.6%) patients had a stable disease at best response. In the subgroup of N=22 (38.6%) patients with somatic PIK3CA mutations, median PFS was 3.1 months (95%CI[2.87-10.9]), while median OS was not reached. In multivariate analysis, somatic PIK3CA mutation was associated with a trend toward a shorter PFS (HR=1.84, 95%CI[0.97-3.99], p=0.06) and OS (HR=2.23, 95%CI[0.88-5.69], p=0.09). Duration of CDK4/6 inhibitor treatment had no overt impact on PFS (HR=0.68, 95%CI[0.38-1.22], p=0.2). Ten (19.6%) patients discontinued everolimus due to toxicity and 17 (29.9%) had at least one dose reduction due to an adverse event. The most grade 3 adverse event were mucositis (10.5%) and hypertriglyceridemia (3.5%), only 1 patient had a grade 3 pneumopathy. At least one mutation trackable by ddPCR was found in N=48 patients. As of July 2022, ctDNA levels have been analyzed in 34 patients (PIK3CAmut: N=19; ESR1mut: N=6; TP53mut: N=4; AKTmut: N=2; CUX1mut: N=1; GATA3mut: N=1; PTENmut: N=1). At baseline, N= 26/34 patients (76.5%) of patients had detectable ctDNA levels. Baseline ctDNA positivity had no prognostic impact on PFS (HR=0.93, 95%CI[0.4-2.13], p=0.86). ctDNA monitoring in the whole cohort will be available for the congress. Conclusion To our knowledge, this is the first prospective study to evaluate the efficacy of fulvestrant-everolimus after progression on CDK4/6 inhibitor. Efficacy data on 57 patients shows that fulvestrant-everolimus is an active regimen in this population. The PFS observed under fulvestrant-everolimus in patients with PIK3CA-mutant mBC appears shorter than previously reported with alpelisib in the BYLIEVE study. Results of ctDNA to monitor the individual response to therapy will be presented at the congress.

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Correlative and longitudinal transcriptomic profiling predicts patient outcomes and the efficacy of neoadjuvant HER2-targeted treatments in the randomized PREDIX HER2 trial

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Background: The PREDIX HER2 trial compared standard neoadjuvant therapy with 6 cycles of docetaxel, trastuzumab, and pertuzumab (DTP), versus 6 cycles of trastuzumab emtansine (T-DM1) in 197 patients with HER2-positive breast cancer. There was no difference in pathologic

complete response (pCR) rate and event-free survival (EFS) between the two treatments (Hatschek, JAMA Oncology 2021). Here we systematically evaluate the prognostic and predictive molecular biomarkers during neoadjuvant HER2-targeting therapy. Methods: Longitudinal fresh-frozen tissue biopsies (pretreatment (n=194) and after 2 cycles (n=167)) and surgical specimens (n=126) were collected and sequenced by RNA-sequencing (RNA-seq). Differential gene expression (DGE) analyses were conducted using zero-inflated negative binomial mixed model, and P-values were adjusted by the Benjamini-Hochberg method. Potential prognostic and predictive markers including PAM50 intrinsic subtype, cancer hallmark signature (n=50) score, tumor infiltrating lymphocyte fraction (n=9), and immune/stromal score were calculated based on normalized count data. The correlations between above biomarkers and pCR and EFS were analyzed using multivariate logistic and Cox regressions, respectively. We integrated the least absolute shrinkage and selection operator (LASSO) regression and bootstrapping algorithm (iteration=10,000, nfold=5) to choose best predictive features. Results: Downregulation of proliferation-related and extracellular matrix pathways (DGEs with false discovery rate (FDR) < 0.05, |log fold change|>1) was observed throughout treatment in both arms. DTP resulted in early (on-treatment vs baseline) inflammatory (IL-17, TGF- β , TNF signaling pathways) and immune (B cell, NK cell and cytokine signaling) responses, whereas late responses occurred in the T-DM1 arm (post-treatment vs on-treatment). Interestingly, a rebound of HER2 and PI3K-AKT signaling was observed within residual disease after T-DM1. Immune and stromal scores showed similar kinetics between the two treatment arms, with increase after first two cycles and later decrease to baseline levels. PAM50 intrinsic subtype at baseline was independently associated with pCR and EFS after adjusting for treatment arm, tumor size, lymph node status, hormone receptor status, and Ki-67. Luminal A (pCR rate, 11.1%, odds ratio (OR), 0.64, 95% confidence interval (CI): 0.49 to 0.84, P=0.001), Luminal B (pCR rate, 20.0%, OR, 0.63, 95% CI: 0.53 to 0.76, P< 0.001) and basal-like (pCR rate, 33.3%, OR, 0.70, 95% CI: 0.53 to 0.93, P=0.02) subtypes had lower pCR rates compared to HER2-enriched subtype (, 68.9%). Patients with basal-like tumors at baseline had worse EFS than those with HER2-enriched tumors (hazard ratio (HR), 4.66, 95% CI, 1.28 to 16.90, P= 0.02). Moreover, pair-wise analyses revealed that patients with HER2-enriched tumors at baseline switching to other PAM50 subtypes after two cycles, had improved pCR (OR, 1.54, 95% CI: 1.31 to 1.80, P< 0.001) and EFS (HR), 0.26, 95% CI, 0.08 to 0.83, P= 0.02) than the remaining patients. Machine learning based analyses identified best biomarkers for pCR (hallmark estrogen response early, hallmark androgen response, hallmark PI3K AKT mTOR signaling) and EFS (NK and Treg cells fraction, hallmark apical surface). Patients with higher hallmark apical surface score could benefit from T-DM1 (HRT-DM1 vs. DTP = 0.13, 95% CI, 0.02 to 0.79, P=0.03) and vice versa (HRT-DM1 vs. DTP = 5.02, 95% CI, 1.06 to 23.76, P=0.04). Conclusion: This study sheds light on how the tumor transcriptome evolves under anti-HER2 therapy and potentially provides prognostic and predictive biomarkers for standard chemotherapy with dual HER2 blockade versus monotherapy with an antibody-drug conjugate. Further investigations evaluating the spatial and single-cell heterogeneity of HER2-positive BC are ongoing.

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5:00 PM - 6:15 PM

P5-02-21

RAB5 is a generic biomarker for ADC efficacy

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Antibody-drug conjugates (ADCs) have demonstrated impressive activity in recent clinical trials in breast cancer. Such targeted therapeutics strongly depends on the presence of target molecules on the tumor cells, and the presence of such target molecules may determine the response of ADCs. However, ADCs are also dependent on cellular uptake, and factors regulating endocytosis as well as intracellular trafficking may strongly influence ADC activity. We have recently demonstrated that the activity of the HER2 targeted ADC trastuzumab emtansine (T-DM1) is dependent on the expression of RAB5A, a protein regulating endocytosis (1). A significant correlation between Rab5A expression and T-DM1 efficacy was found in a panel of HER2 expressing breast- and ovarian cancer cell lines. This result was verified in the I-SPY2 clinical trial where patients with high RAB5A expression were more likely to achieve a pathological complete response following T-DM1 as a neoadjuvant. The result was further validated in patients treated with T-DM1 in the Kamilla study where patients with a high RAB5A had a longer progression free survival. All ADCs should in principle be dependent on endocytosis to exert their activity. This triggered the investigation of proteins regulating endocytosis as predictive biomarkers for ADCs in general. **METHODS:** HER2-positive breast and ovarian cancer cell lines were evaluated with respect to the sensitivity and efficacy of treatment with T-DM1, trastuzumab deruxtecan, sacituzumab govitecan and the targeted toxin MH3B1/rGel. The expression levels of proteins involved in endocytosis and endocytic trafficking including RAB4A, RAB5A and RAB11A were investigated in addition to the molecular drug targets (HER2 and TROP2). Cellular drug sensitivity was correlated to the expression levels of the investigated proteins using both RNA and protein as readout. **RESULTS:** The early endosome marker RAB5A, was found to correlate positively to the activity of trastuzumab

deruxtecan, sacituzumab govitecan and MH3B1/rGel in the HER2 positive cell line panel, confirming the importance of RAB5A expression for the activity of these drugs. A significant correlation was found between RAB5A and drug efficacy using both protein and RNA as a readout. **CONCLUSION:** The present results indicate RAB5A as a generic predictive biomarker for both ADCs and targeted toxins which both depend on cellular uptake for cytotoxic efficacy. The results supports using both protein and RNA as a readout for RAB5A expression and point towards the development of a RAB5A stratification procedure for ADC and targeted toxin treatment. 1. Engebraaten O, Yau C, Berg K, Borgen E, Garred O, Berstad MEB, Fremstedal ASV, DeMichele A, Veer LV, Esserman L, Weyergang A. RAB5A expression is a predictive biomarker for trastuzumab emtansine in breast cancer. *Nature communications* 2021;12(1):6427 doi 10.1038/s41467-021-26018-z.

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Circulating Tumor DNA Genotyping of Intrinsic and Acquired Gene Alterations in Patients With Advanced Breast Cancer Receiving the Cyclin-Dependent Kinase 4/6 Inhibitor Palbociclib: Biomarker Results from POLARIS

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Background: POLARIS is a prospective, real-world study of palbociclib in patients with hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (ABC) in the United States and Canada . We present results from analyses of serial circulating tumor gene alteration profiles from patients treated with palbociclib in the first and second or later lines of ABC treatment to illustrate the potential mutagenic drivers of resistance (intrinsic/acquired) and carrier-mutations (intrinsic/maintained). Methods: The clinical database cutoff date was March 30, 2022 . Patients in the biomarker analysis group provided consent for serial blood sample collection, received ≥ 1 dose of initial palbociclib combination treatment, and had ≥ 1 circulating tumor DNA (ctDNA) measurement available . The Guardant360 platform with somatic single-nucleotide variants in complete or critical exons of 73 genes was used . Tumor gene alteration profiles (at baseline, on-treatment at Cycle 2 Day 1 [C2D1], and at end of treatment [EOT]) were evaluated. Cox proportional hazard models were used to estimate hazard ratios and 95% CIs. Results: Patient samples (n=345) were analyzed and gene alterations were detected in 85% of baseline samples (n=337), 72% of on-treatment samples (n=280), and 85% of EOT samples (n=104). Most frequently altered genes were PIK3CA (38%), TP53 (28%), and ESR1 (15%) at baseline ; TP53 (28%), PIK3CA (24%), and NF1 (10%) at C2D1; and TP53 (40%), PIK3CA (40%), and ESR1 (33%) at EOT . Most frequent gene amplifications (amp) were detected in CCND1 (8.3%), FGFR1 (7.7%), and EGFR (5.9%) at baseline; FGFR1 (5.0%), CCND1 (4.3%), and EGFR (3.2%) at C2D1; and CCND1 (13.5%),

FGFR1 (9.6%), and EGFR (9.6%) at EOT . Baseline mutations of ESR1 and PIK3CA led to shorter real-world progression-free survival (rwPFS) than wild-type (hazard ratio [95% CI], 1.99 [1.38, 2.86] and 1.67 [1.24, 2.25], respectively). Baseline amp of CCND1 and FGFR1 also led to shorter rwPFS than wild-type (2.13 [1.36, 3.34] and 1.93 [1.20, 3.10]). Acquired mutations in ESR1, ATM, and RB1 were observed at EOT . Most frequently acquired ESR1 mutations at EOT were D538G, Y537N, and Y537S . Patients with all mutations cleared at C2D1, had longer rwPFS than those without (hazard ratio [95% CI], 0.58 [0.41, 0.83]). Conclusion: Patients with mutated ESR1 and PIK3CA or CCND1 and FGFR1 amp at baseline had shorter rwPFS than patients with wild-type genes . Genotyping analysis of progression ctDNA highlights the emergence of mutations in estrogen receptor and cell cycle pathways under selective therapeutic pressure and could guide monitoring and therapeutic sequencing for patients with HR+/HER2– MBC. ClinicalTrials.gov: NCT03280303

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Association of Neutrophil-to-Lymphocyte Ratio and Absolute Lymphocyte Count with Clinical Outcomes for Patients with Advanced Breast Cancer in the MONARCH 2 Trial

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Background: Pretreatment neutrophil-to-lymphocyte ratio (NLR) and absolute lymphocyte count (ALC) are putative prognostic factors in patients with advanced breast cancer (ABC). Little information is available on the prognostic value of these immune status markers in patients treated with abemaciclib (ABE). In this study, we investigated the relationship between baseline NLR and ALC and clinical outcomes using data from the phase 3 MONARCH 2 (M2) trial. Methods: The M2 study compared ABE/fulvestrant to placebo (PBO)/fulvestrant in patients with estrogen-receptor positive, human epidermal growth factor receptor 2-negative ABC that had progressed on prior endocrine therapy. The current post hoc analyses used baseline laboratory data and outcome data from the June 20, 2019, cutoff date (median follow-up: 47.7 months). For both baseline NLR and baseline ALC, patients were divided into high and low categories, defined by a cutoff of 2.5 for NLR and $1.5 \times 10^9/L$ for ALC. The association of baseline NLR and ALC with investigator-assessed progression-free survival (PFS) and overall survival (OS) was explored using Cox models stratified by treatment and described using Kaplan-Meier estimates. After assessing the prognostic value of baseline NLR and ALC for PFS and OS using a univariate analysis, a multivariate model was used to determine whether baseline NLR and

ALC were independently prognostic considering additional baseline and disease characteristic factors.

Results: Data were available for 426 and 219 patients in the ABE and PBO arms, respectively. Median baseline NLR was 2.5 and 2.4 in the ABE and PBO arms, respectively. Median baseline ALC was $1.4 \times 10^9/L$ in both arms. The numbers of patients categorized into the high and low categories were well balanced for analysis of both NLR and ALC.

Univariate analyses showed that baseline NLR (< 2.5 , ≥ 2.5) was a prognostic factor for PFS and OS (2-sided $p < 0.0001$). Patients with low baseline NLR consistently had better PFS and OS than those with high baseline NLR, and the treatment effect of ABE against PBO was consistently observed regardless of NLR category (Table 1). Univariate analyses showed that baseline ALC ($< 1.5 \times 10^9/L$, $\geq 1.5 \times 10^9/L$) was also a prognostic factor for PFS and OS (2-sided $p = 0.0116$ and 0.0032 , respectively). PFS and OS were better for patients with high baseline ALC than for those with low baseline ALC, and the treatment effect of ABE against PBO was observed regardless of ALC category (Table 1).

For PFS, the multivariate model was adjusted for Eastern Cooperative Oncology Group performance status (ECOG PS), tumor grade, presence of liver metastasis, and bone-only disease. For OS, the multivariate model was adjusted for sensitivity to endocrine therapy, ECOG PS, presence of liver metastasis, and bone-only disease. When adjusting for these additional prognostic factors, baseline NLR, but not baseline ALC, remained statistically significant in the multivariate model (2-sided $p < 0.0001$).

Conclusions: These exploratory analyses suggest that while both baseline NLR and ALC are prognostic of clinical outcomes, only baseline NLR is independently prognostic of PFS and OS. Low baseline NLR was associated with better PFS and OS outcomes, but the benefit of adding ABE to fulvestrant was similar regardless of baseline NLR status.

Table 1. Summary of outcomes by treatment arm for NLR and ALC categories

Outcome	Factor	Abemaciclib + Fulvestrant Median (95%CI) Months	Placebo + Fulvestrant Median (95%CI) Months	Hazard Ratio (95%CI)
PFS	Low NLR (< 2.5)	21.5 (16.5, 29.0)	11.2 (7.9, 15.0)	0.486 (0.373, 0.633)
	High NLR (≥ 2.5)	14.6 (12.0, 17.4)	7.1 (5.0, 10.2)	0.540 (0.415, 0.703)
	Low ALC ($< 1.5 \times 10^9/L$)	16.4 (14.1, 18.5)	7.4 (5.6, 10.2)	0.458 (0.357, 0.588)
	High ALC ($\geq 1.5 \times 10^9/L$)	17.6 (14.1, 24.2)	11.6 (7.9, 15.7)	0.600 (0.453, 0.794)
OS	Low NLR (< 2.5)	55.5 (48.5, NR)	43.8 (35.8, NR)	0.704 (0.505, 0.982)
	High NLR (≥ 2.5)	36.5 (30.9, 43.6)	33.8 (25.6, 39.8)	0.774 (0.571, 1.050)
	Low ALC ($< 1.5 \times 10^9/L$)	39.0 (34.8, 52.2)	34.4 (26.9, 40.0)	0.750 (0.558, 1.007)
	High ALC ($\geq 1.5 \times 10^9/L$)	51.3 (44.4, NR)	41.7 (35.5, 47.8)	0.735 (0.520, 1.038)

ALC, absolute lymphocyte count; CI, confidence interval; NLR, neutrophil-to-lymphocyte ratio; NR, not reached; OS, overall survival; PFS, progression-free survival.

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12/8/2022

5:00 PM - 6:15 PM

P5-02-24

Whole genome sequencing of long-term, never relapse exceptional responders HER2+ advanced metastatic breast cancer

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Background: Anti-HER2 therapies such as trastuzumab used for the treatment of patients with HER2+ metastatic breast cancer (MBC) have led to significant improvements to disease progression. We previously identified cases from the "Thousand Patient HER2 database" project at Saint Vincent's University Hospital (SVUH) Dublin, of HER2+ MBC long-term durable complete responders to trastuzumab, and reported that Copy Number Aberration (CNA) burden may represent a novel prognostic predictor to trastuzumab response from the exome analysis of in HER2+ MBC "exceptional responders" (ExRs). However, whole-genome sequencing (WGS) allows a better understanding of how CNA affects the MBC genome and to-date, the

complete genome of this “exceptional” cohort has never been described. Methods: We performed WGS analysis to characterise the CNA profiles of 9 ExRs from our HER2+ MBC cohort treated with trastuzumab. Samples were obtained from patients who never progressed/relapsed for more than 5 years (OS > 60 months). DNA was sequenced from tumours (primary or metastases) and matching control (blood or normal tissue) at a mean depth of 60X and 30X, respectively (18 samples). Somatic single nucleotide variants (SNV) were detected using GATK4 Mutect2 and CNA were identified using Control-FREEC. Results: Eighty-five HER2+ MBC were identified with OS > 60 months, of which 28 were ExRs with bone, lung, liver and lymph metastasis who responded exceptionally to trastuzumab, with a mean OS of 108 months (range 61-236 months). This cohort includes patients who were diagnosed between 31 and 80 years old (median=51). WGS analysis revealed CNA in chr6p21 with amplification of CCND3 and in chr17q12 with amplification of RAD51D. SNV were identified in genes involved in the DNA damage repair (DDR) pathway such as ATM, BRCA2, RAD50 and FANCA. On-going analysis will allow the CNA profiles of all ExRs to be presented and their CNA burden calculated in order to investigate the relationship between whole genome CNA burden and HER2+ MBC patient survival. Conclusion: To our knowledge, this is the first study to sequence the whole genome of HER2+ MBC, never relapse exceptional responders. The identification of the genomic aberrations of these metastatic patients increases our understanding of the mechanisms involved in MBC progression. CNA burden may represent a novel prognostic predictor to trastuzumab response and new outcomes for patients, particularly as MBC is generally termed incurable.

Disclosure(s):

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12/8/2022

5:00 PM - 6:15 PM

P5-02-25

Transcriptional profiling of CTCs in metastatic breast cancer patients in the course of CDK4/6 inhibition

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Background: De novo resistance defined as progression within six months and acquired resistance are one of the major problems in the subset of metastatic (M), hormone receptor-positive/HER2-negative (HR+/HER2-) breast cancer (BC) patients without visceral crisis receiving CDK4/6 inhibitors (CDK4/6i) plus endocrine therapy (TX). Here, we aim to identify predictive and monitoring markers of CDK4/6i resistance by conducting transcriptional profiling of circulating tumor cells (CTCs) that represent a real-time snapshot of the heterogeneity. Methods: Blood of (A) 60 HR+/HER2- MBC patients drawn at baseline of Palbociclib plus endocrine TX (TX as first line n=31, second or more lines n=29), (B) 19 HR+/HER2- MBC patients drawn before the initiation of endocrine monoTX (control) and matched blood samples of these patients after six months under TX (n=72) and at the time of progression (n=42) were analyzed. To enlarge the global CDK4/6i cohort at baseline, blood of (C) 32 patients before the initiation of Ribociclib plus endocrine TX was also drawn. Patients with progression within six months were defined as non-responders. Isolation of CTCs was conducted using positive immunomagnetic selection (AdnaTest EMT2/StemCell Select) and preamplified cDNA was analyzed by a multimarker qPCR panel utilizing QuantiNova LNA Probe assays targeting 25 genes involved in the DNA damage -, MAPK -, STAT -, Hippo – pathway or cell cycle, chemokine sensing, multidrug resistance and cell adhesion. qPCR data was normalized to CD45 and data of 20 healthy female donor controls to identify BC CTC specific overexpression signals with a specificity of >90% for all targets. Consumables: QIAGEN, Germany. Statistical analysis included log-rank testing and univariate Cox regression. Results: For first line CDK4/6i

treated patients at baseline, CETN2 and E2F1 signals correlated significantly with worse progression-free survival (PFS) while CETN2 signals also related significantly to non-response. Furthermore, CETN2 and PCNA signals were significantly associated with worse overall survival (OS). Analyzing the Palbociclib cohort after six months of TX, PCNA signals correlated significantly with a decreased PFS while EpCAM signals showed a significant association with OS. In addition, CETN2, CXCR4, EpCAM, MLH3, WWTR1 signals after six months were shown to correlate significantly with a decreased OS and PFS and MAPK1 signals were only found in the non-responders. While non-response was related to appearing (from baseline to six months under TX) ABCC2, JUN and MAPK1 signals, disappearing ABCC2 signals were only found in the responders. Dynamics of ABCC2, CXCR4, EpCAM, JUN, MAPK1, MLH3, STAT1 and WWTR1 signals from baseline to six months under TX correlated significantly with OS and CXCR4 signal dynamics significantly with a worse PFS. At the time of progression, the presence of E2F1, JUN, MAPK1 and STAT1 signals correlated significantly with a decreased OS and in comparison to baseline analysis, the prevalence of ABCC2, EpCAM, E2F1, CETN2 and CXCR4 signals increased. Conclusion: CTC overexpression signals at baseline of targets involved in the cell cycle (CETN2 and E2F1) might be predictive markers for de novo resistance to CDK4/6i as first line TX, while ABCC2 (multidrug resistance), EpCAM (cell adhesion), E2F1, CETN2 and CXCR4 (chemokine sensing) signals could indicate acquired resistance to Palbociclib. In case of disease progression, E2F1, JUN (cell cycle) and targets of the MAPK- and STAT- pathway could be relevant targets for therapeutic strategies beyond Palbociclib TX. Monitoring and prognostic value was shown for single and repeated measurement of signals under TX in genes involved in resistance, cell cycle progression, DNA damage response (MLH3, PCNA), chemokine sensing, cell adhesion and the MAPK-, STAT- and Hippo (WWTR1) pathway.

Disclosure(s):

Sabine Kasimir-Bauer, Prof. Dr. rer. nat.: Pfizer: Contracted Research (Ongoing); QIAGEN: Consulting Fees (e.g., advisory boards) (Ongoing)

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5:00 PM - 6:15 PM

P5-02-26

The 27-gene IO score is associated with pathologic complete response (pCR) in HR+/HER2- breast cancer patients treated with pembrolizumab in the I-SPY2 Trial.

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Introduction

Immune checkpoint inhibitor (ICI) therapy is efficacious for many tumor types and has been approved in both early-stage and metastatic triple negative breast cancer. However, no such approval exists for hormone receptor positive (HR+) breast cancer (BC) which typically has a lower TMB, lower PD-L1 expression, and lower numbers of tumor infiltrating lymphocytes, leaving an unmet need for a biomarker to determine ICI response. The 27-gene IO score has previously demonstrated association with response to ICI therapy in NSCLC, mUC, and TNBC but has not yet tested a cohort of HR+/HER2- breast cancer.

Methods

To determine the ability of the IO score to identify responders with HR+/HER- BC clinical and expression data from publicly available RNA expression data from the I-SPY2 trial were retrieved from Gene Expression Omnibus (GEO) under accession number GSE194040. Expression data were normalized, combined, batch corrected, and log-transformed by the submitting institution. This left an expression matrix of 19134 genes and 988 samples for analysis as well as corresponding clinical data. Within this sample set, 40 patients were HR+/HER- and received pembrolizumab and cytotoxic chemotherapy while 64 patients comprised the control arm (chemotherapy only).

Results

In the I-SPY2 trial, within the 40 patients who received pembrolizumab, 12 patients achieved pCR (30%) and 19 patients were IO+ (47.5%). Of the 12 pCR patients, 9 were IO+ (75%) and of the 28 RD patients, 18 were IO- (64%), resulting in an odds ratio of 5.4 (95% CI 1.2-24.7, p< 0.03). Considering the 64 HR+/HER- patients in the paclitaxel arm, 10 achieved pCR (15.6%) and 21 were IO+ (32.8%). Of the 10 pCR patients, 5 were IO+ (50%) and of the 54 RD patients, 38 were IO- (70%), resulting in an odds ratio of 2.4 (95% CI 0.6-9.3, p>0.2).

Conclusions

Despite a generally low inflammatory tumor microenvironment characteristic of the HR+ BC phenotype, the IO+ group was 3x more likely to achieve pCR with the addition of pembrolizumab to chemotherapy. These data extend on previous findings in neoadjuvant treatment of TNBC and advanced colon cancer that IO score is associated with response only in the presence of ICI therapy, not in the presence of chemotherapy alone. This is the first study to demonstrate the association of IO score with pathologic complete response to immune therapy in hormone receptor positive BC.

Arm	N= (pCR)	IO+ (pCR)	IO- (pCR)	IO score Odds Ratio
Paclitaxel (P)	64 (10)	21 (5)	43 (5)	2.4 (0.6-9.3, p>0.2)
P+Pembro	40 (12)	19 (9)	21 (3)	5.4 (1.2-24.7, p<0.03)

Disclosure(s):

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5:00 PM - 6:15 PM

P5-02-27

Serum thymidine kinase activity as a prognostic marker in women with metastatic breast cancer treated with two different schedules of palbociclib plus second-line endocrine therapy within the CCTG MA38 trial

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Background: Thymidine kinase-1 is a cell proliferation marker downstream of the CDK4/6 pathway, whose activity can be measured in serum to reflect tumor proliferation. The CDK4/6 inhibitor palbociclib (P) is approved for the treatment of patients (pts) with hormone receptor positive metastatic breast cancer (MBC) in first or second line endocrine-based treatment settings. Approximately 10-15% of pts exhibit de novo resistance to P, with circulating levels of thymidine kinase activity (TKa) previously shown as a potential marker of early treatment resistance. Therapeutic strategies to address primary resistance to P are currently lacking. Little is known of the clinical efficacy of alternative dosing schedules of P, and its effect on TKa. Here we report serum TKa measured at different timepoints from samples collected within the MA38 (NCT02630693) study. Methods: MA38 is an open label randomised Phase 2 trial comparing two different schedules of P plus second-line ET in pts with ER-positive, HER2-negative MBC. Pts were assigned to receive physician's choice ET plus either standard P dosing (125mg daily for 21 days on a 28-day cycle), or 100mg daily continuously. Serum samples were collected at baseline (BL; n=135), at 12 weeks (W12; n=122) and 24 weeks (W24; n=95). TKa was measured with DiviTum®, a refined ELISA-based assay (lower limit of detection [LLOD] = 100 DuA). Kaplan-Meier method estimated BL, W12 and W24 (95% CI) median PFS (mPFS; from randomization until progression by RECIST criteria or death) and overall survival (OS; from randomization until death from any cause) in groups of patients defined by dichotomizing TKa as "high" or "low" at the median. Results: MA38 enrolled 180 pts from December 2015 and February 2017 across Canada. Median follow up was 19 months. Overall, the median age was 60, and 90% of pts were post-menopausal. All pts had estrogen receptor-positive disease, and 64% had visceral metastases. On study, 56% received fulvestrant with P, 34% aromatase inhibitor and 10% tamoxifen. TKa was successfully measured in 100% of samples. Median TKa (mTKa) at BL was 234 DuA (IQR 138.5 - 438). BL TKa was not associated with clinical or pathological characteristics. TKa was prognostic at BL with mPFS of 5.5 months (mo) in pts with high TKa vs 16.3 mo with low TKa (HR=2.43; 95% CI, 1.6-3.7; p< 0.001). Similar results were obtained employing other previously reported cut off values. At multivariate analysis, BL TKa was independent from other prognostic factors including age, ECOG status and presence of visceral metastases (adjusted HR= 2.34; 95%CI 1.5- 3.6; p < 0.001). In terms of OS, BL TKa was an independent prognostic factor (adjusted HR=2.0; 95% CI, 1.1-3.7; p=0.02). At 12 mo, OS rate was 68% in pts with high BL TKa vs 92% in low TKa. Both for PFS and OS, no interaction between BL TKa and study arm was observed. At W12 mTKa was 129.5 DuA (IQR 100 - 219.8) and below LLOD (IQR 100 - 180) at W24. At these timepoints, landmark analyses showed no significant difference in PFS according to TKa. However, at W12 high TKa was significantly associated with worse OS (HR 2.0; 95%CI 1.0-4.0; p=0.03), with a similar trend at W24 (HR 2.5; 95%CI 0.9-6.4; p=0.06). Conclusions: Baseline TKa is a reliable prognostic marker of both PFS and OS in pts treated with P and ET, further substantiating previous data. Monitoring TKa during treatment may provide important clinical information. A significant relationship between TKa and assigned treatment arm was not observed, suggesting TKa is not influenced by P treatment dose or intensity. These data confirm the role of baseline TKa as a new marker for patient stratification, and supports further

investigation for the assessment of the clinical utility of TKa as a monitoring biomarker in the advanced setting.

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p27Kip1 V109G single-nucleotide polymorphism (SNP): pinpointing the hormone-receptor positive breast cancer subpopulation that requires CDK4/6 inhibitors in addition to endocrine therapy.

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Background: CDK4/6 inhibitors benefit a limited percentage of hormone receptor-positive breast cancer (HRPBC) patients in the adjuvant setting: according to the MonarchE study, from all patients treated with the endocrine plus CDK4/6 inhibitor combination, 84% were adequately treated with endocrine therapy alone, ~5% experienced benefit from the combination, and 11% were not rescued from relapse by abemaciclib. Given the side effects and the cost, biomarkers to guide treatment decisions in this setting are appealing. We found that the p27Kip1 V109G SNP was enriched in HRPBC patients experiencing relapse despite endocrine treatment. p27Kip1 binds to cyclins and CDKs, restraining cells from cycling by inhibiting the formation of CDK/cyclin complexes and their kinase activity, resulting in less phosphorylation of Rb. A functionally impaired p27Kip1 could render tumor cells insensitive to endocrine therapy, while being rescued by CDK4/6 inhibitors. Thus, this SNP could narrow down the patient population that requires adjuvant CDK4/6 inhibitors. Methods: Isogenic HRPBC cell lines, wild-type or polymorphic homozygous for the p27Kip1 V109G SNP were generated with CRISPR-Cas9.

Cell cycle and cell viability were assessed with BRDU incorporation and colony assays. Immunoprecipitation coupled with western blot (WB) was used to measure the formation of CDK/Cyclin complexes; Rb phosphorylation was assessed by WB. An in vitro kinase assay was set up to measure the CDK4 activity of p27Kip1/CDK/Cyclin complexes. Patients (n=115) with metastatic, HRPBC receiving endocrine monotherapy or in combination with CDK4/6 inhibitors were genotyped for the p27Kip1 V109G SNP, and PFS by genotype and therapy compared with the Kaplan-Meier method. All statistical tests were two-sided. Results: three isogenic polymorphic clones were generated from the wild-type T47-D hormone-positive cell line. The three clones were resistant to hormonal deprivation compared to wild-type cells. The relative plating efficiency (RPE) in the colony assays of the polymorphic clones exposed to hormonal deprivation compared to that of deprived T47-D cells was 550% (clone C1), 165% (clone E1) and 100% (Clone F5); $P < 0.005$. The three clones were also resistant to fulvestrant (Fulv) (300%, 170% and 180%, respectively); $P < 0.005$. Cell cycle (positive BRDU cells) decreased ~3 fold in wild type cells (18% to 6.5%) when exposed to hormonal deprivation or Fulv, but remained unaltered in the polymorphic clones. However, when palbociclib was added to hormonal deprivation or Fulv, the effects in RPE increased and were similar in polymorphic clones and parental cells (>5% RPE compared to vehicle, both in polymorphic and wild-type cells). The p27Kip1 V109G SNP was found in homozygosity in ~15% of metastatic HRPBC patients. When patients received endocrine monotherapy in the first-line setting, polymorphic patients experience rapid failure (N=51) compared to wild-type/heterozygous patients (4.3 vs. 21.1 months; $P < 0.0001$). However, when patients received hormonal plus CDK4/6 inhibitors, the differences disappeared (18.3 vs. 24.3 months; $P=0.85$). Mechanistically, we observed that the formation of CDK2/CyclinA, CDK2/CyclinE and CDK4/Cyclin D1 complexes was >200% higher in polymorphic than in wild-type cells ($P < 0.05$). Regarding CDK4 kinase activity of p27Kip1/CDK/Cyclin complexes, as opposed to wild-type p27Kip1, p27Kip1 V109G was unable to suppress the kinase activity of CDK4 in presence of Fulv or hormonal deprivation. However, palbociclib was able to fully suppress CDK4 kinase activity regardless of the p27Kip1 genotype. Conclusion: Germline p27Kip1 genotyping can constitute a tool for treatment selection: whereas wild-type patients are adequately treated with endocrine monotherapy, polymorphic patients are inherently resistant, but are rescued with CDK4/6 inhibitors. Thus, hormonal+CDK4/6 inhibitor combos could be reserved for the polymorphic patients.

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P5-02-29

WITHDRAWN - Novel Metrics of HER2 Heterogeneity in HER2-Positive and HER2-Low Breast Cancer via High Dimensional Multiplexed Immunofluorescence (HDmIF) Spatial Profiling

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Background: Historically, HER2-directed therapy was limited to tumors identified as HER2-positive, however, binary classification of HER2 as “positive” or “negative” may lose the diversity seen in breast cancer pathology. HER2 intratumoral heterogeneity is associated with distinct outcomes to HER2-directed therapy and, further, HER2-low tumors benefit from certain HER2-directed agents, such as antibody-drug conjugates. We hypothesized that interrogating HER2 heterogeneity (HER2het) across multiple spatial resolutions would more accurately capture HER2 diversity and be associated with clinical outcomes. Methods: We optimized a custom 26-marker fluorescently conjugated antibody panel interrogating HER2 immunofluorescence (IF) expression (HER2exp), HER2 signaling, stromal, and immune markers via NeoGenomics MultiOmyx HDmIF, which leverages serial IF image capture to allow concurrent profiling of all 26 markers on a pathologic section at single cell resolution. We applied 26-marker HDmIF to a tissue microarray of 208 unique patients with matched tumor/normal tissue cores (1-4 cores/patient; total 333 tumor and 307 normal cores). HER2-positive was defined via ASCO/CAP guidelines on clinical sample; HER2-low was defined as HER2 immunohistochemistry (IHC) 1+/2+ but HER2 in-situ hybridization (ISH) negative. In addition to patient-level difference in HER2exp between paired tumor cores, we developed novel computational image analysis-based metrics of HER2het at distinct spatial resolutions: 1) core-level: distribution of HER2exp across each core via Shannon’s Entropy, 2) cellular neighborhood-level: weighted sum of differences in HER2exp of a tumor cell relative to adjacent neighbor cells; 3) single cell-level: proportion of single cells with variation in HER2exp along cell membrane of each individual tumor cell. We evaluated the association of these novel HER2het metrics with patient clinicopathologic features, recurrence-free survival (RFS), overall survival (OS), and diverse antibody markers representing tumor cell intrinsic processes and tumor-immune microenvironment (TME). Results: The 208 unique tumors profiled included 88.9% (185/208) HER2-positive and 11.1% (23/208) HER2-low; 62.5% (130/208) hormone receptor (HR) positive and 37.5% (78/208) HR negative. Median follow-up from diagnosis was 143 months. Among HER2-positive patients, 98.9% (n=183/185) received HER2-directed therapy in the (neo)adjuvant or metastatic setting or were diagnosed prior to FDA approval of trastuzumab for early stage disease. In sum, from 1166 regions of interest in 640 total cores, a total of 1,076,700 single cells were profiled via 26-marker HDmIF. Across all tumor samples,

the HER2het metrics showed only modest inter-metric correlation (Pearson r^2 range 0.04–0.41), suggesting that each metric captures distinct HER2het features. HER2low tumors demonstrated less heterogeneity across metrics than HER2pos tumors yet individual HER2low tumors did demonstrate high HER2het. Among HER2-positive tumors, the single-cell HER2het metric was significantly associated with improved RFS (HR 0.93, 95% CI 0.87–0.99, $p=0.046$) with a non-significant trend for improved OS (HR 0.94, 95% CI 0.88–1.0; $p=0.13$), while remaining HER2het metrics (patient-level, core-level, cellular neighborhood-level) were not significantly associated with RFS or OS. HER2exp and HER2het metrics demonstrated distinct patterns of association with cell-type and spatial TME components. Conclusions: We present novel metrics of HER2 heterogeneity via HDmIF, which offer detailed characterization of the diversity of HER2exp in a large, clinically-annotated cohort with long-term follow-up. Heterogeneity of single cell HER2 membrane expression was associated with RFS and distinct spatial distribution of tumor and immune cell types. Ongoing future efforts include translation of IF-based HER2het metrics to standard HER2 IHC/ISH.

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P5-02-30

Histology-based survival outcomes in HR+/HER2- metastatic breast cancer treated with targeted therapies plus endocrine therapy based on HER2 expression

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Background: About 55% of hormone receptor (HR)-positive metastatic breast cancer (mBC) show a low-level expression of human epidermal growth factor receptor 2 (HER2-low). HER2-low is defined as HER2 immunohistochemistry (IHC) expression of 1+ or 2+ with a negative HER2 amplification by in situ hybridization. The efficacy of the antibody-drug conjugate trastuzumab deruxtecan in HER2-low HR+ mBC has been practice changing. However, there are conflicting data on the prognostic value of low HER2-expression in HR+ mBC with some reports showing no impact on prognosis and other showing inferior outcomes in HER2-low patients when treated with cyclin-dependent kinase 4 and 6 inhibitors (CDK4/6is) in combination with endocrine therapy (ET).

Methods: We retrospectively searched for patients treated at MD Anderson Cancer Center with a diagnosis of HR+ treated with ET in combination with a targeted therapy (CDK4/6is, everolimus or alpelisib). Patients were divided into 3 groups: All histologies, ductal histology (IDC) and lobular histology (ILC). We obtained data on demographics, estrogen (ER) and progesterone (PR) receptor status, HER2 expression, menopausal status, treatment duration and survival status. The Kaplan-Meier product-limit method was used to compare progression-free survival (PFS) and overall survival (OS) between the three different groups stratified by HER2 expression (HER2 low versus HER2 0).

Results: We identified 1,649 patients (64% HER2-low, 36% HER2 0) with HR+/HER2- treated with targeted therapy (CDK4/6is, everolimus or alpelisib) in combination with ET. The median age was around 50 years in all groups, 75% were White, 55% premenopausal, 95% ER-

positive and 83% PR-positive. 68% were treated with CDK4/6is (919 patients treated in first line (1L) and 202 treated in second line), , 30% everolimus and 2% with alpelisib. In the patients who received first 1L CDK4/6is, 70% received an aromatase inhibitor as their ET backbone and 30% received fulvestrant. All the patients who received 1L fulvestrant recurred while on adjuvant AI. PFS and OS were not statistically different between the HER2-low and HER2 0 groups treated with targeted therapies (TT) plus ET or 1L CDK4/6is plus ET regardless of the histology (Table 1).

Conclusion: In this single institution analysis, HER2-low status did not have a significant impact on prognosis in HR+/HER2- mBC treated with TT plus ET or 1L CDK4/6is plus ET.

Table 1. Progression-free Survival and Overall Survival in HR+/HER2- mBC patients treated with targeted therapies (TT) plus endocrine therapy (ET)

	(A) TT + ET in all histologies N = 1,649		(D) 1L CDK4/6is + ET in all histologies N = 919	
	HER2 0 N = 595 (36%)	HER2-low N = 1,054 (64%)	HER2 0 N = 340 (36%)	HER2-low N = 579 (64%)
PFS (mo)	9.1	9.1	11.6	13.0
	$P = 0.434$		$P = 0.273$	
OS (mo)	26.4	28.1	31.2	32.4
	$P = 0.415$		$P = 0.222$	
	(B) TT + ET in IDC N = 1,327		(E) 1L CDK4/6is + ET in IDC N = 731	
	HER2 0 N = 466 (35%)	HER2-low N = 861 (65%)	HER2 0 N = 261 (36%)	HER2-low N = 470 (64%)
PFS (mo)	8.5	9.5	10.1	12.9
	$P = 0.097$		$P = 0.124$	
OS (mo)	26.4	28.8	31.1	34.2
	$P = 0.382$		$P = 0.130$	
	(C) TT + ET in ILC N = 241		(F) 1L CDK4/6is + ET in ILC N = 152	
	HER2 0 N = 95 (39%)	HER2-low N = 146 (61%)	HER2 0 N = 65 (43%)	HER2-low N = 87 (57%)
PFS (mo)	12.6	9.5	16.6	12.1
	$P = 0.266$		$P = 0.648$	
OS (mo)	34.3	27.9	34.7	28.8
	$P = 0.792$		$P = 0.837$	

In patients treated with TT + ET in all histologies (A), in IDC (B) and in ILC (C). In patients treated in 1L with CDK4/6is + ET in all histologies (D), in IDC (E) and in ILC (F)

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Genetic determinants of response to patritumab deruxtecan (HER3-DXd) in hormone receptor-positive/HER2-negative (HR+/HER2-) breast cancer: a correlative analysis from SOLTI TOT-HER3 trial

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Background: Baseline HER3 protein or ERBB3 mRNA levels do not seem to predict efficacy from HER3-DXd in early-stage and advanced HR+/HER2- breast cancer (Prat et al. ESMO Breast 2022; Krop et al. ASCO 2022). Here, we evaluated potential baseline pre-treatment genetic determinants of efficacy to HER3-DXd. Methods: SOLTI TOT-HER3 (NCT04610528) is a window of opportunity, multicenter, pre-operative trial which enrolled, in part A, 77 evaluable patients with untreated HR+/HER2- operable (≥ 1 cm) breast cancer. Patients received a single dose of HER3-DXd (6.4 mg/kg). The primary objective was to evaluate the CelTIL score variation between pre- and post-treatment (day 21) samples. CelTIL combines % of tumor cellularity and % of tumor-infiltrating lymphocytes into a single score. DNA and RNA were purified from pre-treatment baseline FFPE tumor samples. Gene expression was evaluated using a custom 67-gene panel on the nCounter. NGS-based DNA-seq was performed using the VHIO-300 panel, which estimates tumor mutational burden (TMB), identifies copy-number aberrations (CNAs) across the entire genome and calls mutational status of >300 genes. From CNA data, 150 previously defined DNA-based signatures (Xia et al. Nat Comm 2019) trained to capture RNA- and protein-based phenotypes such as the PAM50-related biology were evaluated. Associations of each variable with efficacy (i.e., CelTIL relative changes, and tumor cellularity relative changes) were adjusted for multiple-testing (false discovery rate [FDR] < 5%). The area under the ROC Curve (AUC) was used to estimate the discrimination performance of each variable. Results: RNA and DNA data were obtained from 45 (58%) patients. Baseline characteristics in this subset of patients were generally similar to the original TOT-HER3 population. Among 228 variables (single mutation status, single gene expression, PAM50 signatures, TMB, and DNA CNA-based signatures), 139 (61%) were found significantly associated (FDR < 5%) with CelTIL changes at day 21. Among them, TP53 mutations (n=7) were found associated with higher CelTIL response compared to TP53 wild type (71% [95% CI=-5.4-17.8] vs. 24% [95% CI=15.9-55.4], FDR=2.1%). In addition, RNA-based genes tracking Basal-related biology (e.g., CCNE1, AUC=0.71) or immune expression (e.g., PDCD1, AUC=0.73, or CD68, AUC=0.62), together with RNA/DNA-based signatures tracking proliferation and/or basal-related biology (e.g., retinoblastoma loss-of-heterozygosity [RB-LOH], AUC=0.76), were associated with high CelTIL response. Conversely, RNA/DNA-based signatures tracking endocrine sensitivity/Luminal A-related biology (e.g., Scorr_IE_Correlation, AUC=0.76) were associated with low/lack of CelTIL response. PIK3CA somatic mutations (n=14, 31% of cases), and TMB (range 2.2-12.7) were not found associated with CelTIL

response. Similar overall results were obtained when relative changes in tumor cellularity (instead of CelTIL) was evaluated as the efficacy endpoint. Conclusions: TP53 mutations, immune-related genes, and DNA/RNA-based phenotypic signatures tracking Basal- or Luminal A-related biology such as the DNA-based RB-LOH score or the endocrine sensitivity score (Scorr_IE_Correlation) are associated with CelTIL changes in response to HER3-DXd in HR+/HER2- breast cancer. Further RNA- and DNA-based analyses will be evaluated.

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Differential Gene Mutation Landscape in Patients With PIK3CA-altered and Non-altered Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor 2-negative Advanced Breast Cancer in the SOLAR-1 Clinical Study

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Introduction: The phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha (PIK3CA) is found mutated (mut) in ~40% of patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (ABC); some of these alterations can lead to PI3K pathway hyperactivation and are associated with endocrine resistance and poor prognosis in advanced disease. Alpelisib (ALP), an α -selective PI3K inhibitor and degrader, demonstrated clinical benefit in combination with fulvestrant (FUL) in the SOLAR-1 study in pts with PIK3CA-mut HR+, HER2- ABC. SOLAR-1 (NCT02437318) was a double-blind, placebo (PBO)-controlled, stratified, randomized (per PIK3CA-alt status as determined by QIAGEN PIK3CA RGQ PCR test), Phase III study of ALP in combination with FUL in pts with HR+, HER2- ABC who progressed on/after aromatase inhibitor therapy. Here, we compare the gene alteration landscape in pts with altered (alt) and non-alt PIK3CA and the efficacy of ALP + FUL in pts whose tumors have alterations in both selected genes or cell signaling pathways as well as PIK3CA-alt or non-alt status as determined by next-generation sequencing (NGS).

Methods: In this analysis, retrospective NGS analysis using the FoundationOne CDx 324-gene panel was performed on available FFPE tissue samples. In all, 398 pts were categorized into 2 cohorts based on NGS-tested PIK3CA status. The PIK3CA-alt cohort comprised 237 patients (ALP, n=120; PBO, n=117); the PIK3CA-non-alt cohort 161 patients (ALP, n=81; PBO, n=80). Selected genes altered in >20 SOLAR-1 pts were investigated further. Clinical benefit was assessed by progression-free survival (PFS) based on gene alt status in the PIK3CA-alt and -non-alt cohorts. Hazard ratios (HR) for PFS were estimated using a multivariate Cox PH model by adjusting multiple clinical covariates including age, ECOG performance status, bone lesion, prior CDK4/6 inhibitor treatment, and lung/liver metastasis.

Results: PIK3CA-alt and -non-alt cohorts had differential genomic landscapes; differential PFS benefit was observed among the genes analyzed, including ARID1A, EMSY, FGFR2, MAP3K1, MYC, RAD21, RAD51C, TP53, and a gene set associated with the MAPK pathway. In most pts with analyzed gene alterations, numerically longer PFS was observed with ALP vs PBO in the

PIK3CA-alt cohort than the -non-alt cohort, particularly pts with alterations in ARID1A (median [m] PFS for ALP vs PBO in PIK3CA-alt cohort: 22.11 vs 12.42 mo, HR 0.48; vs mPFS in PIK3CA-non-alt cohort: 6.21 vs 22.31 mo, HR 1.33) and MAP3K1 (PIK3CA-alt cohort: 17.25 vs 7.70 mo, HR 0.50; vs PIK3CA-non-alt cohort: 9.17 vs 5.26 mo, HR 1.32). Full results are found in the Table. Results should be interpreted with caution, as analyses used small sample sizes and were not adjusted for multiple testing.

Conclusions: A differential genomic landscape was observed in PIK3CA-alt and PIK3CA-non-alt populations. Clinical benefit of ALP vs PBO was observed in pts with PIK3CA-alt disease who also had alterations in analyzed genes and/or genes associated with the MAPK pathway. The data from this analysis suggest that, of the genes analyzed, only PIK3CA mutations can predict pt sensitivity to ALP.

Table. PFS in PIK3CA-altered and PIK3CA-non-altered populations by gene alteration

	PIK3CA-alt			PIK3CA-non-alt		
	ALP + FUL mPFS, mo (n)	PBO + FUL mPFS, mo (n)	HR (95% CI)	ALP + FUL mPFS, mo (n)	PBO + FUL mPFS, mo (n)	HR (95% CI)
MAP3K1-alt	17.25 (13)	7.70 (13)	0.50 (0.2-1.22)	9.17 (3)	5.26 (4)	1.32 (0.28-6.13)
MAP3K1-non-alt	10.91 (107)	5.52 (104)	0.56 (0.41-0.77)	7.46 (78)	9.10 (76)	0.88 (0.62-1.25)
ARID1A-alt	22.11 (11)	12.42 (15)	0.48 (0.16-1.41)	6.21 (9)	22.31 (7)	1.33 (0.46-3.79)
ARID1A-non-alt	10.91 (109)	5.52 (102)	0.55 (0.4-0.74)	8.77 (72)	7.36 (73)	0.85 (0.6-1.22)
FGFR2-alt	9.63 (9)	2.78 (9)	0.31 (0.1-0.94)	3.63 (2)	6.47 (1)	1.65 (0.14-19.24)
FGFR2-non-alt	11.01 (111)	5.65 (108)	0.58 (0.43-0.78)	8.77 (79)	9.00 (79)	0.88 (0.63-1.23)
TP53-alt	8.48 (26)	3.68 (36)	0.48 (0.27-0.84)	3.71 (20)	3.75 (17)	0.66 (0.34-1.32)
TP53-non-alt	11.99 (94)	7.29 (81)	0.60 (0.43-0.85)	9.00 (61)	10.84 (63)	0.94 (0.64-1.39)
RAD51C-alt	12.94 (4)	5.52 (10)	0.37 (0.08-1.75)	6.21 (10)	5.40 (8)	0.90 (0.34-2.34)
RAD51C-non-alt	10.97 (116)	5.55 (107)	0.56 (0.42-0.76)	8.77 (71)	9.10 (72)	0.89 (0.62-1.27)
EMSY-alt	7.26 (15)	2.46 (15)	0.50 (0.22-1.18)	4.52 (8)	5.04 (9)	0.70 (0.25-2.01)
EMSY-non-alt	11.01 (105)	5.68 (102)	0.56 (0.41-0.77)	9.00 (73)	9.23 (71)	0.91 (0.64-1.30)
MAPK pathway-alt*	10.91 (23)	3.61 (30)	0.46 (0.25-0.85)	4.44 (19)	5.55 (17)	1.97 (0.95-4.07)
MAPK pathway-non-alt*	11.63 (97)	7.23 (87)	0.59 (0.42-0.82)	9.26 (62)	9.00 (63)	0.77 (0.52-1.13)
MYC-alt	5.8 (13)	6.37 (15)	1.00 (0.45-2.25)	12.81 (15)	3.75 (12)	0.7 (0.31-1.58)
MYC-non-alt	11.63 (107)	5.55 (102)	0.52 (0.38-0.71)	7.46 (66)	9.23 (68)	0.91 (0.63-1.32)
RAD21-alt	6.11 (20)	7.23 (23)	1.03 (0.54-1.96)	12.81 (23)	10.05 (16)	0.89 (0.45-1.77)
RAD21-non-alt	11.63 (100)	5.09 (94)	0.49 (0.35-0.68)	7.39 (58)	9.00 (64)	0.88 (0.59-1.30)

*Includes ERBB2, NF1, ERBB3, KRAS, EGFR, BRAF, and MAP2K1.

Results should be interpreted with caution, as sample sizes are small, and results have not been adjusted for multiple testing.

ALP, alpelisib; alt, altered; FUL, fulvestrant; HR hazard ratio; mPFS, median progression-free survival; PBO, placebo; PFS, progression-free survival; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha.

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5:00 PM - 6:15 PM

P5-02-33

Deep learning-based assessment of HER2-low expression on breast cancer H&E digital whole slide images

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Background: Antibody drug conjugates (ADCs) against HER2 have shown meaningful clinical activity in HER2 low breast cancers, defined as 1+ or 2+ staining on immunohistochemistry (IHC) without gene amplification by in situ hybridization (ISH) techniques,. Given that these methods were originally developed for an accurate detection of HER2 3+, their sensitivity and robustness for the detection of low and ultra-low levels of HER2 are questionable. We have recently described a deep learning algorithm that can detect signatures of HER2 expression based on training utilizing scanned H&E whole slide images (WSI) of breast cancers for which IHC and mRNA expression levels of HER2 were available. Here, we report the application of our algorithm to two independent breast cancer cohorts. Methods: A model was developed based on recognition of invasive breast cancer in whole slide images of H&E staining, and then trained via computational neural network with multiple instance learning for binary classification of cases as HER2 “negative” and HER2 “expressed” (low). For training, true negatives were defined as having HER2 IHC-0 and mRNA level < 7.6. HER2-low cases were defined as IHC-1+/2+ and mRNA >9. IHC-0 cases with mRNA >7.6 were excluded from the training cohorts. The resulting model (HER2Complete) was able to distinguish HER2-negatives from HER2-low cases with an AUC of 0.91 (+/- 0.08). Here we use Her2Complete to assess HER2 in two additional cohorts that include 901 ER+/HER2 IHC-0 and 52 HER2 IHC 0+ breast cancers from MSK and TCGA cohorts, respectively. For the TCGA cohort, concomitant transcriptomics data (RNASeq) as a reference for HER2 mRNA expression were retrieved and “HER2 expressed” defined as RNASeq expression of HER2 greater than the 90th percentile of the geometric mean of expression of three reference genes not expressed in breast tissues (TTN, MUC13, OR10A6). Values less than this reference cut-off in the TCGA cohort were considered “HER2 not expressed.” Results: Among the 901 IHC-0 test cases from the MSK cohort, the model

identified 82 as 'negative', whereas 819 were found to have features of HER2 expression (HER2-Low). Of the 82 negative cases in the MSK cohort, all except 13 cases expressed mRNA levels < 9, and 786/819 of the HER2-low cases expressed mRNA levels >8. Of the 52 IHC 0+ cases in the TCGA cohort, 33 also had "HER2 not expressed" by our reference based RNASeq expression cut-off. Our model identified 15 of these 33 as 'negative', while 15 of the 19 TCGA cases with IHC 0+ and HER2 'expressed' by our cut-off were identified as 'HER2-Low' by our model. Conclusions: AI tools based on the analysis of WSIs of routinely prepared H&E sections may predict HER2 status in breast cancer . This work requires further investigation using treatment response data to demonstrate that cases with morphologic features of low level HER2 expression will respond to ADCs.

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Single-cell Analysis of KN026 in Combination with KN046 in Treating Patients with Advanced HER2-positive Breast Cancer

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Background: KN026 is a novel bispecific antibody that simultaneously binds to two distinct HER2 epitopes (two different HER2 epitopes shared by trastuzumab and pertuzumab). KN046 is a novel bispecific antibody that blocks both PD-L1 interaction with PD-1/CD80 and CTLA-4 interaction with CD80/CD86. Our on-going multi-centered phase II trial (NCT04521179) demonstrated that in advanced HER2-positive breast cancer (HER2+ BC) patients, who have progressed after prior anti-HER2 combinational therapies, the objective response rate (ORR) of this chemo-free therapy of KN026 in combination of KN046 was about 50.0% (SABCS 2021 poster P5-16-04). To explore the underlying mechanism of this regimen, we collected tumor specimens from patients before and after receiving this combinational treatment for single-cell analysis to provide an in-depth description of the tumor immune microenvironment and its correlation with treatment response. Methods: Paired tumor specimens before and after treatment of patients enrolled in the trial were collected for single-cell transcriptome and TCR sequencing. In addition, to reveal the immune cell characteristics of anti-HER2 resistant patients, we compared our data with previously reported single-cell analysis of treatment-naïve HER2+ BC. Results: We obtained 30 specimens from 17 patients, including 17 of pre-treatment and 13 of post-treatment. TCR expansion did not correlate with clinical efficacy. In-depth analysis of subpopulations revealed that compared to treatment-naïve HER2+ BC, these enrolled prior anti-HER2-resistant patients had an additional population of T cells subpopulation characterized by CD4-low and CD8-low in their baseline tumor tissues, and the proportion of this subpopulation was significantly decreased after KN046 plus KN026 treatment in

responding patients. Moreover, we found that patients with baseline CD8+ T/naïve T >1 tended to benefit more from this regimen. Conclusion: We identified a subpopulation of CD4-low and CD8-low T cells that may be associated with anti-HER2 resistance. And decreased of this subpopulation of T cells was associated with better ORR of KN046 in combination with KN026 treatment in heavily pretreated advanced HER2+ BC. Baseline CD8+ T/naïve T ratio in tumor is expected to be a predictor of ORR as well.

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Radiomic biomarkers to predict the efficacy of anti-PD-1 immunotherapy-based combinational treatment in advanced breast cancer: a multi-center study

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Introduction: Immunotherapy, especially immune checkpoint inhibitors, is regarded as one of the major breakthroughs in breast cancer treatment. However, it is an important challenge to accurately locate the patients who benefit from immunotherapy, because there is still a lack of universal and robust predictors of the efficacy of immunotherapy. Radiomics can extract quantitative imaging features in a highthroughput manner and assess tumor microenvironment and heterogeneity. This study investigated the correlation between deep learning radiomic

biomarkers, including its predictive value for immunotherapy response in advanced breast cancer (ABC) patients. Methods: 240 patients with metastatic breast cancer treated with anti-PD-1 immunotherapy in three institutions from February 2018 to January 2022 were studied retrospectively, among which, the data of 61 patients were collected through prospective clinical trials. For these data, 189 ABC patients from prospective clinical trials and Sun Yat-sen University Cancer Center were evaluated as a training set to establish a radiomic model to predict value of immunotherapy, then this model was independently validated with 51 ABC patients from Sun Yat-sen Memorial Hospital. The CE-CT (contrast enhanced computed tomography) images of patients within one month before immunotherapy were delineated with regions of interest (ROI) and radiomics features extraction. Data dimension reduction, feature selection and radiomic model construction were carried out with multilayer perceptron (MLP) deep learning. Combined with the radiomics signatures, independent clinical characteristics and pathological risk factors, the predictive model was established by multivariable logistic regression analysis. ROC curve (receiver operator area under receiver operator area, AUC) and Delong test were used to evaluate and compare the prediction performance of the model. Finally, decision curve analysis (DCA) is used to determine the net benefits predicted by the model. Results: The radiomic biomarker performed well in predicting response to immunotherapy, reflected by the AUCs in the training set (AUC=0.885, 95% CI: 0.829-0.941) and validation set (AUC=0.871, 95% CI: 0.752-0.991), respectively. The accuracy of this radiomics model was better than those of clinical indicators, including PD-L1 expression. Conclusions: By combining deep learning technology and CT images and PD-L1 expression, we developed an independent predictive model that could identify MBC patients most likely to benefit from immunotherapy, and may effectively improve more precise and individualized decision support.

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Proteogenomic profiling of fresh frozen core biopsies from CALGB 40601

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Background: Targeted therapy for HER2+ breast cancer has significantly improved outcomes for this aggressive subtype. However, a subset of patients do not achieve pathological complete response (pCR). In CALGB 40601, a randomized Phase III Trial for neoadjuvant treatment of HER2+ primary breast cancer with Paclitaxel (T: taxane) combined with HER2 antibody therapy (H: Herceptin/Trastuzumab), the small molecule inhibitor Lapatinib (L), or the antibody-inhibitor combination, pCR frequency was 56% for the combination (THL arm), 46% for Trastuzumab (TH arm), and 32% for Lapatinib (TL arm, closed early because of lower efficacy) (PMID: 26527775). While a recent publication reports relapse-free survival (RFS), overall survival (OS), and RNA-based gene expression signatures that can predict pCR (PMID: 33095682), understanding the proteogenomic landscape of treatment response should facilitate identification of alternative and therapeutically tractable protein targets for treatment-resistant tumors. Methods: Microscaled proteogenomic profiling (PMID: 31988290) was performed on treatment-naïve, flash-frozen core needle biopsies from the CALGB 40601 trial obtained from the Alliance for Clinical Trials in Oncology tissue bank. Multi-omics profiling included whole-exome sequencing (WES), RNA-sequencing, and mass spectroscopy-based proteomics and phosphoproteomics from one or two cores from each patient. Results: Eighty baseline core biopsies from 54 patients, including 22 patients from the THL arm, 24 from the TH arm, and 8 from the TL arm, from the CALGB 40601 tissue archive were of sufficient quality to yield genomics, transcriptomics, and/or proteomics profiling data. The frequency of pCR for profiled samples was representative of the overall trial cohort. Linear models were employed to identify baseline determinants of pCR for each arm and to assess differences in genes associated with response between the TH and THL arms. Pathways associated with RNA processing, translation, and the proteasome were elevated in pCR tumors in TH and THL arms, while cell cycle, DNA replication and repair pathways were higher in pCR only in the THL arm. While

enrichment of similar pathways was observed in pCR in the transcriptome, the proteome specifically showed enrichment of pathways associated with extracellular matrix and EMT in non-pCR in the THL but not the TH arm. In particular, “EMT”, “ECM-receptor interaction”, and “extracellular structure organization” constituted the most enriched pathways and GO terms that were higher in non-pCR than in pCR tumors from the combination arm (THL) in the proteomics data despite showing no enrichment in the transcriptomics data. Driving this pathway enrichment were several collagens and matrix metalloproteinases that were significantly elevated in non-pCR tumors at the protein but not the RNA level. Finally, kinase target enrichment of differential phosphorylation sites suggested that the activity of PAK1, a regulator of cytoskeletal remodeling, is elevated in non-pCR tumors from the THL arm ($p=0.006$), but not the TH arm ($p=0.69$). Conclusion: Proteogenomic analysis of archival HER2+ breast cancer core biopsies provides opportunities for identifying proteins and phosphorylation sites in treatment-naïve tumors that are associated with pCR to neoadjuvant Paclitaxel/anti-HER2 therapy. Notably, proteomic but not transcriptomic data showed that ECM and EMT pathways were elevated in non-pCR tumors; thus, signatures encompassing these pathways may serve as biomarkers for aggressive HER2+ breast cancer that is more likely to evade treatment. Non-pCR tumors in the THL arm were also marked by elevated levels of PAK1 target phosphorylation sites, suggesting that this kinase may be a potential therapeutic target in HER2+ breast cancer that is refractory to combination anti-HER2 therapy.

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Multi-omics approach to identify markers of resistance to endocrine therapy + CDK4/6 inhibitors in first line HR+/HER2- metastatic breast cancer (MBC) patients.

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CONTEXT: Endocrine therapy combined with CDK4/6 inhibitor is the standard frontline treatment for the vast majority of HR+/HER2- MBC patients. Despite an overall survival benefit, patients eventually progress and mechanisms of resistance to this combination are not well identified. METHODS: EPICURE is an ongoing pilot prospective cohort study of heterogeneous and massive data integration, ie. multi-omics approach in MBC patients. The present study aims at identifying progression markers in patients with HR+/HER2- MBC receiving frontline endocrine therapy+CDK4/6 by means of transcriptomics, genomics and proteomics data. All patients had a tumor biopsy at the entry in the study (B1) and a biopsy was repeated at progression if feasible (B2). Transcriptomic (RNAseq: NextSeq550, Illumina), genomic (whole exome sequencing: NextSeq550, Illumina) and proteomic (DIA mass spectrometry: TimsTOFPro2, Bruker) were performed on B1 and B2 according to available tumor tissue. RESULTS: Fifty-one patients matching inclusion criteria were included. B1 was done at inclusion for all patients (B1) (n = 51) and B2 was performed in 8 patients. (B2) (n = 8). Eight metastatic sites were biopsied: node (n = 17); liver (n = 16); bone (n = 8); breast local recurrence (n = 5); chest wall (n = 5); skin (n = 4); pleural (n = 3); ovary (n = 1). Transcriptomic, genomic and proteomic analysis of paired biopsies (B1 and B2) was performed in parallel and separately for 8, 7 and 2 patients, respectively. Exploratory data analysis of transcriptomic and proteomic data showed that liver biopsies clustered together. In order to eliminate this anatomic bias, specific genes and proteins of liver metastases were identified by means of DESeq2 analysis (12 liver vs 39 other sites) for transcriptomic data (n = 2654) and LIMMA (4 liver vs 14 other sites) for proteomic data (n = 227), and excluded for the rest of the analysis. Differential analyses (ie. gene expression, non-synonymous mutations and protein expression) between B1 and B2 were performed for each patient. These three kind of lists were finally submitted to ToppGene, DAVID and GOrilla for Gene Ontology terms enrichment analyses. Transcriptomic analyses of the 8 paired biopsies highlighted immune response (IR) in seven B1, IR in four B2 and neurogenesis in three B2. Genomics data evaluation between B1 and B2 pointed out "transposon integration" as an important pathway. Proteomic data of the 2 paired biopsies analysed underlined high immune response in B1, and muscle development/contraction and response to tumor necrosis factor in B2 for one patient. For the second one, liver metabolism in B1 and extracellular matrix and p38 MAPK cascade were emphasised. CONCLUSION: This preliminary study based on transcriptomic, genomic and proteomic data represents an encouraging first step of the EPICURE project. In a near future, additional paired biopsies and other kinds of omics data (epigenetics, radiomics, microbiomics, exposomics) will be available. Furthermore, omics data will be analysed in an integrated manner (ie. artificial intelligence), which will make it possible to detect synergies across the different omics data.

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Leptin receptor (Ob-R)/leptin axis significantly modulates tumour-infiltrating lymphocytes (TILs) and PD-1 expression in early HER2+ breast cancer (BC) emerging as a new surrogate marker for immunotherapy.

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Leptin receptor (Ob-R)/leptin axis significantly modulates tumour-infiltrating lymphocytes (TILs) and PD-1 expression in early HER2+ breast cancer (BC) emerging as a new surrogate marker for immunotherapy. Background: There is strong pre-clinical evidence that obesity produces T-cell dysfunction and high PD-1 expression resulting in a paradoxical benefit from immunotherapy. This effect is driven, at least in part, by leptin that exerts its action through binding Ob-R, which is known to be highly expressed in HER2+ BC. TILs correlate with pathological response and long-term outcomes in BC; however the precise mechanism by which these T-cells are activated in and around tumour remains partially unknown. The primary aim of this study was to investigate the role of Ob-R/leptin axis in modulating TILs and PD-1 expression and its effect in pathological response in early HER2+ BC patients who have received neoadjuvant systemic treatment (NST). Methods: Women with HER2+ BC receiving anti-HER2-based NST followed by surgical resection were evaluated. Patient's height and weight were measured before NST to calculate the body mass index (BMI). Based on the IHC results in diagnostic biopsy, tumors were categorized as HER2+/HR+ and HER2+/HR-. Ob-R expression was routinely measured in the diagnostic biopsy using the BOND RX Research Platform (Leica Biosystems). The Ob-R was classified as over-expressed if there were more than 50% positive cells with weak or strong staining. TILs and PD-1 expression were scored centrally in pre-treatment biopsy. TILs were considered as binary, < 30.0% versus ≥30.0% and PD-1 positive (>1%). Associations with pathological complete response (pCR; ypT0/isN0) were assessed using chi-squared or Wilcoxon test. Results: Of the 74 HER2+ BC patients included in the study, 47 (63.5%) had over-expression of Ob-R, 26 (35.1%) were overweight/obese (BMI ≥25kg/m²), and 42 (56.8%) had pCR status. Ob-R expression was similar regardless of menopausal status, age or HR expression. Patients with Ob-R overexpressed were 21 (80.8%) of 26 with BMI ≥25kg/m² versus 26 (54.2%) of 48 with BMI < 25Kg/m² (p=0.023). Tumors with Ob-R overexpressed had significantly higher mean levels of TILs than those with non-overexpressed Ob-R (21.4% [IQR, 7.5-30] vs 12.4% [IQR, 5-10]; p=0.009). Despite higher rates of TILs, the rate of pCR in Ob-R overexpressed tumours (57.4% [27 of 47 patients]) was not higher than in non-overexpressed tumours (55.6% [15 of 27 patients]; p=0.874). This could be due to the fact that Ob-R-overexpressed tumours had a significant higher median PD-1 expression than Ob-R-negative tumours (2% [IQR, 0.5-7.5] vs 0% [IQR, 0-1]; p< 0.001). Finally, no differences were found in terms of Ob-R expression and pathological response by hormone receptor expression. Conclusions: This multidisciplinary clinical study decodes for the first time how obesity, through the OB-R/leptin axis, might activate TILs but apparently dysfunctional as it is not translated into higher pCR; probably due to the presence of exhausted features such as high PD-1 expression. The role of Ob-R together with PD-1 as a potential biomarker for immunotherapy should be further explored.

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P5-02-39

Efficacy of fulvestrant-based therapies in treating HR-positive, HER2-negative breast cancer with liver metastasis

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Background: Hormone receptor-positive (HR+) metastatic breast cancer (MBC) contributes to nearly 70% of breast cancer-related deaths. The liver is the third most common site for metastasis in breast cancer, and liver involvement has been found to have a poor prognosis. One contributing factor is resistance to hormonal treatments. Furthermore, estrogen receptor alpha gene (ESR1) activating mutations, which are enriched in metastatic tumors of the viscera such as the liver, have been linked specifically to resistance against hormone-blocking therapies. We seek to characterize the efficacy of specific treatment modalities, including hormone therapy, immunomodulators, radiotherapy, chemotherapy, and the role of ESR1 mutations in poor treatment response of MBC with liver metastasis. Methods: We conducted a retrospective matched cohort study of 3388 adults with HR+/HER2- MBC with liver and non-liver involvement, who were treated at MD Anderson Cancer Center from 1997-2021. Patients with liver and non-liver metastasis were matched by age at breast cancer diagnosis, race, BMI, and stage. All patients underwent fulvestrant monotherapy or fulvestrant-based combination therapy with CDK4/6 inhibitors, mTOR kinase inhibitors (everolimus), or PI3K inhibitors (alpelisib). We compared the overall and metastatic survival of patients with liver vs. non-liver metastasis on different treatment regimens. We also evaluated the impact of chemotherapy administered for metastasis. Results: Patients with liver metastasis experienced shorter overall and metastatic survival across all treatment regimens (HR, 1.44; 95% CI 1.34-1.57; P<.001). The addition of targeted therapies to fulvestrant offered a survival benefit over fulvestrant alone in patients with non-liver metastasis. However, this benefit did not extend to the liver metastasis

group. Independent of chemotherapy, liver metastasis was found to be a negative prognostic factor. Patients with first metastasis to the liver did not significantly differ in survival when compared to those who developed liver metastasis at a later stage. ESR1 mutations were identified in only a minority of the cohort (4%), but a higher prevalence of liver metastasis was found in patients with ESR1 mutations (49%) vs. the wild type group (45%). Independent of ESR1 status, patients with liver metastasis were found to have worse survival. Conclusion: We found liver metastasis to be a negative prognostic factor in patients with MBC independent of ESR1 status. While novel fulvestrant-based combination therapies have been promising for MBC, similar survival benefits are not seen in those with liver metastasis. Liver metastasis proves to be aggressive and difficult to treat, and current therapies are insufficient.

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Anthracycline improves the outcome of neoadjuvant trastuzumab-treated breast cancer patients with FcγRIIIA F/F genotype by decreasing the ratios of CD8+PD1+ and CD68+PDL1+ cells

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Background:

Antibody-dependent cell-mediated cytotoxicity (ADCC) is one of the most important mechanisms of trastuzumab. Fragment C Gamma receptor (FcγR) IIA and IIIA polymorphisms influence the affinity of immunoglobulin G (IgG). Recently, FcγRIIA and FcγRIIIA polymorphisms have identified with the efficacy of trastuzumab. However, whether FcγR polymorphisms are associated with the efficacy of trastuzumab in the neoadjuvant setting was unclear.

Patients and methods:

We retrospectively enrolled 101 patients with HER2-positive breast cancer receiving chemotherapy plus trastuzumab at least four cycles as neoadjuvant therapy and mastectomy in Sun Yat-sen university cancer center from May 2015 to March 2021. Among them, twenty patients were excluded because lacking of blood samples. Polymorphisms of FcγRIIA(rs1801274) and FcγRIIIA(rs396991) were examined by nested polymerase chain reaction (PCR) and sanger sequencing. Lastly, we performed multiple immunohistochemistry (mIHC) to examine the expressions of CD8, CD68, CD57, PD1 and PDL1.

Results:

Blood samples (n=81) were successfully detected. No significant differences between FcγRIIA/FcγRIIIA genotypes and clinical characteristics, including age, clinical stages, menstrual status, molecular subtyping, treatment and pathological complete response (pCR) rate. In paclitaxel-based treatment subgroup (n=34), FcγRIIIA polymorphism was significantly correlated with pCR rate ($P < 0.05$, Table1), moreover, the disease-free survivals (DFS) in FcγRIIIA-158V carriers subgroup (high affinity) were significantly longer than that in FcγRIIIA-158 F/F genotype group (low affinity) ($P=0.036$), while that was not significant difference in patients with anthracycline-based treatment (n=47, $P=0.248$), indicating that anthracycline enhanced the efficacy of neoadjuvant therapy in patients with FcγRIIIA F/F genotype (low affinity). So far, there is no recurrence events in paclitaxel-based treatment group with FcγRIIIA-158V carriers genotype. The mIHC showed that the ratios of stroma CD8+PD1+ and CD68+PDL1+ cells were significantly higher in anthracycline-based treatment group (Table2), respectively, indicating that anthracycline improved the efficacy of neoadjuvant targeted therapy

by decreasing the ratios of exhausted immune cells.

Conclusions:

FcγRIIIA-158V genotype is associated with better outcome in HER2-positive breast cancer patients who received paclitaxel combined with trastuzumab as neoadjuvant therapy. Anthracycline improves the outcome of neoadjuvant trastuzumab-treated breast cancer patients with FcγRIIIA F/F genotype by decreasing the ratios of CD8+PD1+ and CD68+PDL1+ cells.

Correlation between FcγRIIIA and pCR

Characteristics	FcγRIIIA		
	F/F (n=47)	V carriers (n=34)	p-value
Total population			
pCR	14	16	0.112
non pCR	33	18	
Paclitaxel-based group			
pCR	5	9	0.049
non pCR	14	6	

Correlation between FcγRIIIA and pCR in total population and paclitaxel-based treatment population.

Ratios of immune cells

Characteristics	%CD68+PDL1+ cells (stroma)		%CD8+PD1+ cells (stroma)	
	Median(range)		Median(range)	
Anthracycline-based	0.01	0.03	0.05	0.002
Median(range)	(0-4.79)		(0-4.94)	
Paclitaxel-based	0.10		0.39	
Median(range)	(0-8.37)		(0-2.42)	

Ratios of immune cells in anthracycline-based and paclitaxel-based treatment group.

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UBE2E3 promotes the progression of HER2-positive breast cancer and influences the efficacy of targeted therapy via EGFR stabilization

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Background: In the past 20 years, the efficacy and prognosis of HER2-positive breast cancer have significantly improved. However, nearly 50% of patients still have residual invasive tumors after chemotherapy combined with dual-targeted neoadjuvant therapy, especially for those with disease progression during treatment. A lack of effective therapeutic regimens results from the failure of targeted therapy, whose heterogeneity is especially worthy of our attention. The aim of this study was to look for efficacy markers and investigate new drug-resistance mechanisms.

Methods: Firstly, the high-throughput sequencing data from 81 patients who received neoadjuvant chemotherapy TCbH (paclitaxel + carboplatin + trastuzumab) was analyzed by the efficacy outcomes. They were divided into 8 patients with stable or progressive disease (SD/PD), 35 with partial response (PR), and 38 with pathological complete remission (pCR). Then, UBE2E3 was chosen from the different expression genes between SD/PD and pCR based on efficacy results and the weighted gene co-expression network (WGCNA). UBE2E3 clinical correlations were investigated using publicly available data from The Cancer Genome Atlas (TCGA) and the Molecular Taxonomy of Breast Cancer International Consortium (METABRIC), and UBE2E3 was validated using immunohistochemistry (IHC) on 200 HER2-positive breast cancer tissue chips. Further, the UBE2E3 knockdown and overexpression stable transfer cell lines were constructed, and the effects of UBE2E3 on cell proliferation, clone formation, and drug sensitivity were verified by live cell imaging, the CCK8 assay, plate cloning, and IC50 assays, respectively. The tumor growth of UBE2E3 in vivo was investigated by an in situ transplantation tumor assay in nude mice. Meanwhile, the p-RB assay of mouse tissues by IHC was used to explore the effect of UBE2E3 on cell proliferation. RNA-seq was used to screen the downstream molecules of UBE2E3. Western blotting was used to verify the results of bioinformatics analysis and to explore the downstream key molecules. The protease inhibitor MG132 and actinomycin CHX were used to look at the effect on the stability of the target protein. Immunoprecipitation and silver staining assays were used to find interacting proteins with the UBE2E3. Results: Ten hub-genes which were efficacy-related were identified by WGCNA analysis, in which UBE2E3 was highly expressed in the SD/PD group ($p < 0.05$). In HER2-positive breast cancer, high expression of UBE2E3 was associated with poor prognosis and decreased disease-free survival both in public data and Fudan University Shanghai Cancer Center (FUSCC) data [HR 2.36, (1.25–4.47), $p < 0.05$]. The experimental results demonstrated that UBE2E3 promoted the proliferation of HER2-positive breast cancer cells, enhanced clone formation, and resisted lapatinib's treatment in cellular phenotype; and that UBE2E3 promoted tumor growth in vivo and upregulated the expression of p-RB. The differentially expressed genes' sets of the RNA-seq between overexpressed cell lines and control showed that overexpressing UBE2E3 activated the EGFR pathway. Further, an immunoblot assay confirmed that UBE2E3 positively regulated EGFR levels and activated the downstream MAPK pathway. The proteasome inhibitor MG132 and CHX assays showed that UBE2E3 could stabilize EGFR proteins. The co-immunoprecipitation and silver staining assays showed that UBE2E3 stabilized EGFR proteins by interacting with c-Cbl. Conclusion: UBE2E3 could negatively affect the efficacy of HER2-positive breast cancer therapy and is significantly associated with poor prognosis. UBE2E3 may serve as a potential marker of efficacy and prognosis for HER2-positive breast cancer in the future. Therapeutic efficacy is affected by UBE2E3, which binds to c-Cbl and causes upregulation of EGFR expression in vivo, which in turn causes the MAPK pathway to be activated and tumor growth to be pushed up.

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Soluble CD163 may be a predictive biomarker of the efficacy of nivolumab plus chemotherapy in patients with HER2-negative metastatic breast cancer (WJOG9917BTR).

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Background: We have conducted a phase II trial (WJOG9917B) to evaluate efficacy of triple therapy with nivolumab, paclitaxel and bevacizumab in patients (pts) with HER2-negative metastatic breast cancer (MBC). Although soluble CD163 has been reported as a potential biomarker for predicting the efficacy of nivolumab in melanoma, however the data is limited in breast cancer. In an ancillary study (WJOG9917BTR), serum level of soluble CD163 were evaluated to elucidate this question. Methods: The main study enrolled 57 pts and showed that median Progression-free survival (PFS) and overall survival (OS) was 14.0 months and 32.5 months, respectively, with a median follow-up of 29.5 months. We have collected blood samples from consenting patients. Serum samples were collected at pretreatment, cycle 1 day 8 and other time points, which were used to measure the concentrations of cytokines, chemokines, and other surrogate proteins. PFS, OS, and response were analyzed in association with the biomarker data using the Kaplan–Meier method, log-rank tests as appropriate. Results: Biomarker study included 50 pts (36 with recurrent BC and 14 with de novo stage IV BC). The median amount of soluble CD163 before treatment was 562.3 (pg/ml) (range: 158.7-1518.0), and the baseline CD163 levels were higher in pts with recurrent than de novo stage IV ($p = 0.0099$). Other clinical factors including tumor subtypes, liver metastasis, response, PFS or OS were not significantly associated with the baseline CD163 levels. The kinetic changes in serum soluble CD163 after treatment were divided into two groups; one group (30 patients, CD163 increased group) had increased soluble CD163 immediately after administration (Cycle 1 Day 8), with a median PFS of 18.2; the other group (20 patients, CD163 decreased group) had decreased CD163 immediately after administration, with a median PFS of 13.6. There was a significantly difference in PFS between these two groups (hazard ratio 0.50 [0.26-0.93], log-rank test, $p = 0.0263$), but not in OS ($p = 0.0548$). These results suggested that the early change of serum soluble CD163 may be a predictive biomarker of efficacy of nivolumab plus chemotherapy in pts with HER2-negative MBC. Conclusions: Soluble CD163 may be a predictive biomarker for early detection of the efficacy of nivolumab plus chemotherapy in pts with HER2-negative MBC. (UMIN000029590)

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5:00 PM - 6:15 PM

P5-02-43

Incidence of HER2-low Expression in HR-positive/HER2-negative and Triple-Negative Breast Cancers in the Integra Connect Database

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Approximately half of primary breast cancers exhibit low levels of human epidermal growth factor receptor 2 (HER2), defined as a score of 1+ on immunohistochemical (IHC) analysis or a score of 2+ on IHC and lack of HER2 gene amplification on in situ hybridization (ISH). Tumors classified as HER2-low represent a target for novel antibody-drug conjugates. In addition, HER2-low expression accounts for about 60% of HER2-negative breast cancers (BC). Real-world studies noted that HER2-low represents 47-54% of hormone positive (HR-positive)/HER2-negative breast cancers, a percentage higher than in the triple negative subgroup, reported at 35%. The goal of this study was to determine the frequency of HER2-low expression in patients with HR-positive/HER2-negative and triple-negative breast cancers (TNBCs) in the real-world and compare it with the published literature. The IntegraConnect (IC) real-world database of 330 thousand breast cancer patients was used for this analysis. Within the IC database, a subgroup of 387 patients with HR-positive/HER2-negative breast cancer and 618 patients with TNBC were abstracted with medical chart curation. The mean age at diagnosis for each group was 56 years and most patients had an ECOG performance status of 0-1. The statistical tests used were the Mann-Whitney test for age at diagnosis and the Chi-squared test for race, major stage, and ECOG at diagnosis. Differences were considered significant at $P < .05$. In the HR-positive/HER2-negative subgroup (n=387), 327 patients were tested by IHC and ISH. Sixty patients were tested by ISH only and were removed as they did not fit the definition of HER2-low. Of the 327 HER2-negative patients, 199 patients exhibited low HER2 expression (IHC1+, n=138 patients; IHC2+/ISH-negative, n=61), accounting for 61% (199/327) of HR-positive/HER2-negative breast cancers. In this group, numerically more patients were HER2-low than HER2-negative across all race subgroups. In the TNBC patient group (n=618), 546 patients tested HER2-negative by ICH and ISH. Patients testing HER2-negative by ISH only were removed (n=72) from the analysis. Of 546 patients with TNBC,

HER2-low expression accounted for 42% (227/546) [IHC1+, n=168; IHC2+/ISH-negative, n=59]. In the Black or AA patients with TNBC subgroup, 37.2% (N=129) were HER2-low compared with 44% (N=353) in White patients. In all TNBC race subgroups, numerically more patients were HER2-negative compared with HER2-low. In addition, the proportion of HER2-low expression was higher in the HR+/HER2-negative subgroup (N=327) than in TNBC (N=546) (61% vs 42%, respectively), corroborating literature reports. In conclusion, analysis of the IC database showed HER2-low expression in 61% of HR-positive/HER2-negative breast cancers and in 42% of TNBC patients. Approximately 37% of Black or African Americans (AA) patients with TNBC expressed low levels of HER2. The frequency of HER2-low expression in TNBC in the IC database at 42% is slightly higher than previous studies that estimate HER2-low expression at 35% of TNBC. The percentage of HER2-low in HR+/HER2-negative breast cancers at 61% is higher than previous reports, which estimate low HER2 expression in patients with primary and recurrent HR+/HER2-negative breast cancers at 47 and 54%, respectively.

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Efficacy analysis of CDK4/6 inhibitors in combination with endocrine therapy treatment in HR+/HER2- breast cancer according to PAM50 intrinsic subtype: primary results of SOLTI-1801_CDK-PREDICT study

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Background: First-line treatment with cyclin-dependent kinase 4 and 6 inhibitors (CDK4/6i) plus endocrine therapy (ET) has demonstrated efficacy in improving progression-free survival (PFS), overall response rate (ORR) and, more recently, ribociclib was also improve overall survival (OS) in hormone receptor-positive/HER2-negative (HR+/HER2-) advanced breast cancer (aBC). Unfortunately, most patients eventually progress and develop secondary or primary endocrine resistance. To date, no clinical or molecular markers have shown clinical utility in this setting. However, data from retrospective analysis suggest that intrinsic subtypes (IS) are prognostic and predict benefit from CDK4/6i+ET (Finn SABCS 2017, Prat. JCO 2021). Here, we have evaluated the impact of IS in PFS and ORR.

Methods: This study prospectively evaluated patients with HR+/HER2- aBC treated in the first-line setting with CDK4/6i + ET from February 2015 to January 2022 across 5 hospitals in Spain. Tumor biopsies had been performed within 90 days prior the patient started the CDK4/6i + ET. RNA from FFPE tumors was analyzed at the nCounter® (Nanostring Technologies) using a 72 custom gene panel including the PAM50 genes. The primary objective is to correlate the baseline PAM50 IS with PFS. The Kaplan-Meier method and multivariable cox model PFS analyses were performed adjusting for previous endocrine sensitivity, visceral disease, and metastatic onset disease. Secondary objectives were to estimate the ORR based on RECIST1.1 and its association with IS and the development of a prognostic algorithm that includes clinical and genomic data.

Results: From May 2020 to May 2022, 113 patients with PAM50 results who met all eligibility criteria, including sample quality, were included. IS distribution was 42.5% Luminal A, 46.9% luminal B, 7.1% HER2-enriched, 0.9% basal-like and 2.6% Normal-like (89.4% luminal vs 10.6% non-luminal). Baseline patient characteristics are shown in table 1. The median follow-up

for PFS was 18.5 m (interquartile range 10.0 – 31.7m). Median PFS for Luminal vs no-luminal subtypes was 26.8 m (95% CI: 18.9 - 43.8 m) and 10.0 m (95% CI: 5.8 - 26.0 m) (adjusted hazard ratio [aHR]= 2.44 95% IC: 1.17 - 5.07). Median PFS by all IS was not reached (NR) for Luminal A (95% CI: 23.0 – NR); 19.5 m luminal B (95% CI: 15.7 - 27.3 m, aHR vs Luminal A= 1.98 95% IC: 1.09 - 3.62), 10.0 m HER2-E (95% CI: 4.4 - NR, aHR vs Luminal A= 2.75 95% IC: 1.05 - 7.18), 12.4 m Normal-like (95% CI: 5.8 - NR, aHR vs Luminal A= 19.35 95% IC: 2.32 - 160.89) and not estimable for basal-like (aHR vs Luminal A= 5.44 95% IC: 1.44 - 20.60). ORR was not significantly higher in Luminal B (55.1%) and HER2-E (57.1%) subtype versus luminal A (46.3%) ($p=0.677$). OS follow-up is still immature.

Conclusions: We confirmed the independent prognostic value of the PAM50 IS in first-line HR+/HER2- breast cancer treated with CDK4/6i+ET. Further gene expression analysis and development of a prognostic composite score is ongoing and will be presented at the conference.

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Baseline patient characteristics

Baseline patient characteristics (n=113)

Median age, years (range)	59 (28-89)
CDK4/6i n, %:	
Palbociclib	61, 54.0%
Ribociclib	36, 31.9%
Abemaciclib	16, 14.1%
Endocrine sensitivity n, %:	
Hormone-sensitive	83, 73.4%
Hormone-resistant	30, 26.6%
Metastatic onset n, %:	
No	55, 48.7%
Yes	58, 51.3%
ECOG PS n, %:	
0	70, 61.9%
1	41, 36.3%
2	2, 1.8%
Disease location n, %:	
Visceral disease n, %:	49, 43.4%
Bone only disease n, %	25, 22.1%
Hepatic disease n, %	28, 24.8%
Menopausal status n, %: *Male patients not included (n=3)	
Postmenopausal	83, 75.5%
Premenopausal	27, 24.5%
Grade n, %:	
1	6, 5.9%
2	74, 72.5%
3	22, 21.6%
Histologic type n, %:	
Non-special type (IDC).	93, 83.0%
Infiltrating lobular carcinoma (ILC)	7, 6.2%
Other	12, 10.7%
HER2 IHQ n, %:	
HER2-0	49, 43.7%
HER2-low (1+ or 2+ with ISH negative)	63, 56.25%

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5:00 PM - 6:15 PM

P5-02-45

An HRD scoring system based on long-focal copy number alterations predictive of PARP inhibitor response

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Homologous recombination deficiency (HRD) is characterized by a defective double-stranded DNA repair mechanism due to alterations in the homologous recombination (HR) pathway. Deleterious mutations in HR pathway genes can help identify potential responders to platinum-based chemotherapies and PARP inhibitors (PARPi), which promote apoptosis in HRD cells. Until recently, the use of PARPi in breast cancer (BC) was limited to advanced or metastatic disease with pathogenic or likely pathogenic germline BRCA (gBRCA) mutations. However, the use of PARPi has expanded to treat early-stage HER2-negative BC with a high risk of recurrence and gBRCA mutations, HER2-negative BC with somatic BRCA mutations, and triple-negative BC. To date, no universal method for HRD scoring is accepted; therefore, biomarkers are needed to stratify patients into PARPi responders and nonresponders more effectively. Because PARPi are used to treat HRD-driven cancers, we aimed to identify genomic consequences of HRD. For HRD-specific features, we calculated the proportion of long-focal total copy number alterations (LF-tCNA), which estimates amplification events for long-focal segments. Aneuploidy is especially prevalent in medullary, metaplastic, and invasive micropapillary BCs. These copy number variations are not necessarily consequences of HRD but can influence HRD scores. Genome-wide loss of heterozygosity (gwLOH) can be a result of HRD and used as a biomarker for HRD. We developed several scoring methods based on LF-tCNA, gwLOH, and aneuploidy scores. These scores were tested as predictors of HRD, defined as known loss-of-function germline mutations in BRCA1, BRCA2, PALB2, or BARD1 (TCGA-BRCA cohort, $n = 1,032$). To calculate the optimal HRD score, we used multivariate logistic regression analysis with HRD as an outcome and LF-tCNA, LOH, and ploidy as predictors. Based on the results of logistic regression, LF-tCNA and ploidy were selected to calculate HRD status. The positive and negative predictive values (PPV, NPV) were used to set the upper and lower thresholds, respectively. Samples with HRD scores above 7 (PPV) have the greatest potential for PARPi and platinum-based therapy response, while scores below -1 (NPV) were considered HRD wild type (WT). To validate the developed HRD score, we tested the score by

combining BC cohorts (MSK_NCI and MET500 cohorts, n = 164) and used gBRCA1/2 pathogenic mutations as an outcome. Our HRD scoring system distinguished HRD WT from HRD-positive samples (AUC = 0.81) more effectively than a previously reported score based on LOH, telomeric-allelic imbalance (TAI), and large-scale state transitions (LST) (AUC = 0.72). We tested our HRD scoring system across tumor microenvironment molecular subtypes. The median HRD score in the basal-like subtype was increased compared to other subtypes, supporting the prevalence of gBRCA1/2 pathogenic mutations in this subtype. Moreover, the number of HRD-positive patients and the percent positive agreement, defined as the proportion of positive test results from our HRD also positive for HR mutations, were calculated for each BC subtype. Only 22% of basal-like HRD-positive samples also carried germline HR pathway mutations, which indicates 78% of HRD-positive patients who might benefit from PARPi or platinum treatment would have been missed by germline HR gene panels. This BC HRD scoring method is a promising tool for identifying HRD patients who may respond to PAPRi and platinum-based therapies, but additional studies are required for clinical validation.

Disclosure(s):

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Targeted capture sequencing allows sensitive genomic profiling of circulating tumor DNA in advanced HR+/HER- breast cancer patients

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Introduction: CDK4/6 inhibitors provide substantial benefits as 1st or 2nd line treatments and are now the standard of care for patients with advanced HR-positive, HER2-negative breast cancer. Recently, we demonstrated that a high-resolution SiMSen-seq assay (SSS) provides a sensitive and robust method for detecting 11 PIK3CA hotspot mutations in cell-free circulating DNA, allowing the identification of patients eligible for alpelisib treatment. Unfortunately, all patients progress at some time point due to intrinsic or acquired resistance. Therefore, detecting additional genomic biomarkers for treatment resistance beyond PIK3CA mutations is crucial. Targeted panel sequencing offers a promising strategy to profile circulating tumor DNA (ctDNA) for genetic alterations in multiple genes associated with treatment response and disease progression. This ongoing study aims to show that a commercial NGS assay (AVENIO ctDNA Expanded Kit, Roche Diagnostics) can (1) detect PIK3CA mutations with similar sensitivity as our high-resolution SSS assay and can (2) simultaneously identify additional genetic alterations in multiple genes, possibly associated with treatment resistance or disease progression. Material and Methods: To this end, we collected plasma samples from 46 metastatic HR+/HER2- breast cancer patients before starting 1st (32 patients) or 2nd (14

patients) line treatment. Samples were analyzed using SSS and the AVENIO ctDNA Expanded Kit, enriching for 77 clinically relevant cancer genes. PIK3CA mutation detection and variant allele frequencies (VAF) were compared between the two methods. Additionally, mFAST-SeqS was used to estimate the tumor fractions in plasma samples. Results: The median z-score from mFAST-SeqS analyses was 2.38 [25–75th percentile: 1.23–4.5], and 17/46 (37%) patients had z-scores ≥ 3 , indicating elevated tumor fractions (>5%). Patients starting 2nd line treatment had significantly higher z-scores than those starting 1st line treatment (median 2.2 vs. 3.8, rank-sum p-value 0.042). One sample repeatedly failed with the SSS assay, leaving 45 samples for a head-to-head comparison. Considering only PIK3CA hotspot mutations covered by both assays, 16 alterations were detected in 14 patients (31%) by the SSS assay and 19 alterations in 17 patients (38%) by the AVENIO ctDNA Expanded Kit. Both assays detected the identical co-occurrence of two PIK3CA mutations in two samples. Two of three mutations only detected with the AVENIO ctDNA Expanded Kit were also observed with the SSS assay but below the pre-defined detection limit. One mutation was only detected by the AVENIO ctDNA Expanded Kit. Overall, we found an excellent concordance rate of 94% between the two assays, confirming the high sensitivity of the panel sequencing assay. Moreover, the VAF of SSS and AVENIO kit were highly correlated (Spearman's rho = 0.97, p < 0.001). Using the AVENIO kit, a large number of additional mutations in 40 genes could be identified in 42/46 (91%) patients with a median of 2.0 variants (range 1-13) per sample. The most frequently mutated genes included PIK3CA (43%), followed by ESR1 (20%), TP53 (20%), MET (17%), SMAD4 (17%), ERBB2 (11%), and BRCA2 (11%). The median VAF was 0.64% (range 0.1-29.8). Further analyses are still ongoing. Conclusion: The AVENIO ctDNA Expanded Kit revealed a high sensitivity and concordance rate for detecting PIK3CA hotspot mutations in plasma samples compared with the high-resolution SSS assay. A major advantage of panel sequencing over a single gene approach is that the interrogation of multiple genes can indicate a true negative PIK3CA result if other variants are present with a high VAF. Moreover, other actionable targets or mechanisms of resistance can be captured simultaneously, thus improving the effective precision treatment of metastatic breast cancer patients.

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5:00 PM - 6:15 PM

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Quantitative proteomic analysis of plasma exosomes from patients with advanced hormone receptor-positive/HER2-negative breast cancer receiving palbociclib and tamoxifen

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Background: A CDK4/6 inhibitor (CDK4/6i) in combination with endocrine therapy (ET) is standard first-line therapy for advanced, hormone receptor (HR)-positive, HER2-negative breast cancer (BC). However, not all patients respond and responders eventually develop drug resistance and disease progression. Exosomes are small extracellular vesicles that are secreted by both normal and tumor cells as a mechanism for intercellular communication. The protein cargo of exosomes reflects biological processes activated in cancer cells and may serve as predictive biomarkers to select patients most likely to benefit from treatment and to identify mechanisms of resistance. Methods: Whole blood was collected in Streck tubes at baseline and at time points during treatment from patients with advanced, HR+/HER2- BC enrolled in a single arm, phase 2 trial of first line therapy with palbociclib plus tamoxifen that was conducted by The Big Ten Cancer Research Consortium (NCT02668666). Plasma was separated and stored at -80C within 48 hours of collection. Different exosome protein isolation methods were evaluated and optimized to maximize protein recovery. Exosome and plasma proteins were extracted, purified, and digested with trypsin. Tryptic peptides were isotopically labeled with Tandem Mass Tag (TMT) 10plex for protein expression level quantitation. Triplicate samples from each patient were analyzed by LC-MS/MS with QExactive HF Orbitrap mass spectrometer. An unsupervised clustering method was used to classify patients based on exosomal proteomic profiles. Results: We developed a sensitive and efficient exosome extraction method to obtain exosome protein from minimal volumes of patient plasma. The optimized exosome isolation method quantitatively identified 800 proteins from a 100 µl plasma sample. Significant enrichment of exosome-specific markers was observed when comparing patient samples with healthy donor samples. A network model was developed to differentiate responders/stable disease patients from non-responders using exosome proteomics data generated from pretreatment plasma samples. Preliminary data from the first 22 patients analyzed (responders, n= 6; stable disease, n=12, and non-responder, n=4) identified a network of 45 proteins that predicted response/stable disease vs progressive disease with high specificity (95%) and sensitivity (89%). We also noted significant differences in the exosome proteomic profiles of patients with de novo vs. recurrent metastatic disease. A network of 22 proteins differentiated de novo vs recurrent metastatic disease with > 85% sensitivity and 78% specificity, providing molecular evidence differentiating the two disease states. This finding is relevant in light of the higher response rate and improved PFS in patients with de novo metastatic disease in this trial, and confirms that this approach may provide molecular insight into mechanisms of primary resistance to CDK4/6i. Results for the entire trial cohort of 46 patients will be presented, along with analysis of serial samples collected at various time points during treatment. Conclusion: This proof-of-concept study demonstrates that an ultrasensitive exosome proteomics platform combined with deep learning methods is ideally suited for developing predictive protein biomarkers and for exploring molecular mechanisms of drug resistance. If results are confirmed, this novel approach holds great promise for identifying protein biomarkers that could be used to select patients unlikely to respond to ET and CDK4/6i in order to spare them ineffective treatment and for selecting participants for clinical trials of

novel agents. Additionally, exosome proteomics data generated from serially collected specimens can be used to identify mechanisms of resistance that emerge during therapy. This approach can be widely applied to other treatment regimens and disease sites. This study was funded by Pfizer.

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Identifying immune-related predictive factors for paclitaxel + bevacizumab therapy in patients with HER2-negative advanced breast cancer- A multicenter retrospective study

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Background: In IMpassion 130 trial, programmed death-ligand 1 (PD-L1) expression was seen in about 40% of participated patients with triple negative advanced breast cancer (TN-ABC) [Schmid, 2018, N Engl J Med], however, actual situation of PD-L1 expression in patients HER2-negative ABC patients including with TN-ABC has not been well studied. Furthermore, no biomarker related to chemotherapy for HER2-negative ABC patients except for PD-L1 in TN-ABC has been identified. Recently, several reports regarding the relationship between peripheral immune-related markers; such as absolute lymphocyte count (ALC) or neutrophil-to-lymphocyte ratio (NLR), and efficacy of eribulin therapy [Miyoshi, 2020, Breast Cancer; Watanabe, 2020, Breast Cancer Res Treat] or paclitaxel plus bevacizumab (PB) therapy [Nakamoto, 2021, Sci Rep], however, the relationship between the efficacy of PB therapy and peripheral immune related markers including dynamic change during the therapy or local immune-related markers is unclear. Therefore, we conducted multi-institutional, retrospective study 1) to evaluate the actual situation of PD-L1 expression and other immune-related markers of the primary site by central review, and 2) to explore biomarkers for first-line PB therapy using

peripheral and local immune-related markers. Patients and methods: We retrospectively reviewed medical records of HER2-negative ABC patients who received PB therapy as first-line (1L) or second-line chemotherapy for ABC. Clinical data including ALC, NLR and serum albumin (Alb) were extracted from medical records, and the pathology of archived tissues of primary and metastatic site (if available) were centrally reviewed including PD-L1 (VentanaR SP142). Statistical analyses were performed using Kaplan-Meier method, log-rank test, Wilcoxon's test, and Cox hazard model. Mixed-effects model for repeated measures (MMRM) to evaluate the relationships between dynamic change in immune-related markers and time-to-treatment termination (TTT) of PB therapy. Results: We identified 156 HER2-negative ABC patients who underwent PB therapy, and 114 out of 156 patients were eligible for analyses. Of 114 patients, 63 patients (55.3%) had recurrent disease, and 65 (57.0%) patients had visceral disease. Eighty-seven out of 114 (76.3%) patients received PB therapy as 1L chemotherapy. Eighty-four specimens (73.7%) were diagnosed as estrogen-receptor (ER) positive, and PD-L1 positivity rate were 3.6% (1/84) in ER+ subgroup and 30.0% (6/20) in ER- subgroup, respectively. Paired biopsy specimens were eligible in 14 patients, and significant elevation of Ki67 labeling index was noted. In patients who received 1L PB (n = 87), there was no positive relationship between maintained ALC (>1,500 or >1,000/ μ L at baseline) or low NLR (< 2.5 or < 3) at the initiation of 1L PB therapy and TTTs. However, low NLR (cut-off at 2.5 and 3) at the initiation of second cycle of PB therapy reduced the risk for treatment-termination as; hazard ratio [HR], 0.427; 95% CI 0.218-0.843; P = 0.0147 and HR, 0.344; 95% CI 0.170-0.731; P = 0.0066, respectively. PD-L1 positive patients (n = 5) showed numerically increased risk of treatment-termination (HR, 2.68; 95% CI, 0.922-6.196; P = 0.0674) for 1L PB therapy, however, there was no significant difference in mortality risk regarding PD-L1 statuses. Multivariate analysis using MMRM disclosed that increase of Alb level was predictive factor for 1L PB therapy (HR, 0.41; 95%CI, 0.18-0.93; P = 0.0338). Conclusion: According to our real-world study, 1) PD-L1 positive rate was lower than that of previous reports, 2) low NLR at the initiation of second cycle of PB therapy and dynamic change in albumin level were identified as predictive factors and 3) PD-L1 overexpression was not a prognostic or a predictive factor for PB therapy in patients with HER2-negative ABC. Funding: Chugai Pharmaceutical CO., LTD.

Disclosure(s):

Junichiro Watanabe, MD, PhD: Chugai Pharmaceutical: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Eisai Co., Ltd.: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Eli-Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Taiho Pharmaceutical Co., Ltd.: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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5:00 PM - 6:15 PM

P5-02-49

Efficacy of subsequent-abemaciclib treatment after disease progression on palbociclib combined with endocrine therapy in patients with ER-positive HER2-negative metastatic breast cancer

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Purpose: Currently, CDK4/6i combined with endocrine therapy (ET) has become the standard of care as first- or second-line treatment for estrogen receptor-positive (ER+) human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer (MBC). However, at present, there are no guidelines for the selection of appropriate treatments after disease progression on prior CDK4/6i treatment combined with ET. Therefore, this retrospective study aimed to verify the efficacy and evaluate predictive factors of clinical outcomes in the patients with ER+/HER2- MBC during subsequent-abemaciclib treatment after disease progression on prior-palbociclib combined with ET.

Methods: In total, 81 patients with ER+/HER2- MBC were treated with palbociclib and ET at our medical center between December 2017 and November 2020. Among them, 25 patients who received subsequent-abemaciclib after disease progression on prior-palbociclib were included. All patients provided informed consent for the indicated treatment. Clinicopathological variables were compared using Fisher's exact test. The Mann–Whitney U test was used to compare categorical variables. PFS and time to chemotherapy (TTC) were estimated using Kaplan–Meier analysis with 95% CIs.

Results: The median age was 69 years, and four women were premenopausal. Stage IV disease occurred in 28.0% (7/25) and visceral metastases were observed in 68.0% (17/25) of the patients. The treatment line of prior-palbociclib was the first-line in 3 (12.0%), second-line in 11 (44.0%), and third- and late-line in 11 patients (44.0%). The median PFS of prior-palbociclib plus ET was 6.3 months (95%CI=5.814–6.786). Subsequent-abemaciclib combined with fulvestrant after disease progression on prior-palbociclib was administered in 64.0% (16/25) of the patients. Median numbers of previous ET and chemotherapy of subsequent-abemaciclib were 2 and 0, respectively. Subsequent-abemaciclib after disease progression on prior-palbociclib resulted in an ORR and clinical benefit rate (CBR) of 16.0% (4/25) and 44.0% (11/25), respectively (Table 1). Kaplan–Meier curve analysis showed that the median PFS was 5.3 months (95%CI=3.082–7.518). Univariate analysis revealed that the best overall response (BOR) ≥PR and progression-free interval (PFI) ≥6 months in prior-palbociclib contributed to better clinical outcomes. Moreover, in multivariate analysis, BOR to prior-palbociclib was the only independent predictive factor for PFS (HR=0.190; 95%CI=0.050–0.722; p=0.015) (Table 2). With regard to grade ≥3 TRAEs in the subsequent-abemaciclib, neutropenia and diarrhea were observed in 16.0% (4/25); appetite loss and fatigue in 12.0% (3/25); leukopenia and anemia in 8.0% (2/25); and thrombocytopenia and liver dysfunction in 4.0% (1/25) of patients. Twelve patients (48.0%) required dose reduction due to TRAEs grade ≥3 in subsequent-abemaciclib. Of them, 10 patients required one dose-level reduction and 2 needed two dose-level reductions. Three patients (12.0%) required dose discontinuation: two had uncontrollable

appetite loss and nausea and one had pneumonia. Of the 25 patients, 12 were not administered any prior chemotherapy and the median TTC in those treated with subsequent-abemaciclib was 33.9 months (95%CI=11.334–56.136). Next-line treatment after disease progression on subsequent-abemaciclib in the patients who were not administered prior chemotherapy was performed in 2 (8.0%) who were treated with ET and in 12 (48.0%) who were treated with chemotherapy (1 taxane-based, 7 eribulin, and 4 oral 5-fluorouracil). The median PFS in patients treated with chemotherapy after disease progression on subsequent-abemaciclib treatment was 6.2 months (95%CI=3.484–8.916).

Table 1. Best overall response rate in patients with ER+/HER- MBC who were treated with subsequent-abemaciclib after disease progression on prior-palbociclib

	n=25	%
Response		
CR	0	0
PR	4	16.0
Long SD	7	28.0
SD	5	20.0
PD	9	36.0
ORR	4	16.0
CBR	11	44.0

ER, Estrogen receptor; HER2, human epidermal growth factor receptor 2; MBC, metastatic breast cancer; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ORR, overall response rate; CBR, clinical benefit rate.

Table 2. Univariate and multivariate analyses of the progression-free survival in patients with ER+/HER2- MBC treated with subsequent-abemaciclib after progression on prior-palbociclib

Factor	Univariate		Multivariate	
	HR (95%CI)	p-value	OR (95%CI)	p-value
Age (years) (≥70/<70)	0.737 (0.321-1.695)	0.473		
Menopause (yes/no)	0.712 (0.237-2.134)	0.544		
BMI (≥25/<25)	2.278 (0.868-5.978)	0.094		
Nuclear grade (3/1or 2)	1.155 (0.500-2.670)	0.736		
Disease stage at initial diagnosis (stage IV/I-III)	0.653 (0.256-1.666)	0.372		
Previous lines of ET in the context of metastatic disease (≥2/1)	0.696 (0.279-1.735)	0.436		
Previous lines of chemotherapy in the context of metastatic disease (≥2/1)	0.680 (0.148-3.122)	0.620		
Combined ET with abemaciclib (fulvestrant/AI)	0.816 (0.342-1.950)	0.648		
BOR of prior-palbociclib (CR, PR/long SD, SD, PD)	0.169 (0.053-0.532)	0.002*	0.190 (0.050-0.722)	0.015*
PFI of prior-palbociclib (≥6 months/<6 months)	0.329 (0.134-0.808)	0.015*	0.836 (0.298-2.348)	0.734
Number of metastatic sites (≥2/1)	0.853 (0.244-2.980)	0.804		
Visceral metastasis (yes/no)	0.763 (0.303-1.922)	0.566		
Bone only metastasis (yes/no)	1.381 (0.313-6.093)	0.670		

HR, Hazard ratio; CI, confidence interval; BMI, body mass index; AI, aromatase inhibitor; CR, complete response; OR, odds ratio; PR, partial response; SD, stable disease; PD, progressive disease; BOR, best overall response; ET, endocrine therapy; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; MBC, metastatic breast cancer; PFI, progression-free interval. *p<0.05.

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Do thymidine kinase 1 (TK1) plasma concentration and activity play a role in therapy management of metastatic breast cancer patients treated with CDK4/6 inhibitors?

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Introduction: CDK4/6 is a checkpoint kinase, regulating the transition of the S into the G2 phase of the cell cycle. As a cell transverse through the cell cycle, thymidine kinase 1 (TK1) is expressed and represents a direct marker of proliferative activity which might indicate therapy efficiency of CDK4/6 inhibitors (CDK4/6i), the first choice of therapy in case no sign of visceral crisis is detected in hormone receptor positive (HR+), HER2 negative (HER2-) metastatic breast cancer (MBC) patients. We here determined whether the activity and/or concentration of TK1 in plasma samples of MBC patients treated with CDK4/6i harbours predictive, monitoring or prognostic value. Methods: Blood of 90 HR+/HER2-MBC patients drawn at baseline of CDK4/6i (Ribociclib/Palbociclib) plus endocrine treatment and 18 HR+/HER2-MBC patients drawn before initiation of endocrine monotherapy (control), as well as available matched blood samples of these patients after six months under TX (n=90), 12/24 months before progression (n=72/24) and at the time of progression (n=52) are available. TK1 concentration in plasma samples was measured by competitive ELISA (ABIN809094, Shanghai BlueGene Biotech Co., LTD, China) and TK1 activity of matched plasma samples by competitive, two-step chemiluminescence immunoassay (REF 310960, Diasorin, Stillwater, US). Statistical analysis was conducted via log-rank test and univariate or multivariate Cox regression. Results: Currently, baseline samples were evaluated for TK1 concentration (n=106) and activity (n=90). The mean value for TK1 activity was 12.69 U/L and the median value was 8.37 U/L in the entire cohort. Values ranged from 0.89 to 79.50 U/L and the standard deviation was determined to be 12.64 U/L, which is similar to the mean value. In contrast to the control group, high TK1 activity

(Cut-off: mean or determined by ROC analysis and maximal Youden's Index for PFS < six months) was significantly correlated with decreased progression free survival (PFS) in the CDK4/6i cohort (p-value < 0.05 in log rank test and univariate Cox regression). In addition, using multivariate Cox regression analysis including clinical parameters (e.g. therapy line, prior chemo- or endocrine therapies, type of CDK4/6i accompanying endocrine therapy, number of sites of metastases, visceral metastases, menopausal status), TK1 activity was found to be an independent marker for PFS. High TK1 activity (Cut-off: mean or determined by ROC analysis and maximal Youden's Index for PFS < six months or already deceased patients) at baseline was significantly correlated with shorter time from baseline to death in the CDK4/6i cohort (p-value < 0.05 in log rank test and univariate Cox regression) but not in the control cohort. For TK1 concentration analysis, the mean value was 21.76 ng/ml and the median value was 18.57 ng/ml in the entire cohort. Values ranged from 7.35 ng/ml to 46.66 ng/ml and the standard deviation was determined to be 11.16 ng/ml, which is half of the mean value. In contrast to TK1 activity measurements, no significant association of TK1 concentration with PFS or overall survival (OS) was detected in the CDK4/6i cohort. Currently, all remaining samples during the course of treatment are evaluated for TK1 activity and concentration and final statistical analysis of the complete data set will be available at the meeting. Conclusion: Our preliminary results indicate that TK1 activity, in contrast to TK1 concentration, determined before starting CDK4/6 inhibition could be a suitable predictive and prognostic biomarker for estimating response to treatment. Our final analysis will clarify, whether TK1 could also serve as a monitoring marker during treatment.

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5:00 PM - 6:15 PM

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Single-cell transcriptome reveals distinct peripheral blood immune landscapes associated with sensitivity to anti-HER2 treatment in HER2-positive metastatic breast cancer patients

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Background: Different immune cell states reflect distinct tumor microenvironment and led to various clinical outcomes for cancer patients. However, very few studies examined the contribution of peripheral blood (PB) immune landscapes to the treatment response due to the limited applications. This study aimed to explore the circulating immune cell landscapes associated the sensitivity to cytotoxic chemotherapy with trastuzumab in HER2 positive metastatic breast cancer patients. Methods: Whole blood were drawn at baseline and after 2 cycles of trastuzumab plus cytotoxic chemotherapy from six patients (3 responders and 3 non-responders). Approximately 3,500 to 10,000 peripheral blood mononuclear cells per patients were profiled using single-cell RNA sequencing (scRNA-seq). scRNA-seq data were further processed and analyzed using Seurat package version 3.1. Cell populations were clustered using the Louvain algorithm and subsequently annotated using known marker genes. Differential abundance in cell population was quantified using MiloR and differentially expressed genes were detected using MAST between responders and non-responders. Results: After removing low quality cells, a total of 65,295 cells were clustered into 18 clusters. CD8 Effector T, CD4 Naïve T, CD4 Effector T, Cytotoxic NK, Naïve B, Plasma B and Monocytes were significantly enriched in responders compared to non-responders. Especially, CD8 Effector T, NK, Plasma B and Classical Monocytes showed distinct patterns that those cells were enriched in pre-treatment than post-treatment of responder but not in non-responder. From the differentially expressed gene analysis, cytotoxic or costimulatory marker genes (GZMK, GZMA, GNLY, CCL5, NKG7, PRF1) were enriched in responders. While, exhausted or coinhibitory marker genes (DNAJB1, LGALS9, HAVCR2) were enriched in non-responders. Gene set enrichment analysis revealed four pathways associated with T cell, B cell receptor signaling, NK cell mediated cytotoxicity and Cytokine-cytokine receptor interaction which showed differences between responders and non-responders following chemotherapy. Finally, validation with flow cytometry using independent cohort showed that constant expression manner in HAVCR2, LGALS9 and LGALS3 genes. Conclusions: Single-cell transcriptome analysis identified distinct PB immune landscapes associated with treatment response in HER2-positive metastatic breast cancer patients. Differential abundance and unique gene expression programs of immune cell populations could serve as potential predictive biomarkers for anti-HER2 therapy.

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P5-02-52

Predictive and prognosis value of PIK3CA mutations in HER2-positive breast cancer treated with tyrosine kinase inhibitors (TKIs): a systemic review and meta-analysis

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Background: PIK3CA mutations is one of the most frequent gene alterations in breast cancers, which was reported to be related to the treatment response of anti-HER2 regimens. However, the relationship between PIK3CA mutations and treatment response of a tyrosine kinase inhibitors (TKIs) is still unclear. We thus conducted a systemic review and meta-analysis to investigate the predictive and prognosis value of PIK3CA mutations in HER2-positive breast cancer treated with TKIs. Methods: The following databases were searched from inception to July 2022: Medline, Embase and the Cochrane Library. Abstracts from conferences were also reviewed for inclusion. The critical information was extracted from eligible studies. Results: A total of 16 reports including 17 studies were assessed for eligibility, enrolling 1706 patients. Ten studies including 902 patients were in the neoadjuvant setting, the pCR rate is significantly higher in PIK3CA wild-type (WT) patients than in mutated-type (MT) patients (OR = 0.45; 95% CI: 0.31-0.65; P < 0.001). Seven studies including 804 patients were in the metastatic setting, the pooled objective response rate (ORR) is significantly higher in PIK3CA WT patients than in MT patients (OR = 0.40; 95% CI: 0.23-0.70; P = 0.001), and similarly, the clinical benefit rate (CBR) in WT patients is also higher (OR = 0.43; 95% CI: 0.19-0.98; P=0.045). A total of 4 metastasis studies reported progression free survival (PFS), and 2 of them reported overall survival (OS), revealing a marginally significant relationship between PIK3CA mutation and worse PFS (HR = 0.82; 95% CI: 0.67-1.00; P=0.052) and OS (HR=0.63 , 95%CI : 0.39-1.02; P=0.062). No evidence of publication bias was found in both the neoadjuvant setting and metastatic setting. Conclusion: Our findings indicate that PIK3CA mutations is significantly associated with a lower rate of pCR when treated with TKI-containing regimens in neoadjuvant chemotherapy of early-stage HER2-positive breast cancer, and is significantly associated with lower ORR and CBR in metastatic HER2-positive breast cancer.

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P95HER2 Expression in HER2-Positive Breast Cancer

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Background: -HER2-positive breast cancer subtype accounted for around 15-20% of all breast cancer. -The introduction of HER2-targeted therapy such as trastuzumab and pertuzumab has

remarkably increased the patients' prognosis of HER2-positive breast cancer. -However, resistance exists due to impaired drug binding to HER2 receptor and constitutive activation of HER2 downstream signaling pathways. -P95HER2 isoform is a truncated form of HER2 that retains the C terminal domain but lacks an N terminal trastuzumab binding site, leading to trastuzumab resistance in HER2-positive breast cancer. -A new P95HER2 antibody is developed to target the extracellular domain of p95HER2 in formalin-fixed paraffin-embedded (FFPE) HER2-positive breast cancer tissues by using hematoxylin and eosin (HE) staining method. Objectives: To evaluate the expression of P95HER2 and its clinicopathological characteristics in HER2-positive breast cancer. Methods: We assessed 68 HER2-positive patients (IHC 3+ or IHC 2+/in situ hybridization [ISH]+) from Fudan University Shanghai Cancer Center (FUSCC) who underwent breast cancer surgery and were treated with adjuvant chemotherapy (taxane or anthracycline or combination) plus trastuzumab from 2014 to 2016. P95HER2 HE antibody is provided by Simcere Pharma. In this study, we compared 27 patients with primary trastuzumab resistance with 41 non-relapse breast cancer patients. 14 patients have not received trastuzumab targeted therapy. P95HER2 staining of either 1+, 2+ or 3+ observed in any tumor area in HE slides was considered to be P95 HER2 positive. Chi-square test was used to determine the relationship between P95HER2 expression of patients' characteristics. The main outcome measures were disease free-survival (DFS), distant disease-free survival (DDFS) and overall survival (OS) by using log-rank test. Univariable and multivariable Cox regression analyses were used to identify independent factors related to prognosis. Results: From 2014 to 2016, we assessed the expression of P95HER2 expression in 68 HER2 positive breast cancer patients from FUSCC. Median follow-up was 45 months. In our study, 19 (27.9%) were P95HER2 positive. P95HER2 positive expression rate is higher in premenopausal patients than in postmenopausal patients (68.4% vs 38.8%, $P=0.028$). Univariable analysis showed that higher T-stage ($P=0.018$), higher N-stage ($P=0.001$) and P95HER2 positive expression ($P=0.033$) were associated with worse DDFS. Multivariable analysis showed that higher T-stage (hazard ratio, 6.019; 95% CI, 1.205-30.078; $P=0.029$) and P95HER2 positive (hazard ratio, 2.349; 95%CI, 1.03-5.358; $P=0.042$) independently predicted worse DDFS. P95HER2 positive was significantly associated with shorter 5-year DDFS (42.1% vs 67.6%, $P=0.028$), but has no significant difference in DFS (36.8% vs 59.5%, $P=0.072$) and OS (74.8% vs 81.2%, $P=0.685$). Conclusions: P95HER2 positive was found more in premenopausal patients and was associated with a higher metastasis rate, indicating that P95HER2 expression tends to be a more aggressive isoform type of HER2-positive breast cancer. P95HER2 may serve as a therapeutic target for anti-HER2 therapy.

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Application of low-pass whole genome sequencing for the detection of Homologous Recombination Deficiency in breast cancer

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Background: Homologous recombination deficiency (HRD), broadly defined as a loss of the cellular mechanism underlying homologous recombination, is often observed in breast cancer. HRD causes distinctive perturbations to tumor genomic architecture that allow for its molecular identification, while also rendering HRD+ cancers vulnerable to specific chemotherapeutic interventions. This makes the molecular identification of HRD a promising avenue in precision medicine of breast cancer. Specific features of HRD include the presence of large-scale transitions (LST), telomeric allelic imbalance (TAI) and Loss of Heterozygosity (LOH). Each are

readily detectable via targeted next generation sequencing (tNGS) or via array-based genotyping. However, genome-wide approaches for HRD detection using cost-effective methods, such as low-pass sequencing (LP-WGS), remain relatively under-explored. Here, we investigated whether HRD signals can be successfully re-capitulated using LP-WGS technology and benchmarked our results against the current field standard (both tNGS and array genotyping). Methods: LP-WGS and tNGS was performed on 96 samples across a range of tumor types (including N=17 breast cancer samples). LP-WGS libraries were prepared using Nextera (Illumina) using 0.4ng DNA input, and sequenced to 0.5-1x coverage. tNGS libraries were prepared using TSO500 (Illumina) using 40-80ng input, and sequenced to >150x unique read coverage. Regions of CNV were estimated using CNVKit v0.9.6, and regions of LOH were estimated using a novel ancestry-aware method. Small variant detection was performed using the TSO500 v2.2.0.12 analysis pipeline. SNP array analysis of 12 tumor samples using Oncoscan (ThermoFisher) was also performed. CNV and LOH estimates derived from LP-WGS, TSO500 and SNP array data were calculated using Jaccard similarity, treating the SNP array data as the “ground truth”. Results: We benchmarked HRD signals derived from LP-WGS compared to the array-based calls and observed near perfect sensitivity for CNV gains across samples (Jaccard index=1.0), as well as for CNV losses between LP-WGS and SNP array (Jaccard index=1.0). We additionally noted that LPS-WGS calls captured both CNV loss and gains that were not detectable via the SNP array. For TAI, LP-WGS re-capitulated 7/10 unique signals also identified via array. We also observed high concordance between regions of the genome called LOH between both platforms (median Jaccard index=0.70, IQR=0.254), but noted an attenuation of sensitivity in samples where estimated tumor heterogeneity was high. We also evaluated LP-WGS CNV calls against the TSO500 assay and noted high sensitivity (96%; 94%) and specificity (89%; 91%) for both CNV gains and losses, respectively. Conclusions: Workflows incorporating LP-WGS can support the detection of HRD genome-wide, paving the way for a more affordable assay that may help to inform clinical decision making in the future treatment of breast cancer.

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Long-term oncologic outcome of unselected triple-negative breast cancer patients according to BRCA1/2 mutations: a comprehensive single institution study

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Background Triple-negative breast cancer (TNBC) is known to have a higher risk of early recurrence and relatively low risk of late recurrence compared to luminal type breast cancer. Among all subtypes of breast cancer, TNBC is more likely to have BRCA1/2 germline mutation which showed prevalence rate from about 10% to 20% in previous reports. To date, there are only few studies about the effect of BRCA1/2 mutations on the long-term oncologic prognosis in TNBC patients. We analyzed long-term oncologic outcome in unselected TNBC patients according to BRCA1/2 mutations in a comprehensive single institution. Methods Among 11,994 patients who underwent primary breast cancer surgery at Samsung Medical Center (SMC) between June 2008 and January 2016, 1,628 (13.6%) were TNBC patients. Of those, patients with inadequate and unavailable samples at SMC biobank and patients with follow-up duration less than 12 months and who had distant metastasis at presentation were excluded from the study, and 953 patients were enrolled. A retrospective study was conducted and BRCA1/2 genetic testing was done with SMC biobank samples through Next Generation Sequencing (NGS). Results Among 953 unselected TNBC patients, 122 patients (12.8%) had BRCA1/2 mutations: 91 (9.5%) were in BRCA1, and 32 (3.4%) were in BRCA2. One patient had both BRCA1/2 mutations. BRCA1/2 carriers were more likely to have personal history of ovarian cancer (9.0% vs. 0.5%, $p < 0.0001$), family history of breast cancer and/or ovarian cancer (40.2% vs. 9.4%, $p < 0.0001$), bilateral breast cancer (4.9% vs. 1.2%, $p = 0.0105$), and higher nuclear grade (86.0% vs. 74.0%, $p = 0.0250$). The median follow-up duration was 80.9 months. There were no significant differences in disease-free survival (DFS), distant metastasis-free survival (DMFS), overall survival (OS), and breast cancer-specific survival (BCSS) ($p = 0.375$, 0.268, 0.413, and 0.133, respectively) between BRCA1/2 carriers and non-carriers. However, BRCA1/2 carriers showed significantly worse contralateral breast cancer (CBC)-free survival than non-carriers ($p < 0.0001$). Sixty and 120-months cumulative recurrence rate were 18.5% and 31.2% for BRCA1/2 carriers versus 19.3% and 22.7% for non-carriers ($p = 0.834$ and 0.136, respectively). However, cumulative recurrence rate at 150 months showed absolute but not statistically significant difference between BRCA1/2 carriers and non-carriers (36.2% versus 23.5%, $p = 0.080$). Cumulative CBC recurrence rate on 60, 120- and 150-months estimates were 6.7%, 18.7% and 25.5% for BRCA1/2 carriers versus 1.1%, 2.7% and 5.2% for non-carriers which showed statistically meaningful difference ($p = 0.025$, 0.006 and 0.018, respectively). Sixty months, 120- and 150-months cumulative expire rate were 11.2%, 15.6% and 27.7% for BRCA1/2 carriers versus 14.3%, 20.7% and 20.7% for non-carriers ($p = 0.319$, 0.202 and 0.549, respectively). Discussion In this unselected cohort of patients with TNBC, we found 12.8% (122 patients among 953) prevalence of BRCA1/2 mutations. The median follow-up duration was 80.9 months. There was no significant difference in DFS, DMFS, OS and BCSS by BRCA1/2 mutation status in long-term follow up. However, BRCA1/2 carriers showed significantly worse CBC recurrence rate at 60, 120- and 150- months. And also, BRCA1/2 carriers had 12.7% higher risk of recurrence than non-carriers at 150 months, which was not statistically meaningful but showed absolute difference. Among patients with CBC recurrence, 41.3% (12 patients among 29) were BRCA1 carriers, over 85% had TNBC type of recurred CBC and approximately 80% underwent chemotherapy. In conclusion, we demonstrated that CBC recurrence risk is relatively high in TNBC patients with BRCA1 mutation and showed high chance to receive chemotherapy. Therefore, long-term follow up and appropriate genetic counseling, risk assessment should be done properly for BRCA1/2 mutation carriers in TNBC patients.

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Adiposity and immune-related gene expression in the breast tumor microenvironment

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Background: Extreme adiposity has been associated with tumor progression and increased mortality after a breast cancer diagnosis, but the underlying mechanisms remain unclear. Pre-clinical and in vitro analyses suggest that higher levels of adiposity impair anti-tumor immunity, but studies in human breast cancer patients are lacking. Previously, we found that higher levels of subcutaneous adiposity had stronger associations with breast cancer outcomes than did higher levels of visceral adiposity or overall obesity measured by BMI, underscoring the

importance of measuring adipose tissue distribution as well as overall body size to understand the adiposity-cancer link.

Methods: We identified women with a first-primary, stage 2 or 3 invasive breast cancer diagnosed and treated at Kaiser Permanente Northern California between 2005 and 2015. Using diagnostic computed tomography scans collected as part of routine clinical care, we measured subcutaneous (SAT) and visceral adipose tissue (VAT) areas in cm² at the third lumbar vertebra. We calculated body mass index (BMI) from clinically-collected height and weight. We isolated RNA from 251 FFPE breast tumors collected at biopsy or excision; these were a preliminary, random sample within each immunohistochemical subtype groups from an ongoing study that will analyze 1400 breast tumors. We verified RNA quality prior to performing NanoString BC 360™ assays to calculate the PAM50 molecular intrinsic subtype and measure the expression levels of genes related to immune cell abundance and anti-tumor immune activity. Using linear regression models, we examined the mean change in log₂ gene expression (dependent variables) associated with each adiposity exposure (BMI, SAT and VAT as independent variables).

Results: Mean (SD) age at diagnosis was 56 (13); a majority of women were either overweight (BMI 25- < 30-kg/m²: 30%) or obese (BMI>30-kg/m²: 35%), and most were diagnosed with stage 2 (61%) vs. stage 3 (39%) breast cancer with representation from each PAM50 subtype: n (%) Luminal A, 46 (18%) Luminal B, 56 (22%), HER2-overexpressing 26 (27%), and 82 (33%) basal-like. In unadjusted analyses, expression of genes related to macrophages, PD-1 and TIGIT increased with increasing subcutaneous adiposity, whereas expression of genes related to mast cells decreased (see Table 1). We found a similar (though non-significant) pattern for BMI. Associations with increasing visceral adiposity were closer to the null. After adjusting for PAM50 subtype, age and stage at diagnosis, only the association of increasing subcutaneous adiposity with increasing PD-1 expression remained statistically significant.

Conclusion: Excess subcutaneous adiposity was associated with increased PD-1 expression, whereas excess visceral adiposity or obesity defined by BMI were not. These results from the first 251 samples of an ongoing study of 1400 tumors provide evidence from human breast cancer patients to demonstrate the importance of measuring body composition to assess adipose tissue distribution and support the hypothesis that excess adiposity impairs anti-tumor immunity.

Association of Adiposity Measures with Immune-Related Gene Expression in the Breast Tumor Microenvironment (n=251 patients with stage 2-3 breast cancer at Kaiser Permanente Northern California)

Association of Adiposity Measures with Immune-Related Gene Expression in the Breast Tumor Microenvironment
(n=251 patients with stage 2-3 breast cancer at Kaiser Permanente Northern California)

Outcomes: (component genes)	Exposures								
	Body Mass Index at diagnosis (per 5-kg/m ² increase)			Subcutaneous adipose tissue (per 1-SD [126 cm ²] increase)			Visceral adipose tissue (per 1-SD [80 cm ²] increase)		
	Beta	95% CI ¹	p-value	Beta	95% CI ¹	p-value	Beta	95% CI ¹	p-value
Immune-related signatures (component genes)									
Interferon Gamma Signaling (STAT1, CXCL9, CXCL10)	0.03	(-0.07, 0.13)	0.6	0.04	(-0.10, 0.17)	0.6	-0.05	(-0.19, 0.09)	0.5
Inflammatory Chemokines (CCL2, CCL3L1, CCL4, CCL7, CCL8)	-0.03	(-0.12, 0.07)	0.6	-0.02	(-0.15, 0.10)	0.7	-0.08	(-0.21, 0.05)	0.2
Macrophages (CD163, CD68, CD84)	0.06	(-0.01, 0.13)	0.089	0.09	(0.00, 0.19)	0.054	0.00	(-0.10, 0.10)	>0.9
Mast Cells (MS4A2, CPA3, HDC, TPSAB1)	-0.10	(-0.21, 0.00)	0.053	-0.09	(-0.23, 0.06)	0.2	-0.08	(-0.23, 0.08)	0.3
Major Histocompatibility Complex II (MHCII: HLA-DPA1, HLA-DPS1, HLA-DGE1, HLA-DRA, HLA-DRB1, HLA-DMA)	0.00	(-0.11, 0.10)	>0.9	0.04	(-0.10, 0.18)	0.6	-0.03	(-0.19, 0.12)	0.7
Programmed Death-1 (PD-1: PDCD1)	0.09	(0.00, 0.18)	0.061	0.14	(0.02, 0.27)	0.023	0.03	(-0.10, 0.16)	0.7
Programmed death-ligand 1 (PD-L1: CD274)	0.06	(-0.03, 0.14)	0.2	0.07	(-0.04, 0.19)	0.2	-0.04	(-0.16, 0.09)	0.6
Programmed death-ligand 2 (PD-L2: PDCD1LG2)	0.01	(-0.07, 0.09)	0.8	0.02	(-0.09, 0.13)	0.7	-0.08	(-0.20, 0.03)	0.2
Transforming Growth Factor-β (TGF-β: TGFB1)	0.04	(-0.02, 0.10)	0.2	0.08	(0.00, 0.16)	0.062	0.01	(-0.08, 0.09)	0.9
T-cell immunoreceptor with immunoglobulin and ITIM domain (TIGIT)	0.08	(-0.03, 0.18)	0.14	0.14	(-0.01, 0.28)	0.060	-0.02	(-0.16, 0.13)	0.8
Regulatory T cells (Tregs: FOXP3)	0.03	(-0.05, 0.11)	0.5	0.05	(-0.07, 0.16)	0.4	-0.06	(-0.18, 0.07)	0.4

¹ 95% Confidence Interval

² A 1-unit increase represents a doubling in the log expression level of the genes in the signature

1 95% Confidence Interval

2 A 1-unit increase represents a doubling in the log expression level of the genes in the signature

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Variant Classification Discordance: A real-world experience of genetic test results in a community-based setting

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BACKGROUND Accurate interpretation of hereditary cancer germline genetic variants is critical to ensuring appropriate care. Myriad Genetics has developed tools that are instrumental in the accurate classification of variants, including a previously described history-weighting algorithm (Pheno), mutation co-occurrence statistical analysis (MCO), and in trans haplotype analysis. Differences in classification are known to occur among commercial testing laboratories, however the rate at which a single provider may observe variants with a different classification has not been reported. Here, we compared genetic test results from multiple laboratories ordered by a single surgical community-based practice with the classifications from Myriad's testing laboratory. **METHODS** Variants initially reported as a "variant of uncertain significance" (VUS) on hereditary cancer test results from multiple commercial laboratories ordered by a single surgeon at a community-based, comprehensive breast center from June 2013 to May 2021 were evaluated and compared to the classifications from Myriad. In total, 212 variants were submitted for comparison. After review, 42 variants were excluded because they had not been observed previously in Myriad-tested patients. Therefore, 170 variants were eligible for comparison. Variants were classified as pathogenic/likely pathogenic, VUS, and benign/likely benign for comparison. Descriptive statistics were used for analysis. **RESULTS** Discordant classification was observed between Myriad and other testing laboratories for 28.2% (48/170) of the variants compared. Initially, all 170 variants were classified and reported by other testing laboratories as VUS, however, 15 variants (8.8%) were subsequently reclassified by other testing laboratories (N=13 were reclassified as benign/likely benign; N=2 were reclassified as pathogenic/likely pathogenic). Among all variants compared, 23.5% (40/170) were definitively classified by Myriad as benign/likely benign. For 90.0% (36/40) of these variants, evidence driving the classification relied upon Pheno (32 variants), MCO (4 variants), and in trans haplotype analysis (8 variants), with some variants having multiple lines of evidence. Other in-

house specific rules were used for the remaining classifications (4/40;10%). Fifty-five percent (22/40) of the discordant classifications were seen in high-risk genes including APC, BRCA1/2, MLH1, MSH2, MSH6, PMS2, PALB2 and STK11, and 45% (18/40) were in moderate-risk genes including ATM, BARD1, BRIP1, CHEK2, and RAD51C. Of the 13 variants reclassified by other testing laboratories as benign/likely benign, six were classified as VUS by Myriad. Notably, two variants classified by Myriad as VUS were reclassified by other laboratories as pathogenic/likely pathogenic. CONCLUSIONS These data indicate that even in a single practice, significant discordance in variant classification exists based on the chosen laboratory. Myriad definitively classified nearly one-quarter of variants classified as VUS by other laboratories, likely due to the use of Myriad's laboratory-developed classification tools. The degree of discordance observed here reflects the need for continuous laboratory investment in variant classification tools and evaluation of genetic variants, enabling physicians and patients to receive accurate results to facilitate appropriate medical management decisions.

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5:00 PM - 6:15 PM

P5-03-04

PIK3CA mutation prevalence in hormone receptor positive breast cancer patients in United Arab Emirates

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Background: The Phosphatidylinositol-4,5-bisphosphonate 3-kinase catalytic subunit alpha (PIK3CA) gene is mutated in about 30-40% of hormone receptor positive/human epidermal growth factor receptor 2 negative (HR+/HER2-) breast cancer (BC) patients. For HR+/HER2- advanced breast cancer patients with disease progression following endocrine-based therapy, the NCCN guideline recommends testing for PIK3CA mutations with tumour or liquid biopsy to identify suitable patients for targeted therapy with alpelisib, an oral α -specific PI3K inhibitor in combination with fulvestrant. The primary objective of this study was to evaluate the proportion and distribution of PIK3CA mutational landscape of HR+ve BC patients at the largest cancer centre in the United Arab Emirates (UAE). Material and methods: Retrospective review of consecutive HR+ve BC patients at Tawam Hospital for whom PIK3CA testing was requested. DNA was extracted from the samples and a targeted resequencing assay was used for mutation detection in exons 7, 9 and 20 of the PIK3CA gene. Sequencing was carried out using the Next Generation Sequencing platform Ion GeneStudio S5 Prime System with a detection limit of 2-5% of the mutant allelic content. Results: 124 patients with HR+ve BC were enrolled in the present study. The pathology samples were considered unsuitable/unsatisfactory in 18

cases. The median age was 51.5 years (range 31-90). All patients were female, 54% were post-menopausal and 49% presented with de-novo metastatic disease. Of the 106 eligible patients, PIK3CA mutations were detected in 33 (31%) patients, the most common being H1047R (45%) and E545K (30%) mutations in exons 20 and 9, respectively. Other less common mutations included C420R mutations (6%) in exon 7, E542 (6%) in exon 9 and H1047Y (3%) in exon 20. 9% of patients had more than one hotspot mutations, primarily in exons 9 and 20. Of the 12 HER2 +ve patients tested, 3 had PIK3CA mutations, most commonly the H1047R mutation in exon 20. Conclusion: The prevalence of PIK3CA mutations and the presence of most common hotspot mutations in exons 20 and 9 was consistent with prior published studies. The clinical relevance of PIK3CA mutations in HER2 +ve BC patients needs further assessment.

Disclosure(s):

Fathi Azribi, MD: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); BMS: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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P5-03-05

Distinct molecular differences between African American/Black and White women with Triple Negative Breast Cancer

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Introduction: Triple-negative breast cancer (TNBC) is an aggressive disease that lacks well-defined molecular targets. It accounts for 15-20% of all breast cancers and disproportionately affects women of color due to both limited access to treatment and genetic variation. Recent studies identified BRCA1(or 2) and the PIK3CA/AKT1/PTEN axis as targets for treatment, but these studies neglected to account for genetic variations between race. Here, we present molecular differences between African American/Black (AA) and White (W) women with TNBC to highlight the importance of accounting for race to develop effective therapy and improve long-term outcomes. Methods: This study utilized the TCGA Firehose Legacy Breast Carcinoma dataset on cBioPortal. Subjects with breast cancer and negative ER, PR, and HER2 scores were stratified into AA (n=32) and W (n=69) subgroups. Data was analyzed to compare the most altered genes, copy number variation (CNV), and survival rates between the subgroups. The logrank test was used to obtain the hazard rate. The GISTIC2 model was used to assess CNV and G-scores (G; amplitude of aberration x frequency of occurrence). Results: The main genetic differences were in PIK3CA and BRCA1(or 2) genes. PIK3CA was detected as one of the ten most altered genes in TNBC, but this alteration was found in less than 10% of the TNBC cases. Of the 10%, PIK3CA was altered in 19% of W and 9% of AA subgroup. BRCA1(2) were altered in 10%(7%) of W but 0%(3%) of AA. Additionally, structural differences in chromosomes contributed to different survival outcomes. Both groups had co-amplification in 8q, but a significant hazard rate difference ($z = 5.32, p < 0.001$) was found for the W compared to the AA for the MYC gene. Further, the W had significantly higher amplification at 3q ($G = 0.8$ in W; 0.45 in AA). It is important to note that the PIK3CA gene lies in the 3q.26 region, meaning this gene is amplified significantly in the W subgroup. The AA group had a significant deletion at 8p.23 ($G=0.5$ in W; 0.8 in AA). Deletion of 8p causes MYC amplification, a targetable alteration. Conclusion: Our analysis reveals critical differences between AA and W subgroups with TNBC. Thus, it is clear that targeting the PIK3CA or BRCA1(2) gene benefits the W more than the AA

population. To alleviate the disproportionate burden that AA women with TNBC face, more effort must be geared to find solutions specific to the AA subgroup. A greater sample size will help determine whether MYC amplification is unique to the AA subgroup, and if so, it could be targeted to improve outcomes of AA women with TNBC. Nevertheless, more data and research is needed to understand causes and decrease the rate of disparate outcomes in patients with TNBC.

Disclosure(s):

So Hyeon Park, MS: No financial relationships to disclose

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P5-03-06

Effect of Sleep Traits on Subtype Specific Breast Cancer Survival: a Mendelian Randomization Analysis

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Background There is increasing interest in the relationship between sleep traits and both quality of life and survival in breast cancer. Recent work has found that oestrogen receptor positive (ER+) tumour cells are more likely to spread, via the circulation, at night than in the morning, providing support for a potential role of sleep characteristics influencing metastasis and therefore survival from breast cancer. The aim of this study was to investigate causal effects of sleep traits on subtype-specific breast cancer survival. **Methods** Single-nucleotide polymorphisms (SNPs) identified from GWAS associated with sleep traits with were used as a genetic instruments for Chronotype (N=697,828), Insomnia (N=1,331,010), Sleep Duration (N=446,118), Napping (N=452,633), Daytime sleepiness(N=452,071) and Ease of Getting up (N=461,658). All instruments were identified in data from UK Biobank, except chronotype and insomnia, which were identified in meta-analyses of UK Biobank and 23andme. For all instruments female-specific effect estimates were used. For these SNPs, summary statistics of their association with breast cancer survival were obtained from GWAS meta-analyses of European women from the Breast Cancer Association Consortium (BCAC), (N=91,686, with 7531 breast cancer specific deaths over a median follow-up of 8.1 years). To estimate the causal effect of the sleep traits on breast cancer survival, we applied two-sample MR for both overall and subtype-specific breast cancer (Luminal A-like, Luminal B-like, Human Epidermal Growth Factor 2 (Her2) positive, Her2 negative and triple negative (TNBC)). Further stratification by tumour characteristics at diagnosis and treatment received was also used. Sensitivity analyses were used to assess the robustness of main analyses to MR assumptions. **Results** For every hour increase in sleep duration, we observed worsening 5-year breast cancer specific survival in patients with ER+ tumours who received endocrine therapy (HR: 2.55, 95% CI: 1.10, 5.82) and for all patients receiving aromatase inhibitors (HR: 9.57, 95% CI: 1.61, 57.10). Conversely, improved 5-year survival was observed in patients with ER- tumours who received chemotherapy (HR: 0.30, 95% CI: 0.10, 0.87) and all patients receiving taxanes (HR: 0.23, 95% CI: 0.05, 0.98). We also observed that an increase in daytime sleepiness improved 15-year survival in patients both overall (HR: 0.34, 95% CI: 0.14, 0.80) and with lymph node negative tumours at diagnosis (HR: 0.12, 95% CI: 0.02, 0.64). Detailed sensitivity analyses are ongoing. **Conclusions** The current study uses a causal approach to identify potential effects between sleep patterns and breast cancer survival and confirms the previously observed relationships with increased sleep duration and worse survival in ER+ breast cancer. The

reasons for opposite effects seen in those with ER- and those receiving taxanes needs further mechanistic work. Although the improved survival in relation to increased daytime sleepiness appears to be in-keeping with previous findings, this may largely reflect shorter sleep duration. Further work accurately characterising sleep quality, rather than duration in those with breast cancer, examining the effects on quality of life and survival and establishing mechanisms are needed.

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Rebecca Richmond, n/a: No financial relationships to disclose

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P5-03-07

Prevalence of Pathogenic Variants in Cancer Predisposition Genes in Women with Young Onset Breast Cancer

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Introduction: Approximately 5% of breast cancers are diagnosed in women 40 years of age or younger. Known risk factors for young-onset breast cancer are few and can only account for a very small proportion of cases. In this study, we evaluated the contribution of mutations in 24 breast cancer predisposition genes in unselected Canadian women diagnosed with breast cancer at age 40 or younger. Methods: This study is a sub-study of the larger Reducing the bUrden of Breast cancer in Young women (RUBY) Study. In the RUBY study, women diagnosed with breast cancer at the age of 40 years or younger are recruited at the time of diagnosis from 33 centres across Canada. Participants in RUBY provided detailed demographic and clinical data, in addition to provision of serial biospecimens. Participants could elect to consent into the genetics substudy, and have genetic testing performed for pathogenic variants in 24 breast cancer predisposition genes, including ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, FAM175A, MLH1, MRE11, MSH2, MSH6, NBN, PALB2, PMS2, PTEN, RAD50, RAD51C, RAD51D, RECQL, STK11, TP53 and XRCC2. Sequencing was performed and all potentially pathogenic variants were confirmed with conventional Sanger sequencing. Pathogenic and likely pathogenic mutations were reported for all 24 genes. CanRisk scores for likelihood of having a pathogenic variant in 8 cancer predisposition genes (BRCA1 BRCA2, PALB2, CHEK2, ATM, RAD51C, RAD51D, and BRIP1) were generated for each participant. Results: 714 women consented and genetic testing was performed on the

blood samples provided as a component of the RUBY study. The mean age of the participants was 35.8 years (range 23-40 years), and the mean CanRisk score was 13.7 (range 2.3-98.0). Overall, 150 pathogenic mutations (21.0%) were detected in 147 women (three participants had mutations in two genes). The most common pathogenic variants detected were in BRCA1 (48), BRCA2 (40), CHEK2 (24), ATM (10), and PALB2 (9), representing 87.3% of all pathogenic variants identified. The mean CanRisk score was 28.8% (range 3.2-98.0%) for those identified with a pathogenic variant compared to 9.6% (range 1.0-88.9%) for those with a negative result ($p < 0.0001$). The prevalence of pathogenic variants was 32.9% for women age 20-30 years, 27.5% for 31-35 years, and 16.7% for 36-40 years. Conclusions: Twenty-one percent of women with breast cancer at age 40 or younger had a pathogenic variant in a breast-cancer predisposition gene. The great majority of these pathogenic variants were found in genes (BRCA1, BRCA2, CHEK2, PALB2) for which there are validated breast cancer treatment recommendations. All women with young-onset breast cancer should be offered germline genetic testing at the time of breast cancer diagnosis to make informed surgical and medical treatment decisions.

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Joint associations of mammographic breast density and obesity on the presence of crown-like structures in the breast adipose tissue of breast cancer patients

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Background: Obesity is an established risk factor for postmenopausal breast cancer and is associated with poor outcomes. Accumulating evidence suggests crown-like structures in the breast adipose tissue (CLS-B), a marker of local inflammation, play a role in explaining the obesity-breast cancer association. However, it is unknown whether breast tissue composition (i.e., the amount of fibroglandular tissue in the breast relative to fat) is related to CLS-B.

Objective: We evaluated whether breast tissue composition, as reflected by mammographic breast density, is associated with breast adipose tissue inflammation, as indicated by the presence of CLS-B, and whether the combination of breast density and obesity increases the presence of CLS-B among newly diagnosed breast cancer patients.

Methods: We examined the presence of CLS-B, detected by CD68 immunohistochemistry, in breast adipose tissue obtained via mastectomy from a quadrant uninvolved by tumor among 254 women with stage I–III breast cancer treated at Emory University Hospitals (2007–2012). Patient characteristics, including mammographic breast density (assessed on a mammogram up to 5 years before breast surgery) and body mass index (BMI) at diagnosis, were abstracted from electronic medical records. Mammographic density was assessed using the Breast Imaging Reporting and Data System (BI-RADS) density classification (1=almost entirely fat; 2=scattered fibroglandular densities; 3=heterogeneously dense; and 4=extremely dense); density was further categorized as fatty (BI-RADS 1-2) and dense (BI-RADS 3-4). Age and multivariable (MV)-adjusted logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the independent and joint associations of breast density (dense vs. fatty) and obesity (BMI ≥ 30 kg/m² vs. < 30 kg/m²) on the presence of CLS-B. Multivariable models adjusted for age (continuous, years) and parity (nulliparous, parous) with mutual adjustment of BMI (continuous, kg/m²) or mammographic breast density (dense, fatty) depending on the model.

Results: Women with obesity were more likely to have fatty breasts than women without obesity

(52% vs. 27%). Obesity was strongly associated with the presence of CLS-B in age-adjusted (OR=3.11, 95% CI: 1.79, 5.48) and multivariable models (MV-OR=3.70, 95% CI: 1.96, 7.15). There was no apparent association between dense breast tissue and presence of CLS-B in the age-adjusted model (OR=1.04, 95% CI: 0.59, 1.85). After additional adjustment for BMI and parity, we noted that women with dense breasts had higher odds of having CLS-B compared to those with fatty breasts (MV-OR=2.13, 95% CI: 1.07, 4.41). MV-ORs from the joint model (common referent: not obese, fatty breasts) were 1.54 (95% CI: 0.62, 4.24) for women without obesity but with dense breasts, 3.18 (95% CI: 1.15, 9.56) for women with obesity and fatty breasts, and 6.24 (95% CI: 2.23, 19.2) for women with obesity and dense breasts.

Conclusions: Our findings suggest that dense rather than fatty breast tissue is associated with breast adipose tissue inflammation among women with breast cancer. Results of the joint analyses suggest obesity is more strongly predictive of CLS-B presence than breast density. However, density may be an important risk factor for CLS-B among women without obesity while patients with obesity and dense breast tissue are the most likely to have CLS-B present. Future studies may consider the mechanisms by which density leads to increased presence of CLS-B.

Joint Associations Table

Table 1. Joint associations between mammographic breast density (MD) and body mass index (BMI) on the presence of crown-like structures in breast adipose tissue (CLS-B) among 254 women diagnosed with invasive breast cancer (stage I-III) at Emory University between 2007 and 2012

Characteristic	Total N	N with CLS-B	Unadjusted		+Age		+Age, Parity	
			OR	95% CI	OR	95% CI	OR	95% CI
Combined MD¹ & BMI²								
Fatty & not obese	44	8	1.00	—	1.00	—	1.00	—
Dense & not obese	121	28	1.35	0.59, 3.43	1.48	0.63, 3.81	1.54	0.62, 4.24
Fatty & obese	46	20	3.46	1.36, 9.49	3.50	1.37, 9.63	3.18	1.15, 9.56
Dense & obese	43	22	4.71	1.84, 13.10	5.00	1.94, 14.0	6.24	2.23, 19.20

Abbreviations: BMI=Body mass index; CI=Confidence interval; CLS-B=Crown-like structures in breast adipose tissue; MD=Mammographic density
¹Fatty= BI-RADS classifications (1) almost entirely fat and (2) scattered fibroglandular densities; Dense = BI-RADS classifications (3) heterogeneously dense and (4) extremely dense
²Not obese = BMI <30 kg/m² at diagnosis; Obese = BMI ≥30 kg/m² at diagnosis

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Maret L. Maliniak, MPH: No financial relationships to disclose
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Cell composition changes in healthy breast tissue is associated with advancing age and epigenetic age acceleration

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Introduction: Risk factors for breast cancer include advancing age, lifetime estrogen exposure, and breast density. DNA methylation-based estimates of age are elevated in breast tissue of healthy women compared with paired blood samples, and the degree of age acceleration is associated with lifetime estrogen exposure. However, no prior work has examined cell compositional changes associated with breast epigenetic aging. In this study we estimated the abundance of different cell types in healthy breast, computed using gene expression data, and

investigate cell composition changes that accompany advancing chronologic age and breast epigenetic age acceleration. Methods: DNA/RNA were extracted (AllPrep, Qiagen) from breast tissue specimens from 192 healthy women aged 19-90 years who donated breast tissue to the Susan G. Komen Tissue Bank at the Indiana University Simon Comprehensive Cancer Center. Transcriptome analysis was performed using the QuantSeq 3'mRNA-SeqFWD kit to generate RNA sequencing libraries. DNA methylation age was estimated using beta-values from Illumina EPIC 850K array platform. Age acceleration is defined using the residual of a linear regression of methylation age on chronologic age. Cell deconvolution was performed using CIBERSORTx to estimate the abundance of adipocytes, luminal epithelial cells, basal myoepithelial cells, vascular endothelial cells, lymphatic endothelial cells, immune cells (dendritic cells & macrophages), pericytes & smooth muscle cells, and fibroblasts. We examined cell composition changes with chronologic age, and with age-adjusted measures of acceleration in 6 epigenetic clocks: the Horvath Pan-tissue, Hannum, Phenotypic, Grim, Skin & Blood, and Epigenetic Pacemaker clocks, as well as the DNA methylation-based estimate of telomere length, DNAmTL. Results: Advancing chronologic age was associated with an increase in the imputed proportion of adipocytes ($R=0.40$, $p<0.0001$), vascular endothelial cells ($R=0.23$, $p=0.0033$), and immune cells (dendritic cells & macrophages) ($R=0.29$, $p=0.00016$), and a decrease in the proportion of luminal epithelial cells ($R=-0.43$, $p<0.0001$), and basal myoepithelial cells ($R=-0.27$, $p=0.00047$). Epigenetic age acceleration was significantly associated with increases in proportions of luminal epithelial cells ($p<0.0001$ for age-adjusted Hannum, Phenotypic, Grim, and Skin & Blood clocks, $p<0.05$ for Pan-tissue) and basal myoepithelial cells ($p<0.0001$ for Phenotypic and Skin & Blood clocks), and decreased proportions of adipocytes and vascular endothelial cells ($p<0.0001$ for Hannum, Phenotypic, Grim, and Skin & Blood clocks, $p<0.05$ for Pan-tissue). Conclusion: Using gene expression data in healthy female breast tissue, we identified significant changes in cell-type-specific abundance that accompany advancing chronologic age, with an increase in adipocytes and immune cells, and a decline in luminal epithelial cells and basal myoepithelial cells. By contrast, epigenetic age acceleration in breast tissue is associated with decreasing proportions of adipocytes and vascular endothelial cells and a rise in basal myoepithelial cells and luminal epithelial cells. Our findings suggest distinct patterns of cellular composition changes that accompany normal aging compared with accelerated aging in breast tissue.

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The impact of single nucleotide polymorphisms on return-to-work after taxane-based chemotherapy in breast cancer

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Background Return-to-work (RTW) after breast cancer may be challenging for breast cancer survivors, especially those who experience adverse effects. Neuropathies are common adverse effect of taxane-based chemotherapy. Single nucleotide polymorphisms (SNPs) in genes related to taxane metabolism and transport, neural function, and neural- or DNA-repair may influence the risk of taxane-induced adverse effects, potentially impacting patient recovery and RTW. We examined the association of such SNPs with RTW in premenopausal breast cancer survivors. Methods We used Denmark's nationwide population-based health registries to ascertain data on premenopausal women aged 18–55 years diagnosed with non–distant

metastatic breast cancer during 2007–2011, who were candidates for adjuvant combination chemotherapy including cyclophosphamide and docetaxel. Only women employed at diagnosis were included. We collected archived tumor tissue from nationwide pathology departments and genotyped 26 SNPs in 20 genes using TaqMan assays. For each SNP, we categorized the women as wildtype, homozygote or heterozygote. Follow-up continued from the date of primary surgery to the first of RTW (defined as 4 consecutive weeks of work), recurrence, maternity leave/childbirth, other malignancy, retirement, death, emigration or 25th September 2017. We computed the cumulative incidence of RTW and used Cox regression models to calculate unadjusted hazard ratios (HRs) and 95% confidence intervals (CIs) of RTW. Results We included 1,963 women. Women who were homozygotes for the phase 1 metabolizer CYP3A5 rs776746 (n=15) had lower cumulative incidence of RTW than wildtypes (n=1,600) and heterozygotes (n=249), 7%, 25% and 17% at six months, 57%, 87% and 88% at two years, and 82%, 94% and 94% at end of follow-up, respectively. Compared with wildtypes, CYP3A5 rs776746 homozygotes had delayed RTW throughout follow-up (HR 0-10 years: 0.48, 95% CI: 0.26, 0.86). No other SNPs were associated with RTW. Conclusions Among 26 SNPs, CYP3A5 rs776746 was associated with delayed RTW after breast cancer among premenopausal women. Our findings may help identify women at risk of a poor clinical course, who may benefit from enhanced supportive care during treatment and follow-up.

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DNA repair genes are more frequently mutated in non-white populations of metastatic breast cancer (MBC) patients

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Background: Although improvements in detection, therapeutic development and molecular profiling have decreased MBC mortality over the last twenty years, clinical outcomes are not being equally realized among all patients. Representation and enrollment into clinical trials are often not reflective of the general MBC population in terms of race and ethnicity, with Black and Hispanic patients being largely and often underrepresented. Not only does this imbalance translate into overall access to novel agents, but the lack of understanding of therapeutic efficacy in minority populations and tumor-based molecular differences reduce the use of truly personalized treatments for these groups. There is an opportunity to improve clinical outcomes for all patients with MBC, starting with a better understanding of the degree of any potential differences in underlying tumor molecular biology between racial groups. Methods: We utilized data from two cohorts of patients whose tumors underwent molecular profiling to examine differences in the frequency of genetic mutations across racial groups with MBC. The first cohort included 856 MBCs whose genomic profiles were retrieved from the AACR Genomics Evidence Neoplasia Information Exchange (GENIE) publicly available database. The second cohort included a separate set of 91 patients with MBC from an ongoing precision medicine program sponsored by the Side-Out Foundation (SOF). While the GENIE data were collected at 19 large academic cancer centers, the SOF data are derived from patients treated in the community setting. We compared the relative distributions of age and reported ethnicity between datasets, and compared the 20 most frequently mutated genes in each racial group across datasets. The analysis across races included 73 genes that were examined for differences in mutation frequency using Fisher's Exact test and Pearson Chi-Square test ($p <$

0.05 uncorrected). Results: Although the GENIE set was significantly larger, race distribution was not statistically significant across the two populations. The combined populations included 831 white patients (88.4%), 43 Black patients (4.6%), 30 Asian patients (3.2%), and 35 Hispanic patients (3.7%). The age of initial (59.61) and metastatic (61.19) diagnosis was older in the SOF population compared to the GENIE population (48.81, 53.14; $p < 0.001$). Hispanic patients (46.92) were diagnosed with MBC at a younger age compared to White patients (53.78; $p < 0.001$). Of the 73 genes analyzed, 11 genes were found less frequently mutated in whites compared to non-whites including, NTRK1, SDHA, MSH6, TCF3, FANCC, GNAS, COP1, RECQL4, WRN, BCL6, and U2AF1. When the same 73 genes were examined for differences across racial groups, alterations of 22 genes reached statistical significance. The gene(s) with the largest difference compared to white patients were RECQL4 in black patients (13.95% vs 5.29%; $p = 0.019$), WRN in Asian patients (16.63% vs 2.53%; $p < 0.001$), and RECQL4 and ERBB2 in Hispanic patients (16.13% vs 5.29%; $p = 0.019$, $p = 0.020$). Of the 22 genes that were more frequently altered in the non-white population, 6 have roles in DNA repair including RECQL4, WRN, ERCC2, BLM, MSH6, FANCC. 4/22 are receptor tyrosine kinases (RTKs), including NTRK2, RET, ERBB3, and ERBB2, and 3/22 have roles in immune function, including BCL6, CIITA, and TLR4. Conclusion: Analysis of genomic alterations derived from 2 independent real-world molecular profiling-based cohorts identified in non-whites MBC patients a set of candidate “actionable” genes involved in DNA damage repair, RTK expression, and immune function. Although these results require further validation, considering the relatively small samples sizes of the non-white populations, these findings may provide actionable targets for non-white patients with MBC that could be utilized in future trials.

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Circular RNAs express heterogeneously across different breast cancer subtypes and correlate with invasive disease-free survival

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Background: Circular RNAs (circRNAs) are a large class of RNAs derived from back splicing and subsequent circularization of precursor mRNAs. Due to their circular structures, circRNAs are protected from exonuclease-induced degradation and are thereby comparatively more stable than linear RNAs. circRNAs have been implicated in the progression of multiple types of cancers but few studies have systematically examined how circRNAs associate with different subtypes of breast cancer and prognosis. Methods: We conducted a nested case-control study of prospectively ascertained participants in the Chicago Multiethnic Breast Cancer Cohort (ChiMEC), in which patients without recurrence were matched with patients with recurrence on time to recurrence, age of diagnosis, tumor stage, and clinical subtype. We performed whole exome capture RNA sequencing on tumor samples that passed quality control. We then used CIRIquant to identify circRNAs by aligning back-splice junction (BSJ) reads to pseudo-circular

reference sequences and retained circRNAs that had a BSJ read count of 2 or greater in at least 5 patients. After normalization using the trimmed mean of M-values method, we used edgeR to model circRNA expression via a negative binomial distribution and performed differential expression (DE) analyses of circRNAs by ER and HER2 status, as well as between Black (self-reported) and White patients. Furthermore, we conducted survival analyses for each circRNA using Cox proportional hazards models to assess how the expression of each circRNA associated with survival outcomes of invasive disease-free survival (IDFS) and overall survival, while adjusting for age at diagnosis, stage, and HER2 status. Results: A total of 123 of 126 sequenced patients were included in the analysis, including 56 Black patients, 59 White patients, and 8 patients from other racial groups. The mean age of diagnosis was 51.9 years of age (SD 13.2) with 68% ER+, 48% PR+, and 30% HER2+ patients. We identified 16,927 high-confidence circRNAs. In the crude DE analysis, we found 489 circRNAs differentially expressed between patients with ER+ compared to patients with ER- tumors and 33 circRNAs between HER2+ vs. HER2- at a false discovery rate of 0.05. After adjusting for race and grade, we discovered 187 circRNAs differentially expressed by ER status and 38 by HER2 status. In the DE analysis by race, we found 88 circRNAs that were differentially expressed between Blacks and Whites. After adjusting for grade, ER, PR, and HER2 status, 14 circRNAs remained significantly different between racial groups. After a median of follow up of 8 years, 41 patients died, 41 patients had invasive recurrent diseases, and 2 patients had second primary breast cancers, for a total of 57 events in the IDFS analysis. Because of the matching study design to limit the impact of known prognostic factors, none of known prognostic factors (stage, ER, PR, HER2, grade, and race) were statistically associated with IDFS. In the survival analyses, we discovered two circRNAs (hsa-GSK3B_0001 and hsa-CMPK1_0006) that met the Bonferroni threshold for significance for their associations with IDFS but did not detect any circRNAs that were significantly associated with overall survival after correction for multiple testing. Discussion: This preliminary study demonstrates that multiple candidate circRNAs were differentially expressed between BC subtypes and racial groups, and several circRNAs were associated with IDFS. Future studies are warranted to validate our findings and cement the portability of these circRNAs as prognostic biomarkers across populations.

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Prevalence of germline BRCA mutations in unselected Korean patients with HER2-negative breast cancer: A Prospective cohort study

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Backgrounds Since OlympiAD study, National Comprehensive Cancer Network guideline recommends assessment of germline BRCA1/2 mutation in all patients with recurrent or metastatic breast cancer to identify candidates for PARP inhibitor therapy, which is not always possible in clinical practice due to limited resources for testing. Data on the prevalence of gBRCA mutation is still lacking, especially in patients with non-high risk for hereditary breast and ovarian cancer syndrome. In this study, we investigated prevalence of gBRCA mutation in unselected Korean patients with HER2-negative advanced BC in a prospective cohort and analyzed oncologic outcome. Methods Eligible patients were diagnosed with HER2-negative advanced BC and had initiated palliative systemic treatment. Peripheral blood was prospectively drawn from each patient and gBRCA mutation status was assessed by next generation sequencing using NGeneBio BRCAaccuTest®. In 100 patients, somatic mutations including BRCA1/2 from tumor tissue were investigated using targeted panel sequencing. To estimate the prevalence of gBRCA mutation with margin of error to be no more than $\pm 4\%$ at the 95% confidence interval in a population size of 20,000, 583 patients were to be enrolled. Results A total of 583 patients were enrolled between Oct 2019 and Mar 2022, and the

prevalence of gBRCA mutation was analyzed in 570 patients, excluding ineligible patients. Median age was 54 years old (range 26-87) and 567 patients were female. 475 patients had HR+/HER2- BC and 94 patients had triple negative breast cancer (TNBC). The overall prevalence of gBRCA1/2 pathogenic mutation was 7.3% (42/570) in unselected patients. The prevalence of gBRCA1 mutation was 1.6%(9/570) overall, 0.8%(4/475) in HR+/HER2- BC, and 5.3%(5/94) in TNBC. The prevalence of gBRCA2 mutation was 5.8%(33/570) overall , 6.3%(30/475) in HR+/HER2- BC, 3.2%(3/94) in TNBC. Prevalence in low risk TNBC (>60 years at first BC diagnosis, no known family history of relevant cancer and unilateral breast cancer) was 10.5% (2/19, all 2 patients had gBRCA2 mutation). Prevalence in low risk HR+/HER2- (>40 years at first BC diagnosis, no known family history of relevant cancer and unilateral breast cancer) was 5.9% (18/307, 17 patients had gBRCA2 mutation). The overall prevalence of gBRCA1/2 pathogenic mutation in Korean patients with low risk HER2-negative advanced BC was 6.1%. The result of somatic mutation, treatment patterns and clinical outcome according to gBRCA1/2 mutation will be further analyzed. Conclusions The prevalence of gBRCA mutation among Korean patients with HER2-negative advanced BC classified as low risk (6.1%) in this study supports routine testing of gBRCA mutation in this population.

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P5-03-15

Application of 21-gene Breast Recurrence Score® assay to evaluate prognosis and benefit of adjuvant chemotherapy in BRCA1 and BRCA2 pathogenic variant carriers with early stage, estrogen receptor positive breast cancer

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Background: Minimal data exists for the utilization of the Oncotype Dx® assay specifically in breast cancers associated with BRCA1/2 pathogenic variants (PVs). It is unknown whether estrogen receptor positive (ER+) breast cancer associated with an inherited BRCA1 or BRCA2 (BRCA1/2) PV is more aggressive than disease seen in patients who do not carry an inherited PV, and whether there are differences between BRCA1 and BRCA2. In prostate cancer patients with inherited cancer predisposition due to a BRCA2 PV, more aggressive cancers are observed, which influences first-line treatment. Limited data exists for the optimal management of early stage ER+ breast cancer in BRCA1/2 PV carriers. Comparing Recurrence Score® (RS) results in ER+ breast cancer patients with an inherited BRCA1/2 PV (cases) versus matched patients who test negative for a PV in BRCA1/2 (controls) may inform whether biologically more aggressive breast cancer is seen in BRCA1/2 carriers and optimal treatment approaches. Methods: A retrospective case control study was performed to compare RS results in women with breast cancer with an inherited BRCA1/2 PV versus patients who tested negative for an inherited BRCA1/2 PV. Female breast cancer patients seen between 2005-2020 at NorthShore University Health System with ER+Her2- early stage invasive breast cancer with 0-3 lymph nodes who completed genetic testing for BRCA1/2 were eligible for enrollment. BRCA1/2 cases were defined as individuals with an inherited PV in BRCA1/2 and controls were negative for BRCA1/2 or other known breast cancer risk gene PVs tested. Subjects were excluded if they had neoadjuvant therapy (hormonal or cytotoxic chemotherapy). Eligible cases were matched to control patients by age, grade, and stage. The Recurrence Score result was obtained by

chart review; if not previously evaluated, Oncotype Dx assay was performed by Exact Sciences. Statistical analysis of the primary outcome used the paired t-test to determine mean difference in RS results between BRCA1/2 PV carriers and patients negative for a PV in BRCA1/2 using a 1:1 matched pairs design. Results: A total of 46 matched cases and controls were analyzed. Median age was 50 with a range of 28-74. Of the cases, 18 had a BRCA1 PV and 28 had a BRCA2 PV. Cases and controls were well matched for age (> 50 and ≤ 50); race, grade, stage, and progesterone receptor status. As expected, a higher number of BRCA1/2 carriers were treated with mastectomy while more of the controls received breast-conserving surgery. Chemotherapy was utilized more frequently in the cases (67.4%) versus the controls (54.4%). The average RS result was higher in the cases (27) than the controls (21.3) by a mean difference of 5.7 ($p = 0.0195$). Using Oncotype Dx cutoffs of low < 18 , intermediate 18-30 and high ≥ 31 , a statistically significant difference in RS result was noted in the cases versus controls. For cases in the highest risk group (Oncotype Dx ≥ 31), only 20% of their matches also had a score in the highest risk group while 35% had a score in the lowest risk group. Subgroup analysis showed that the cases had the largest difference in RS result from their controls in premenopausal women (age ≤ 50), BRCA1 carriers, and the node negative population. Conclusion We present one of the largest data sets available to date of a well-matched cohort of cases and controls which shows that BRCA1/2 PV carriers are more likely to have a higher Recurrence Score result than their matched controls when matched for age, grade, and stage. These findings suggest ER+ breast cancer in BRCA1/2 PV carriers is biologically more aggressive. Further investigation is warranted to evaluate how this important finding impacts adjuvant therapy recommendations for BRCA1/2 PV carriers.

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5:00 PM - 6:15 PM

P5-03-16

Changes in preferences for ovarian cancer prevention strategies during the COVID-19 pandemic: Results of a discrete choice experiment.

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Background: The COVID-19 pandemic influenced patient health care decisions, but there is little information about the pandemic's impact on decisions about cancer risk reduction. This includes women at elevated risk of breast or ovarian cancer considering risk-reducing salpingo-oophorectomy (RRSO), risk-reducing salpingectomy (RRS), or other preventive measures. During the pandemic patients needed to balance their concerns about cancer risk reduction with their risks associated with elective health procedures, a risk which changed as vaccines became available. Methods: To address the impact of the COVID-19 pandemic on cancer prevention decision making, we recruited N=396 pre-menopausal women with a personal history of breast cancer or familial history suggestive of increased breast and/or ovarian cancer risk between 4/2019 and 3/2022. We conducted a discrete choice experiment in which patients were asked to choose between two scenarios that specified type of surgery (RRSO, RRS vs. non-surgical surveillance), age of menopause (natural versus immediate), quality of menopausal symptoms (mild, moderate, severe), and risk of ovarian cancer, heart disease, or osteoporosis. Risk of ovarian cancer for the scenarios provided varied in discrete intervals from

0% to 40%. We examined temporal trends during the pandemic using interactions with time coinciding approximately with the beginning of pandemic, peak vaccination period, and the Omicron wave. Results: We identified significant temporal interactions on a woman's prevention decisions. In 2019, women at higher risk of ovarian cancer were more likely to choose prevention scenarios that favored lower ovarian cancer risk (odds ratio [OR] = 0.48; 95% CI = 0.37, 0.69 per 10% increase in ovarian cancer risk difference). This association decreased through the pre-vaccine period of 2020 by OR=2.61/month (95% CI = 1.21, 5.65). By June 2020, the effect of a 10% increase in ovarian cancer risk on intervention choice had attenuated substantially (OR=0.84, 95% CI 0.67, 1.00). By January 2022, the effect strengthened (OR= 0.69, 95% CI .49, .88), but had not reached pre-pandemic levels. Before 3/2020, natural age of menopause (versus immediate) had a strong impact on the choice of a scenario (OR=3.56, 95% CI 1.65-7.65). At the beginning of the pandemic, the effect was reduced by 0.47/month (95% CI 0.22-0.99). The rate of attenuation slowed over time, such that the effect of having a natural age of menopause on choice was OR= 1.56 (95% CI 0.65, 2.46) by January 2022. Tests for temporal interactions were statistically significant for both ovarian cancer risk and age of menopause. Conclusions: Our results suggest that over the course of the pandemic, women seemed more accepting of higher risks of ovarian cancer and immediate (post treatment) menopause when considering preventive options. There was an inverse U shape curve of the effect of ovarian cancer risk on choices over time (Figure A), but the strength of the relationship had not reached pre-pandemic levels by January 2022. This may reflect patient tolerance for side effects as the pandemic evolved. These results suggest that factors such as ovarian cancer risk and delay of menopause influenced personal prevention choices, but that these choices were influenced by events related to events that hallmarked the COVID-19 pandemic.

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P5-03-17

BRCA1/2 gene mutations in patients with high-risk breast cancer in a tertiary-level hospital in Guatemala

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Objectives, to establish the frequency of BRCA1/2 mutation rate in high-penetrance breast cancer susceptibility population. Methods Based on NCCN guidelines for testing criteria for high-penetrance breast cancer susceptibility genes genetic counseling was offered to 140 breast cancer patients in the hemato-oncology unit of Roosevelt Hospital at Guatemala City performing test with NGS and MLPA technology from 2019 to 2021. Results The overall BRCA1/2 mutation rate high-risk patients were 23% (33/140). Of the patients with mutations, 66.6% (22/33) had BRCA1 mutation, 33.3% (11/33) had BRCA2 mutation, of the mutated population the median age was 45 years. Regarding the phenotype in the mutated population, 75% were triple negative, 16% luminal and 9% with Her2 overexpression. Of the patients carrying the BRCA1 mutation, we identified the c.212+1G>A mutation in 40% of the patients, possibly a founder mutation. In the triple negative population and under 45 years of age, the percentage of patients with BRCA 1/2 mutation is 40.9 (88.8% BRCA1 and 11.1% BRCA2). Conclusions: we found a percentage of BRCA 1/2 mutations in the selected population (NCCN criteria) similar to that reported in other Latin American countries, highlighting the high percentage of BRCA mutations in women under 45 years with triple negative phenotype, previous reports have highlighted the frequency of the c.212+1G>A mutation of BRCA1 in breast cancer patient in Guatemala, in this study 40% of the BRCA1 mutations correspond to said mutation, considering it as a probable founder mutation.

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Co-occurring alterations in PALB2 germline carriers identified by liquid biopsy in patients with advanced breast cancer

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Introduction: PALB2 is a BRCA complex-interacting protein and has an essential role in homologous recombination and repair (HRR). PALB2 germline (gPALB2) mutations are found in 1 – 4% of breast cancer patients and can be incidentally identified by liquid biopsy testing. Recent data has shown the efficacy for PARP inhibitors (PARPi) in breast cancer gPALB2 carriers, highlighting the importance of understanding genomic drivers in this group of patients. Here we present the genomic landscape of patients with advanced breast cancer (aBC) with incidental gPALB2 mutations identified by liquid biopsy testing. Methods: Genomic results were queried for aBC patients who had Guardant360 (G360) testing as part of routine clinical care from October 2020 – March 2022. Eligible patients had must have a diagnosis of breast cancer and an incidental gPALB2 alteration identified on G360, defined by presence of ClinVar loss-of-function single nucleotide variant (SNV)/indel mutation. Co-occurring somatic alterations in these patients were then analyzed after removing synonymous and variants of uncertain

significance. Analysis of HRR-related alterations, such as loss of heterozygosity and/or copy number loss, was performed in a subset of patients. Clinical demographics and clinical status (newly diagnosed or progressing at the time of G360 testing), were extracted from test requisition forms. Results: A total of 48 patients had gPALB2 alterations: 60% had indels and 40% SNVs. gPALB2 variant allele frequencies (VAF) were >30% for all patients (median VAF: 49.7, range: 34.1-66.6). All patients were female with a median age of 59 years (range: 31-84); 29 (60%) were tested at progression whereas the rest were tested at diagnosis. 36 (75%) patients with gPALB2 had co-occurring somatic alterations across 23 genes. The most commonly mutated genes were TP53 (47%), ESR1 (23%), and PIK3CA (19%); other mutated genes had less than 7% frequency. Notably, 95% of patients with co-occurring ESR1 alterations and 70% found to harbor PIK3CA co-occurring alterations were tested at progression. Other clinically relevant findings include co-occurring somatic alterations in MTOR (4%) and HRR-related genes ATM, ARID1A, CHEK2, FANCA (4% each; one patient had both ATM and CHEK2 somatic alterations). No somatic BRCA1/BRCA2 alterations were identified in gPALB2 patients. For 33 (69%) patients with gPALB2, additional HRR-related biomarker analysis was performed resulting in identification of 3 (9%) patients with copy number loss, one who had CHEK2 and PALB2 single copy number loss, resulting in PALB2 biallelic loss. In the overall cohort, an additional 33 patients were identified with uniquely somatic PALB2 alterations. Conclusions: Carriers of gPALB2 alterations comprise a rare subset of aBC patients analyzed by liquid biopsy. These patients have co-occurring somatic alterations identified in genes that have been reported in published cohorts of aBC patients without gPALB2 alterations. Assessment of additional somatic HRR-related alterations may identify other patients with PALB2 findings who could benefit from PARPi. Clinical studies are needed to assess how patients with gPALB2 and co-occurring mutations may have altered response and/or resistance to therapies, including standard-of-care regimens and PARPi.

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P5-03-19

Frequency of germline TP53 p.R337H variant among women at risk of hereditary breast cancer in a public health system of Central-West of Brazil

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Background: Breast Cancer (BC) is one of the most common cancers diagnosed in Li-Fraumeni Syndrome (LFS). Most studies about the frequency of germline pathogenic variant (PV) TP53 p.R337H have been conducted in the South and Southeastern regions of Brazil reaching rates as high as 8% of detection. There is a lack of data on the frequency of this germline PV in other Brazilian regions, especially among patients without access to genetic tests. Objective: This study aims to evaluate the detection rate of TP53 p.R337H in patients (pts) at risk of hereditary breast cancer (HBC) and describe the clinical and demographic profile of the study cohort. Methodology: Hereditary cancer risk assessment based on the National Comprehensive Cancer Network Criteria (NCCN), version 1.2020, was performed in women with BC who were being followed in a public hospital (DF, Brazil) between January 2021 and January 2022. All pts eligible for germline genetic testing according to HBC NCCN criteria were referred for genetic counseling and genetic testing. For those patients who could not afford a comprehensive genetic test, a real time PCR test specifically searching for TP53 p.R337H variant was performed. In case of TP53 p.R337H detection in the proband, genetic counseling and familial variant testing were offered to family members. Results: Among 221 pts eligible for this study,

180 pts performed germline testing, including 100 pts tested only for the TP53 p.R337H variant (real-time PCR) and 80 pts performed out of pocket BC multigene panel testing (including TP53 sequencing). This cohort was mostly represented by pts from Central-West (47%) and Northeast (35%) regions of Brazil. The median age of BC diagnosis was 44 y.o. (18 - 78). Invasive ductal carcinoma represented 92% (n=203) of the tumors, 50% were ER/PR+ HER2-, 25% HER2 +, 25% ER/PR- HER2- (triple negative). Regarding stage at diagnosis, 59% (n=130) were stages IIB-IIIC and 13% IV. The detection rate of TP53 p.R337H was 1.1% (2/180). Among the pts who met the revised Chompret criteria for LFS, this frequency was 5% (2/40). One of them was diagnosed with a stage IIIB IDC ER/PR+HER2- at 28 y.o. and had no relevant family history of cancer. The other pt was diagnosed with a stage IV IDC ER/PR+HER2- at 44 y.o. and the family history revealed four sisters and one niece with BC, and one nephew with brain tumor at 4 y.o. The family members from these two families received genetic counseling and genetic testing. Cascade testing was able to identify 12 additional carriers. All carriers were referred for post-testing follow-up. Conclusion: According to these results, we expect to identify at least one p.R337H carrier in each 90 BC pts treated in the Federal's District Public Health setting who fulfill HBC NCCN criteria. In a limited resources setting, in Brazil, testing the TP53 p.R337H variant with PCR is a low-cost test that should be considered at least for pts that meet the revised Chompret criteria. The overall detection rate of TP53 p.R337H carriers was lower in comparison to other Brazilian studies from the South/Southeast of the country. Both cases identified in this cohort had advanced local disease or metastatic disease at BC diagnosis, raising the concern about the importance of LFS diagnosis, and high-risk surveillance and risk reduction strategies in this subgroup of pts. Despite the low detection rate of TP53 p.R337H in this cohort, there was a high familial impact through cascade testing.

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5:00 PM - 6:15 PM

P5-03-20

Mutations of TP53 and genes related to homologous recombination repair in breast cancer with germline BRCA1/2 mutations

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Background Germline mutations of breast cancer susceptibility gene BRCA1 and BRCA2 (gBRCA1/2) are associated with elevated risk of breast cancer in young women in Asia. BRCA1 and BRCA2 proteins contribute to genomic stability through homologous recombination (HR)-mediated double strand DNA break repair (DDR) in cooperation with other HR-related proteins. In this study, we analyzed the targeted sequencing data of the breast cancer patients with gBRCA1/2 mutations to investigate the landscape of HR-related gene mutations and their clinical implications. **Materials and Methods** Data of the breast cancer patients with pathogenic gBRCA1/2 mutations and qualified targeted next generation sequencing, SNUH FiRST cancer panel, were analyzed. Single nucleotide polymorphisms, small insertions and deletions were analyzed with functional annotations using ANNOVAR. HR-related genes were defined as ABL1, ATM, ATR, BARD1, BRCA1, BRCA2, CDKN1A, CDKN2A, CHEK1, CHEK2, FANCA, FANCD2, FANCG, FANCI, FANCL, KDR, MUTYH, PALB2, POLE, POLQ, RAD50, RAD51, RAD51D, RAD54L, and TP53. Mismatch-repair genes were MLH1, MSH2, and MSH6. Clinical data were analyzed with cox proportional hazard models and survival analyses. **Results** Fifty five Korean breast cancer patients with known gBRCA1/2 mutations and qualified targeted

NGS data were analyzed. Ethnically distinct mutations in gBRCA1/2 genes were noted, with higher frequencies of Val1833Ser (14.8%), Glu1210Arg (11.1%), and Tyr130Ter (11.1%) in gBRCA1 and Arg2494Ter (25.0%) and Lys467Ter (14.3%) in gBRCA2. Considering subtypes, gBRCA1 mutations were associated with triple-negative breast cancers (TNBC), while gBRCA2 mutations were more likely hormone receptor-positive breast cancers. At least one missense mutation of homologous recombination (HR)-related genes were observed in 44 cases (80.0%). The most frequently co-mutated gene was TP53 (38.1%). In patients with gBRCA1/2 mutations, however, genetic variations of TP53 occurred in locations different from the known hotspots of those with sporadic breast cancers. The patients with both gBRCA1/2 and TP53 mutations were more likely to have TNBC, high Ki-67 values, and increased genetic mutations, especially of HR-related genes. Survival benefit was observed in the TP53 mutants of patients with gBRCA2 mutations, compared to those with TP53 wildtypes. Conclusion Our study showed distinct genetic landscape of breast cancer patients with gBRCA1 and gBRCA2 mutations in the Asian populations. Further studies on precision medicine are needed for tailored treatments of patients with genetic diversity among different ethnic groups.

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5:00 PM - 6:15 PM

P5-03-21

A COMPARISON OF BREAST CANCER SURVIVAL ACROSS DIFFERENT TUMOUR BIOLOGY IN YOUNG WOMEN: A MULTICENTRIC DATABASE STUDY IN KLANG VALLEY, MALAYSIA

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Background: OBJECTIVE: This study aims to determine the 5-year overall survival of young breast cancer according to tumour biology in Malaysia. METHODOLOGY: Multicenter retrospective study with convenience sampling method used to recruit the patients. All young women aged 50years and below with breast cancer who underwent surgery/ under follow up from 1st January 2014 to 31st December 2017 in Hospital Tengku Ampuan Rahimah (HTAR), Klang, Hospital Selayang and Hospital Putrajaya were included. Categorical data were analyzed using Chi-Square analysis and Fisher's Exact Test. 5-year overall survival was calculated using Kaplan Meier. Cox Regression to estimate hazard ratio for mortality in patients with different tumour biology. Recurrence were analysed using Chi-Square analysis. RESULTS: A total of 360 patients were recruited predominantly within 41years to 50years of age (63.9%). The majority of the patients were Malays (66.4%). Most of the patients were in Stage II (39.4%) with a significant number of patients in Stage III and IV (25.0% & 26.4% respectively). 56.1% had tumour biology of Luminal A followed by Triple negative (21.7%), HER2 Enriched (12.2%) and Luminal B (10%). Kaplan Meier analysis showed that the 5-year overall survival was 58.3%. There were no statistical significance across the tumour biology subtypes. Among the tumour biology groups, Triple Negative had the highest probability of survival with 54.5%. CONCLUSION: We observed that Triple Negative had the highest probability of survival at 5years while Luminal B (HER 2 Positive) had the lowest probability. The 5-years overall survival was not statistically significant with accordance to locoregional recurrence rate and in different tumour biology. Keywords: Breast cancer, young women, tumour biology, overall survival, locoregional recurrence

Disclosure(s):

Mee Hoong See, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

P5-04-01

Screening Patterns of Mammography and Breast Magnetic Resonance Imaging Following Cancer Genetic Testing in an Integrated Health Care System

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Background

Patients at high-risk for breast cancer with genetic mutations are recommended to receive annual breast MRI in adjunct to annual mammography. Despite 15 years of clinical guidelines, uptake of annual breast MRI remains low. Further, little is known about screening patterns across genetic test results in patients tested for hereditary cancer susceptibility as part of usual care.

Methods

We conducted a retrospective cohort study in an integrated health system among women aged ≥ 18 years old, without prior breast cancer who had genetic testing for high penetrance hereditary cancer susceptibility genes between January 1, 2010 and December 31, 2018. Genetic test orders and results (pathogenic or likely pathogenic (P/LP) variant(s), negative, or variant of uncertain significance (VUS)) were obtained from health system administrative and laboratory data. Mammogram and breast MRI use data were extracted from electronic health records and claims data. To characterize screening patterns, we calculated average proportion of time covered (PTC) as the number of days covered by mammography and/or breast MRI divided by the number of days from screening eligibility until the earliest censoring event: end of observation period, reached age 75 years, breast cancer diagnosis, death, bilateral mastectomy, or disenrollment in the health system. Per National Comprehensive Cancer Network (NCCN) guidelines, women with P/LP variants in BRCA1/2, TP53, PALB2, CHEK2, ATM, and NF1 became eligible for screening on either the day they received their genetic test result or reached age eligibility and received one year of covered time for each mammogram or MRI imaging procedure received. Per Healthcare Effectiveness Data and Information Set (HEDIS) performance measures, all other women became eligible for screening at age 50 years and received two years of covered time for each mammogram received. Average PTC was calculated overall, by genetic test results, and by screening type. Poisson regression was used to determine the association between average PTC and patient-level factors (age at test, race/ethnicity, and genetic mutations) and guideline factors (recommended screening age state).

Results

Of 1,167 women meeting the inclusion criteria, 140 (12%) had P/LP in high penetrance breast cancer susceptibility genes (Table 1). Average PTC for individuals with a high penetrance susceptibility gene was 34.4% for MRI, 47.6% for mammogram, 63.2% for either MRI or

mammogram, and 19.0% for both screening tests. The average PTC for those who tested negative, had VUS only, and had P/LP variants in genes unrelated to breast cancer was 50.3%, 44.4%, and 40.6%, respectively. Poisson regression model showed that among those with P/LP variants in high penetrance breast cancer genes, average PTC for annual MRI was positively associated with recommended screening initiation age ≥ 40 years (incident rate ratio [IRR]=2.07, 95% confidence interval [CI]: 1.94-2.20), higher absolute lifetime risk of breast cancer (IRR=1.38, 95% CI: 1.31-1.49), being 40-59 years old at genetic testing (IRR=1.04, 95% CI: 1.01-1.06), and non-Hispanic White race/ethnicity (IRR=1.10, 95% CI: 1.06-1.14).

Conclusions

Use of breast screening in women who had a P/LP variant(s) in high penetrance breast cancer susceptibility genes was low and not consistent with clinical guidelines, but comparable to the use of screening in women with negative and VUS results. Our findings suggest the need to improve screening in high-risk women with known genetic mutations and women at average risk.

Table 1. Average PTC by NCCN and HEDIS recommendation.

Table 1. Average PTC by NCCN and HEDIS recommendation.

	MRI		Mammogram		MRI or mammogram		MRI and mammogram	
	N	PTC (Range)	N	PTC (Range)	N	PTC (Range)	N	PTC (Range)
NCCN								
Overall	129	34.4 (0-100.0)	118	47.6 (0-99.6)	118	63.2 (0-100.0)	118	19.0 (0-99.0)
<i>BRCA1</i>	55	34.7 (0-95.6)	49	47.1 (0-99.6)	49	72.9 (0-99.6)	49	18.1 (0-87.6)
<i>BRCA2</i>	48	31.9 (0-91.0)	43	47.9 (0-97.4)	43	61.8 (0-98.9)	43	17.7 (0-84.0)
<i>TP53</i>	3	6.4 (0-19.1)	3	19.0 (0-57.0)	3	25.4 (0-57.0)	3	0
<i>PALB2</i>	4	33.0 (0-85.0)	4	53.5 (0-88.1)	4	65.1 (0-90.5)	4	21.4 (0-58.4)
<i>CHEK2</i>	14	53.6 (0-100.0)	14	53.2 (0-99.0)	14	74.6 (0-100.0)	14	32.2 (0-99.0)
<i>ATM</i>	4	25.6 (0-62.8)	4	49.9 (0-84.5)	4	61.6 (0-95.9)	4	13.9 (0-51.5)
<i>NF1</i>	1	0	1	40.1 (NA)	1	40.1	1	0
HEDIS								
Overall	-	-	608	48.9 (0-100.0)	-	-	-	-
Negative	-	-	475	50.3 (0-100.0)	-	-	-	-
VUS	-	-	104	44.4 (0-100.0)	-	-	-	-
Other	-	-	29	40.6 (0-100.0)	-	-	-	-
P/LP	-	-	-	-	-	-	-	-

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5:00 PM - 6:15 PM

P5-04-02

Comparative analysis between screening mammography performed in patients at usual risk and patients at high risk for breast cancer in the early detection program for breast cancer in Brazil

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Introduction: Breast cancer is currently considered a public health problem, being the most frequent in women in Brazil. In the past, and in places where screening programs are not very successful, the diagnosis was made during the clinical examination, being carried out late, which compromised the prognosis and survival of the patient. To avoid late diagnosis, an attempt is made to have the strategy of appropriate screening programs that make an early detection by applying the test to the asymptomatic population and identifying lesions in the pre-clinical stage. Objectives: To analyze the incidence of reports highly suggestive of malignancy in patients undergoing mammography in Brazil between 2013 and 2021. Methodology: A retrospective and analytical cross-sectional study of the notifications available in the cancer information system (SISCAN) was carried out. The incidence of report notifications by the Breast Imaging Reporting Data System (BI-RADS) classification system was compared between high-risk and normal-risk women for breast cancer. In addition to the information regarding the BI-RADS report, they were analyzed comparing epidemiological data between high-risk and normal-risk women. Other variables analyzed were the age group of the screened population and the size of the nodule according to the BI-RADS. Results: In the period analyzed from 2013 to 2021, 16,065,383 screening mammograms were performed and reported in Brazil. Of these, 13,167,259 mammograms were performed on women at normal

risk, while 2,898,124 mammograms were performed on women reported as high risk. To analyze the difference between the reports in women at usual risk and those at high risk, the relative risk between them and the number necessary to cause harm was calculated, having found a relative risk of 0.5412 (CI 95 % 0.5341 - 0.5483) in B4 and a relative risk of 0.433 (95% CI 0.4203 - 0.4462). As for the number needed to deal damage, it was observed 203 (95% CI 198 - 209) for B4 and 788 (95% CI 754 - 825) for B5. Discussion: Although the need for breast cancer screening programs to reduce mortality is already well established, some aspects of screening do not have much consensus. In our study, as proposed in the literature, the incidence of reports suggestive of malignant breast lesions was higher in high-risk women. This finding may be consistent with the fact that women with risk factors are more likely to develop breast cancer than those with usual risk. Some studies show that exams from high-risk patients tend to be examined in greater detail, in order to have a higher false positive rate than low-risk patients, just as low-risk patients have a higher false negative rate. Conclusions: Our study showed an increased prevalence of reports suggestive of malignancy in high-risk patients when compared to usual-risk patients. Such findings may mean that high-risk patients have a higher prevalence of malignancy, but also that clinicians review the examinations of high-risk patients more carefully, increasing the rate of reports suggestive of malignancy in these patients.

Reports of mammograms performed in the target population and in high-risk women in Brazil between 2013 and 2021

	Populaç Target	High-risk women	Relative risk (p-value)
B0	1.439.841 – 11%	373.683 – 13%	0.8481 (p < 0.05)
B1	4.906.097 – 37%	1.009.350 – 35%	1.0698 (p < 0.05)
B2	6.452.900 – 49%	1.409.596 – 49%	1.0076 (p < 0.05)
B3	279.335 – 2,1%	67.966 – 2,3%	0.9046 (p < 0.05)
B4	76.329 – 0,6%	31.045 – 1,1%	0.5412 (p < 0.05)
B5	12.757 – 0,1%	6.484 – 0,2%	0.4330 (p < 0.05)
Total	13.167.259 – 100%	2.898.124 – 100%	

Risco relativo a depender do tamanho do nódulo e o laudo BI-RADS entre mulheres de alto risco e risco habitual

	<=10mm	11-20mm	21-50mm	>50mm
BI-RADS 0	0.8806 (IC 95%: 0.8562 - 0.9056)	0.8725 (IC 95%: 0.8423 - 0.9037)	0.8315 (IC 95%: 0.7729 - 0.8946)	1.0341 (IC 95%: 0.8816 - 1.2129)
BI-RADS 3	1.4464 (IC 95%: 1.2925 - 1.6186)	1.7870 (IC 95%: 1.5040 - 2.123)	1.2183 (IC 95%: 0.6933 - 2.1408)	0 pacientes de risco habitual com >50mm e B3
BI-RADS 4	2.281 (IC 95%: 1.8479 - 2.8156)	1.9252 (IC 95%: 1.5848 - 2.3387)	1.5548 (IC 95%: 1.2454 - 1.9409)	1.1081 (IC 95%: 0.6290 - 1.9521)
BI-RADS 5	2.9962 (IC 95%: 1.9727 - 4.5506)	1.4758 (IC 95%: 1.0655 - 2.0442)	1.7349 (IC 95%: 1.3405 - 2.2453)	0 pacientes de risco habitual com >50mm e B5

Disclosure(s):

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12/8/2022

5:00 PM - 6:15 PM

P5-04-03

Analyzing the performance of Thermalytix, an AI-based breast cancer screening solution, in a community setting

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Background: Despite improvements in treatment strategies, breast cancer survival rates remain low in India due to a lack of awareness and late stage of presentation. If diagnosed and treated early, breast cancer survival rates improve. Screening mammography, the gold standard in cancer diagnosis, is not feasible in a resource-constrained setting. Niramai's novel breast cancer screening technology, Thermalytix™, applies Artificial Intelligence (AI) over thermography, to give an automated interpretation of the breast thermal images. The portable Thermalytix test has been so far used to screen 60000 women in community settings across India and Kenya. This study is a recent evaluation of the test in rural setting.

Methods: Women who provided written consent and who underwent Thermalytix tests in community-based screening camps at primary health centers (PHCs) in Afzalpur Taluk of Gulbarga District, Karnataka, India between 01 August 2021 to 15 June 2022 were included in this study. Five thermal images in multiple views were analyzed using Niramai's patented algorithm. Automated analysis of the thermal images produced a screening report and triaged the participants for follow-up. In case of abnormal thermal activity, Thermalytix triaged women as 'red' and were referred to the district hospital for follow-up with breast ultrasound and/or other investigations and were recorded into the following three categories: Normal (BI-RADS 1), Abnormal - benign (BI-RADS 2/3) and Abnormal - malignant (BI-RADS 4/5). If no abnormal thermal patterns were detected by Thermalytix, women would be recommended routine screening.

Findings: The analysis included 3531 women were included in the analysis and the median age in the cohort was 42 years. Of them, 97 (2.74%) women were triaged 'red' by Thermalytix indicating a suspicion of breast abnormality. As on 15 June 2022, 29 (30%) out of 97 women underwent standard follow-up investigations of which two cases of carcinoma breast, one case of phyllodes, one case of tuberculosis mastitis and seven other benign cases were identified, indicating that Thermalytix has a positive predictive value of 35.71% (11/29) in detecting benign

and malignant breast lesions. Furthermore, a Patient experience questionnaire was used to assess their experience. 98.71% women were being screened for breast cancer for the first time in their lives. 93.9% women said they were very satisfied with Thermalytix screening experience and remaining 6.1% said they were satisfied, thus aiding in strong acceptability and adoption of the test.

Interpretation: In resource-constrained settings such as India, where less than 2% of the women in the country have ever got screening for breast cancer, the portable, no-radiation Thermalytix test is an accessible breast cancer screening solution. Thermalytix's patient-friendly features - privacy-aware, painless, comfortable, and radiation-free make it favorable for population screening in India, and thus, can increase the uptake of breast cancer screening. With the device's capacity to fit into a backpack, it can make breast cancer screening accessible to even remote areas with limited resources. However, following up on women who were found to be Thermalytix positive still remains a challenge. Future studies will ensure that follow-up after abnormal breast screening is part of the approved clinical protocol.

Results of the screening program

Total no.of woman screened by Thermalytix between 01 August 2021 to 15 June 2022	3531
Women screened 'red' by Thermalytix - suspicious of breast abnormality	97
Women who underwent follow-up investigations	29
Women with abnormal findings as per Breast ultrasonography	11
Fibroadenoma	7
Breast Tuberculosis	1
Invasive Ductal Carcinoma	2
Phyllodes	1

3 malignancies and 8 benign lesions found in 29 Thermalytix RED patients

Disclosure(s):

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5:00 PM - 6:15 PM

P5-04-04

Does reducing the frequency of regularly scheduled physical examinations affect recurrence detection in patients with early breast cancer?

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Purpose: Follow-up care of patients with early breast cancer (EBC) usually includes routinely scheduled physical examinations. While ASCO guidelines recommend a physical exam every three to six months for the first three years, there is little evidence to support this schedule. Health care systems continue to be challenged to meet the future growth in demand from

increasing numbers of diagnosed patients and long-term survivors, scarcity of health care workers, and the need to control health care costs. Despite recognition that new follow-up models are needed, there continues to be no generally accepted well follow-up strategy. We evaluated recurrence detection patterns of patients transferred into a single centre survivorship program that follows ASCO recommendations.

Methods: Consecutive patients with EBC referred to the Wellness Beyond Cancer Program (WBCP) between February 1, 2013, and January 1, 2019, who had breast cancer recurrence, were reviewed. Descriptive analyses were used to present patients and disease characteristics stratified by type of recurrence and mode of cancer detection.

Results: Of 206 recurrences, 135 were distant recurrences (65.5%), 41 were ipsilateral breast recurrences (19.9%), and 30 were contralateral new breast cancers (14.6%). Patient reported symptoms lead to the detection of the majority of distant recurrences (125/135, 92.6%). The most common symptoms of recurrence were bone pain (24.8%), dyspnea/cough (13.1%), abdominal pain (10.7%). Ipsilateral breast recurrences were both quite frequently detected by patients (22/41, 53.7) and by routine mammographic surveillance (17/21, 41.5%). Contralateral breast cancers were primarily detected by imaging 83.3% (25/30). Only 2/206 (1.14%) recurrences/new primaries were detected by a healthcare provider at routinely scheduled follow-up visits. There was a statistical difference in recurrence detection between image detected vs. self-detected in the following factors: grade 3 (26.5% vs 51%, $p < 0.007$), triple negative breast cancer (3.9% vs. 15.1%, $p=0.03$), and HER2 disease (18.4% vs. 9.8%, $p=0.04$).

Conclusions: Despite regularly scheduled in-person follow-up visits following ASCO guidelines, healthcare providers rarely detect recurrences. Our data suggests that 30,000 – 35,000 follow-up visits were required for the healthcare providers to detect these 2 recurrences. This leads to further need for proper survivorship programs with patient and provider education, and concentration on targeted surveillance. Provided patients attend regular screening tests, our data points to less frequent in-person follow-up being associated with non-inferior breast cancer-related outcomes. Future prospective studies are required looking at different models of follow-up.

SABCS Abstract Table

		Image-Detected (n=51, %)	Self-Detected (n=152, %)	p-value*
Grade	1	7 (14.3)	20 (13.8)	0.007
	2	29 (59.2)	51 (35.2)	
	3	13 (26.5)	74 (51.0)	
Breast-Cancer-subtype	ER-Positive	45 (88.2)	118 (77.6)	0.10
	HER2-Positive	5 (9.8)	28 (18.4)	0.04
	HER2-Unknown	7 (13.7)	7 (4.6)	
	Triple-Negative	2 (3.9)	23 (15.1)	0.03
Type-of-Recurrence	Distant	9 (17.7)	125 (82.2)	<0.001
	Local	17 (33.3)	22 (14.5)	
	Contralateral	25 (49.0)	5 (3.3)	

The categorical variables are presented in number and frequency (%), and the continuous variable is presented in median and range. *P-value of Chi-squared tests or Mann-Whitney U-Test

Disclosure(s):

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5:00 PM - 6:15 PM

P5-04-05

Predictors of guideline-incongruent breast cancer screening in an urban comprehensive cancer center

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Background: Guideline-congruent breast cancer (BC) screening is imperative to systematically curb BC mortality. This study was conducted to identify predictors of BC screening behaviors congruent with guidelines from various nationally recognized organizations (e.g, American Cancer Society, National Comprehensive Cancer Network, American College of Radiology) among high- and average-risk women, and to elucidate the alternative screening behaviors of women who were incongruently screened. Methods: Medical records of 6,090 women who received at least two screening mammograms from January 2016 to March 2018 at the Karmanos Cancer Institute were reviewed to determine breast cancer risk status (classified by the Tyrer-Cuzick model) and breast density status to determine whether breast cancer screening was concordant with risk-driven screening guidelines. Breast density was determined by BI-RADS density scoring, with non-dense breasts defined by a score of A or B, and dense breasts as C or D. For women at average-risk of breast cancer, incongruent screening was defined as receiving supplemental imaging in the interval between screening mammograms. For high-risk women, incongruent screening was defined as not having a recommended supplemental image in the interval between screening mammograms. Further, we examined BC risk, breast density, age, and race as predictors for guideline-concordant screening. Results: The screening cohort included 73.3% Black and 26.7% White women of whom 86.5%

were classified as average-risk, 7.7% intermediate risk and 5.8% high risk. Further analyses focused on women with average and high-risk of breast cancer. Among both average- and high-risk women, 390 (6.9%) were incongruently screened, however the rate of incongruent screening was much higher among high-risk vs. average risk women (97.7 vs. 0.9%, $p < 0.01$). Among average-risk women, incongruent screening was more likely among women with dense vs. non-dense breasts (2.0% vs 0.1%, $p < .01$). High-risk women were more likely to be incongruently screened if they had non-dense compared to dense breasts (99.5% vs 95.2%, $p < .01$). Younger women more likely to be incongruently screened among average-risk women (55.11 [SD = 10.24] vs 62.20 [SD = 9.73]; $t_{5267} = 4.87$, $p < .01$, $d = 0.73$), whereas older women were more likely to be incongruently screened among high-risk women, although this difference was not statistically significant (52.38 [SD = 7.27] vs 47.50 [SD = 8.57]; $t_{351} = 1.87$, $p = .06$, $d = 0.67$). There was no significant impact of race and incongruent screening for individual risk-level categories. With the exception of rendering the age effect non-significant, preliminary multivariable analyses did not significantly change the results. Further analyses will be conducted to assess the relationship between predictive factors and incongruent screening. Conclusions: An apparent lack of adherence to evidence-based screening guidelines for BC has led to underutilization of supplementary breast imaging for women at high-risk for BC. Further interventions are needed to promote increased supplemental imaging for this group of women.

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P5-04-06

Breast Imaging Recommendations for Females <40 Years of Age with $\geq 20\%$ Lifetime Breast Cancer Risk: Practice Patterns at a Specialized Clinic

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Background— There are limited data to guide breast cancer screening recommendations among females < 40 yrs of age with elevated lifetime breast cancer risk not driven by a known germline mutation. The American Cancer Society recommends initiating screening at age 30, while the National Comprehensive Cancer Network (NCCN) recommends 10 yrs younger than the youngest affected relative (YAR). Both support screening MRI in addition to annual mammogram (MMG). This study describes practice patterns related to screening imaging recommendations and patient (pt) follow-through in young females with $\geq 20\%$ lifetime breast cancer cared for in a specialized clinic.

Methods— At the Brigham and Women's Hospital high-risk breast clinic, specialized advanced practice providers, surgeons and oncologists perform risk assessment including use of the Tyrer-Cuzick (TC) risk model, and provide risk management recommendations. For this study, we identified pts age < 40 yrs with $>20\%$ lifetime breast cancer risk, no known genetic mutation or high-risk breast lesions, and ≥ 1 first or second-degree relatives (FDR or SDR) with breast cancer. We evaluated factors associated with recommendation for i) early screening initiation, defined as prior to age 40, and ii) use of supplemental imaging modalities.

Results— 335 pts met study criteria: 20% were age < 30, 36% were 30-34, and 44% were 35-39. Mean lifetime risk by the TC model was 32% (SD: 10%). Early screening was recommended in 75%; these pts were more likely to have an affected FDR (71% vs. 48%, $p < 0.001$) and younger affected relatives (median age of YAR: 44 vs. 55, $p < 0.001$). Among pts whose YARs were age < 50, early screening was recommended in-line with NCCN guidelines for 99% of pts with FDRs < 50 vs. 80% of pts with only SDRs < 50 ($p < 0.001$). Among pts whose YARs were age ≥ 50 , early screening was recommended contrary to NCCN guidelines in 51%. Factors associated with an early screening recommendation in this subgroup were having received a prior MMG (62% recommended early screening vs. 33% with no prior MMG) as well as being older at time of risk discussion (median age 37 in early screening group vs. 34 in routine screening group) and having younger affected relatives (median age of YAR: 53 vs. 56) (all $p \leq 0.01$). Regarding use of supplemental imaging, 35% were recommended screening MMG alone, while 65% were also offered screening MRI or ultrasound (US). Factors most strongly associated with offering MRI/US included having heterogeneously or extremely dense breasts, normal BMI, greater extent of family history, younger affected relatives and higher TC scores (Table). All except extent of family history remained statistically significant in multivariable analysis. Among those offered supplemental MRI/US who were eligible to initiate screening, 48% had pursued MRI, 7% US +/- MRI, 27% MMG alone, and 18% had no screening imaging at a median follow-up of 17 months.

Conclusions— These data suggest that providers in our high-risk breast clinic are using nuanced clinical judgment related to screening recommendations in pts < 40 yrs with elevated lifetime risk. Those with affected FDRs at age < 50 were consistently recommended early screening initiation, while practice recommendations varied more for pts with only SDRs age < 50 or those with YAR age ≥ 50 , suggesting a need for consensus criteria as to when to initiate screening in these subgroups. Multiple factors impacted recommendations for screening MRI/US, most notably breast density.

Factors associated with offering supplemental screening with MRI/US

	Recommended MMG alone (row %)	Offered MRI/US (row %)	p-value	MVA Odds Ratio	MVA p-value
Breast density					
Non-dense	25 (66%)	13 (34%)	<0.001	0.34	0.02
Heterogeneously dense	28 (30%)	65 (70%)		ref	--
Extremely dense	16 (20%)	64 (80%)		1.20	0.64
No prior MMG	47 (38%)	77 (62%)		0.49	0.04
BMI (kg/m²)					
<25.0	46 (25%)	137 (75%)	<0.001	ref	--
25.0-29.9	29 (38%)	48 (62%)		0.52	0.05
≥30.0	41 (59%)	29 (41%)		0.28	0.001
Family history					
0 FDR + 1 SDR	22 (54%)	19 (46%)	0.002	1.47	0.39
0 FDR + ≥2 SDR	29 (39%)	46 (61%)		1.55	0.26
1 FDR + 0 SDR	30 (42%)	42 (58%)		ref	--
1 FDR + ≥1 SDR	29 (26%)	81 (74%)		1.58	0.24
≥2 FDR + any SDR	6 (16%)	31 (84%)		1.39	0.58
Median age of YAR (IQR)	50 (44-55)	45 (39-50)	<0.001	0.96	0.006
Mean TC lifetime risk (SD)	27 (7)	32 (10)	<0.001	1.07	0.001

Disclosure(s):

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5:00 PM - 6:15 PM

P5-04-08

Breast cancer screening using ultrasound increases recall, biopsy, and cancer detection rates

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Title: Breast cancer screening using ultrasound increases recall, biopsy, and cancer detection rates

Background: Ultrasound is often used as an adjunct to mammography for breast cancer (BC) screening. Usage of screening ultrasound (US) varies by state, likely due to differences in state-specific breast density notification laws and mandates requiring insurance coverage of supplemental screening for women at elevated risk of breast cancer. Screening US can increase cancer detection rates among women with dense breasts, but may increase recalls and benign biopsies. As more states adopt policies mandating insurance coverage for

“medically necessary” breast cancer imaging, it is important to understand the impact to screening US utilization and subsequent service utilization. This analysis examines use of screening US by state as well as associated rates of recall, biopsy, and cancer detection.

Methods: We analyzed deidentified administrative claims. We included women aged 18-74 years with ≥1 claim for screening mammography in 2018. First claim was index date. Continuous enrollment was required in a commercial (COM) or Medicare Advantage (MA) plan from 1/2016 to index date (baseline period) and from index date to 6 months after (follow-up period). Recall, biopsy, and cancer detection rates were calculated for the follow-up period. Recall was defined as ≥1 claim for mammography, diagnostic ultrasound, or MRI in the follow-up period. We used CPT/HCPCS codes to identify procedures. Screening US was identified by CPT 76641 (complete) with modifier 50 (bilateral) or LT/RT (left/right). Using ICD codes, cancer detection was defined as ≥1 claim for DCIS or invasive BC. We examined screening US rates by insurance type, state, and age. Proportions were compared with chi-squared tests.

Results: 939,410 women met study criteria (70% COM, 30% MA; Tables 1-2). In the COM population, recall, biopsy, and cancer detection rates with screening US were approximately two-fold higher than without (recall: 26.1% vs. 11.8%; biopsy: 5.0% vs 1.6%; cancer detection: 1.0% vs. 0.4%). In the MA population, recall, biopsy, and cancer detection rates with screening US were roughly three-fold higher than without (recall: 23.6% vs 9.0%; biopsy: 5.2% vs 1.6%; cancer detection: 1.9% vs 0.7%). In NY, NJ, and CT, the rate of screening US usage was > 14 times higher than in all other states (29.1% vs 1.9%). These three states had higher recall and biopsy rates, but similar cancer detection rates compared to all other states (recall: 14.4% vs. 11.4%; biopsy: 2.5% vs 1.7%; cancer detection: 0.6% vs. 0.5%). All proportion differences reached statistical significance (p < 0.001).

Conclusion: Screening US was associated with increases in recall and biopsy, but modest increases in absolute cancer detection rates. Observed state by state variation of screening US is likely driven by laws requiring zero patient payment insurance coverage of “medically necessary” imaging which, as is the case with NY, NJ, and CT, is interpreted to include screening US. Our results demonstrate that screening US may lead to a large increase in recall rates and biopsies without consequentially improving the cancer detection rate.

Table 1: Recall, biopsy, and cancer detection rates by age with and without use of adjunctive breast screening ultrasound in a commercially insured U.S. population

Age	Recall		Biopsy		Cancer Detection	
	With Screening US (n=37,021)	Without Screening US (n=623,865)	With Screening US (n=37,021)	Without Screening US (n=623,865)	With Screening US (n=37,021)	Without Screening US (n=623,865)
18-39	35.5%	20.2%	8.2%	2.6%	N/A*	0.3%
40-44	29.6%	16.5%	5.9%	2.0%	0.9%	0.2%
45-49	26.6%	13.5%	5.1%	1.6%	0.7%	0.3%
50-54	25.3%	11.5%	4.7%	1.5%	1.0%	0.4%
55-59	24.3%	9.9%	4.6%	1.4%	1.0%	0.5%
60-64	23.6%	9.5%	4.3%	1.4%	1.4%	0.6%
65-69	22.7%	9.6%	4.4%	1.5%	1.8%	0.7%
70-74	22.6%	10.3%	5.0%	1.7%	N/A*	0.8%
Overall	26.1%	11.5%	5.0%	1.6%	1.0%	0.4%

* values are suppressed to comply with requirements for data release

Table 2: Recall, biopsy, and cancer detection rates by age with and without use of adjunctive breast screening ultrasound in a Medicare Advantage (MA) U.S. population

	Recall		Biopsy		Cancer Detection	
	With Screening US (n=6,100)	Without Screening US (n=272,408)	With Screening US (n=6,100)	Without Screening US (n=272,408)	With Screening US (n=6,100)	Without Screening US (n=272,408)
Age						
18-39	N/A*	16.5%	N/A*	N/A*	N/A*	N/A*
40-44	N/A*	15.4%	N/A*	N/A*	N/A*	N/A*
45-49	31.2%	11.9%	N/A*	1.5%	N/A*	N/A*
50-54	19.3%	11.6%	N/A*	1.6%	N/A*	0.4%
55-59	28.9%	10.5%	7.4%	1.4%	N/A*	0.5%
60-64	25.3%	10.1%	6.8%	1.6%	N/A*	0.5%
65-69	25.4%	9.0%	5.3%	1.6%	2.2%	0.7%
70-74	22.4%	8.7%	4.9%	1.6%	1.8%	0.8%
Overall	23.6%	9.0%	5.2%	1.6%	1.9%	0.7%

* values are suppressed to comply with requirements for data release

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5:00 PM - 6:15 PM

P5-04-09

Analysis of an update to a novel breast cancer screening web-app

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Introduction

A minority of women with breast cancer in Mexico are diagnosed through a screening program with a low rate of national coverage of about 20%, which translates into late diagnosis and worse outcomes. The detection of high-risk groups through easy-access interventions is essential to increase the screening rate.

OBJECTIVE

To identify and analyze patients at high risk of breast cancer, through a web app specially designed for this purpose.

MATERIAL AND METHODS

The web app stratified respondents according to breast cancer risk into 4 categories: very high risk (symptomatic), high lifetime risk, average risk (usual screening recommendations), or low risk. The app was programmed to guide patients to a risk-based information page or urge them to seek medical advice if indicated (https://cuccuanl.com/tamiz_mama/). The web app also provided the contact information of our center, or an appointment could also be scheduled within the app. Distribution was made via social media.

An upgrade of the app was launched, which expanded the functionality with the inclusion of the Gail model to identify women with a high lifetime risk for developing breast cancer and the option for a simple interpretation of mammographic results. In version 2.0, the patients were divided into 2 populations, the first one which already had a breast imaging test but wished to know what the BIRADS score obtained meant and the other group were those who answered a simple survey similar to the one available on version 1.0, with added questions to calculate the Gail model risk.

RESULTS

The web app was originally released in October 2021 with a total number of 1,012 women answering the survey. The update was released in June 2022 with 406 new subjects. 281 patients wished for a risk calculation with no prior breast imaging tests and 124 patients already had a breast image diagnosis test that wanted a simple interpretation. Table 1 depicts the answers given between both versions.

Among the group of patients that had a mammography but had doubts about the result 12.9% (n=16) reported a BIRADS 0, 12.1% (n=15) BIRADS 1, 46% (n=57) BIRADS 2, 14.5% (n=18) BIRADS 3, and 14.4% (n=18) BIRADS 4 or 5.

To date 41 patients have booked an appointment at the cancer prevention clinic directly within the webapp for further evaluation.

DISCUSSION AND CONCLUSION

The changes in the criteria of high risk did not translate into changes in the proportion of patients considered at high lifetime risk of breast cancer, but these changes made might be more specific for subsequent screening and chemoprevention strategies. The app persisted with a high proportion of symptomatic patients.

The results of integration of the simple mammography interpretation were surprising, with a high proportion of subjects with indication for a biopsy founded. In the Mexican population there is a significant gap between the screening mammography and the first consultation with a specialist, averaging 113 days from an abnormal screening test to a diagnosis of breast cancer (1), which delays treatment initiation resulting on a worst outcome.

These kinds of apps may empower patients to seek earlier consultation if warranted or educate patients on their personal risk for developing cancer so they may have a closer adherence to early detection programs. These results and subsequent updates might help evolve the app into something more akin to a digital navigator for patients.

Bibliography

1)Unger-Saldaña K, Cedano Guadamos M. Delays to diagnosis and barriers to care for breast cancer in Mexico and Peru: a cross sectional study. The Lancet Global Health. 2020 Apr 1;8:S16.

Table 1

	Version 1.0 (n= 1003)	Version 2.0: Cohort that didn't have a screening test to interpret (n=281)
Very high risk (Symptomatic Patient)	12.8% (n=128)	13.2% (n=37)
High lifetime risk (V1: Positive family history, ≥5-year OCP use; V2: ≥1.7% Gail Index, Prior radiotherapy, ≥5-year OCP use)	18.2% (n=183)	15.3% (n=43)
Normal screening recommendation (≥40 years without additional risk factors)	16.8% (n= 169)	17.8% (n=50)
Low risk of breast cancer (<40 years without additional risk factors)	52.1% (n=523)	53.7% (n=151)

Results stratified by risk groups between version 1.0 and 2.0

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5:00 PM - 6:15 PM

P5-04-10

Consensus guidelines for breast cancer staging during pregnancy. A Delphi Study.

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Background: Breast cancer is the second most common cancer occurring during pregnancy with limited evidence for appropriate staging (1,2). A Delphi study was performed to develop consensus guidelines. Methods: Guideline recommendations were constructed based on available evidence and included statements targeting highlighted areas of uncertainty from a clinician-based survey. Statements were divided into two domains: one focused on indications for staging and the second addressed imaging selection. A two round Delphi study was performed. Medical, radiation and surgical oncologists from Australia and New Zealand were invited to participate. Participants who had worked in their field for >5 years were considered experts. Participants voted using a 9-point Likert scale selecting from 1 (strongly disagree) to 9 (strongly agree). Consensus was achieved when >75% participants selected < 3, or >7 for a statement. Statements that did not reach consensus in the first round were refined and re-presented for subsequent voting. Results: 15 Australian and New Zealand experts agreed to participate: 8 medical oncologists, 3 radiation oncologists and 4 breast surgeons. 87% (13/15) of participants completed round one. Of the 18 recommendations, six did not meet consensus. These were revised, with seven recommendations re-presented in round two. 11/13 (85%) participants completed round two, with one further recommendation achieving consensus. Consensus was achieved on indications for staging including women with locally advanced or inflammatory breast cancer and clinical suspicion of metastatic disease. Staging should be delayed until after pregnancy if it will not immediately change management decisions. Staging should not routinely be used in stage I and II breast cancers. Where staging is indicated, it was agreed that visceral disease should be screened for; however, consensus was not achieved for whether screening for bone metastases should be performed. There was consensus for liver ultrasound as the imaging modality of choice for liver metastases screening. Participants did not agree on whether chest x-ray or CT chest was best practice for pulmonary metastases nor optimal imaging for bone metastases. There was also discord as to whether there is a role for PET scan. Conclusion: Consensus guidelines have been developed to standardise breast cancer staging during pregnancy. Consensus was achieved for indications for staging and use of liver ultrasound to screen for liver metastases. Optimal staging practices for bone and

pulmonary metastases warrants further investigation. Acknowledgements: We thank the experts who participated in this Delphi study. References: 1. Lee YY, Roberts CL, Dobbins T, Stavrou E, Black K, Morris J, et al. Incidence and outcomes of pregnancy-associated cancer in Australia, 1994–2008: a population-based linkage study. *BJOG Int J Obstet Gynaecol*. 2012;119(13):1572–82. 2. Cottreau CM, Dashevsky I, Andrade SE, Li DK, Nekhlyudov L, Raebel MA, et al. Pregnancy-Associated Cancer: A U.S. Population-Based Study. *J Womens Health*. 2019 Feb 1;28(2):250–7.

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5:00 PM - 6:15 PM

P5-05-01

Personalized Cancer Monitoring (PCM): a novel ctDNA tool to detect molecular residual disease in patients with early-stage breast cancer

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Introduction: Identification of Molecular Residual Disease (MRD) in patients with breast cancer with circulating tumor DNA (ctDNA) presents a strategy to identify patients at high risk of relapse. Approaches that detect ctDNA at lower concentrations are required to increase sensitivity and improve on the lead time between ctDNA detection and clinical relapse. Here we present results using novel highly sensitive tumor-informed sequencing assays for ctDNA detection of MRD based on detection of multiple patient specific mutations in ctDNA. Methods: 62 stage II-III breast cancer patients (23 hormone receptor positive HER2 negative (HR+HER2-), 20 HER2+, 15 triple negative breast cancer (TNBC) and 4 unknown receptor status) enrolled in the ChemoNEAR sample collection study were included. All patients received neoadjuvant chemotherapy, followed up by surgery, with samples taken at diagnosis, and post-surgery every 3 months for the first two years, followed by every 6 months for up to five years. Tumor DNA from FFPE samples and germline was Whole Exome Sequenced to identify patient specific mutations and design anchored-multiplex PCR (AMP™) Personalized Cancer Monitoring (PCMTM) assays to track mutations in plasma. Cell free DNA was extracted from 613 plasma samples (median volume 4ml, range 0.5-4.5ml) and sequenced with PCMTM assays, with 37-177 variants (median 52) per panel, to a depth of 100,000x per locus. A proprietary algorithm was used to identify ctDNA. Results: At a median follow-up of 52.7 months post-surgery (range 15.3-96.4 months), ctDNA was detected in 25.8% (16/62) of patients, with detected ctDNA levels ranging from allele frequency (AF) of 0.01%, to 32.5% (median 0.24% AF). Detection of ctDNA was associated with a high risk of future relapse (HR 65.4, 95% CI 14.5-293.7), with a median lead-time from ctDNA detection to clinical relapse of 13.7 months (range 3.9-58.9). MRD was identified in 76.9% (10/13) of patients who relapsed. ctDNA was detected prior to relapse in both patients with brain only relapse, but with a reduced lead time over clinical relapse (5.73 and 3.90 months), which was previously not achievable with digital PCR MRD-detection assays. Of patients with assessable baseline samples, 81% (39/48) had ctDNA detected. No patients with undetected ctDNA, or detectable ctDNA with AF < 0.1%, relapsed during follow-up, whereas ctDNA was detected at baseline in all 10 patients who relapsed during follow-up (p=0.1). Conclusions: PCMTM detected breast cancer relapse with a long lead-time over clinical relapse, and strong association with relapse free survival, an advancement over previously published data with digital PCR MRD detection. Prospective, interventional trials are now required to assess whether treatment on the basis of MRD detection improves outcome, including the TRAK ER Trial (NCT04985266).

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5:00 PM - 6:15 PM

P5-05-02

Estrogen receptor 1 (ESR1) mutations in circulating tumor DNA (ctDNA) from patients with ER+/HER2- metastatic breast cancer (mBC) treated with lasofoxifene plus abemaciclib in the ELAINE 2 study

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Introduction: Use of long-term endocrine therapy (ET) for ER+ breast cancer often leads to acquired ESR1 mutations (mutESR1), causing endocrine resistance, tumor progression, and poor prognosis. An unmet clinical need exists for treating ER+ mBC patients with mutESR1, particularly after progression on CDK4/6 inhibitors (CDK4/6i). ELAINE 2 is an open-label, phase 2, multicenter trial evaluating safety and efficacy of lasofoxifene (LAS [selective estrogen receptor modulator]) plus abemaciclib (Abema [CDK4/6i], provided by Eli Lilly) in patients with ER+/HER2- and mutESR1 mBC who progressed after prior ET. Preliminary data with LAS plus Abema showed median progression-free survival of 55.7 wks, objective response rate of 50%, and 24-wk clinical benefit (CB) rate of 69%, with an acceptable safety and tolerability profile. Here, we report ESR1 ctDNA mutant allele frequency (MAF) and correlations of ESR1 MAF

changes with CB.

Methods: ELAINE 2 patients with detectable ctDNA mutESR1 at baseline (BL) were analyzed. Oral LAS 5 mg/day and Abema 150 mg BID were taken until disease progression, death, unacceptable toxicity, or withdrawal from the study. ctDNA was assessed by the Sysmex-Inostics SafeSeq assay—which detects mutESR1 at low allele fractions—at BL, every 4 wks, and end of treatment. MAF changes from BL to wk 4 were characterized as decreased (decrease in ESR1 MAF or none detected [ND]), increased (increase in MAF), or equivocal (in polyclonal patients [>1 mutESR1] with some MAF increasing and decreasing trends).

Correlations of MAF change at 4 wks with CB at 24 wks were explored.

Results: 29 patients (median of 2 prior metastatic therapies: 97% CDK4/6i, 79% fulvestrant, 48% chemotherapy) had BL mutESR1 of Y537S (66%), D538G (45%), Y537N (28%), and other less frequently detected mutations; 14 (48.3%) patients were polyclonal. 26 of 29 patients had evaluable BL and wk-4 ctDNA results: 21 patients had decreased MAF (81% [54% with ND]), 3 (12%) had increased, and 2 (8%) had equivocal ESR1 MAF changes (Table). CB at 24 wks was seen in 17 patients with a decrease, 2 with an increase, and 1 with equivocal MAF change. A sensitivity of 89.5% and specificity of 20% were calculated for predicting CB based on direction of ESR1 MAF change. The positive predictive value (PPV) for CB with decreased MAF was 81% and the negative predictive value (NPV) for an increased MAF was 33%. Of the 14 (54%) patients with ND ESR1 MAF, 13 had CB resulting in 87% sensitivity, 50% specificity, 93% PPV, and 33% NPV.

Conclusion: In ELAINE 2, 81% of patients had decrease/cleared (ND) mutESR1 after 4 wks of LAS plus Abema, which correlated with clinical benefit. All mutESR1 detected appear targeted with this therapy. High sensitivity and favorable PPV were observed in patients with decreased MAF, and even more so in those with ND MAF; however, increased MAF was less specific and not as predictive of treatment failure. Our results indicate that ESR1 liquid biopsy evaluation may be an adequate non-invasive surrogate marker for monitoring patients on treatment. Further study in a larger population of women with endocrine-resistant mBC and acquired mutESR1 is warranted to explore this potential for monitoring treatment response or resistance to this novel LAS-Abema combination.

Table. Change from baseline to week 4 in ESR1 MAF and clinical benefit at 24 weeks.

Clinical benefit at 24 weeks	MAF change at 4 weeks (n=26)		
	Decreased/ND	Increased	Equivocal
Yes	17 (65%)	2 (8%)	1 (4%)
No	4 (15%)	1 (4%)	1 (4%)
	Decreased/ND/Increased (n=24)		
Sensitivity*	89.5% (95% CI, 65.5–98.2)		
Specificity*	20.0% (95% CI, 1.05–70.1)		
PPV	81.0% (95% CI, 57.4–93.7)		
NPV	33.3% (95% CI, 1.80–87.5)		
	ND only (n=14)		
Sensitivity*	86.7% (95% CI, 58.4–97.7)		
Specificity*	50.0% (95% CI, 9.50–90.5)		
PPV	92.9% (95% CI, 64.2–99.6)		
NPV	33.3% (95% CI, 1.80–87.5)		

CI, confidence interval; MAF, mutant allele fraction; ND, none detected; NPV, negative predictive value; PPV, positive predictive value.

*Sensitivity and specificity analyses do not include equivocal results.

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12/8/2022

5:00 PM - 6:15 PM

P5-05-03

Characterization of the genomic landscape of breast carcinoma patients with NF1 alterations using comprehensive cell-free tumor DNA next-generation sequencing

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Background: NF1 (neurofibromin type 1) encodes neurofibromin, and is commonly altered in many cancers, including breast cancer. NF1 suppresses breast cancer by not only negatively regulating RAS signaling but also by independently acting as a transcriptional co-repressor of the estrogen receptor (ER). In this study, we analyzed the genomic landscape of patients with NF1 alterations from a large genomic database to define what unique patient characteristics were associated with NF1 alterations. Methods: Retrospective analysis of the Guardant Health database based on samples from the commercially available Guardant360® plasma-based circulating tumor DNA (ctDNA) assay. Samples were queried between June 2020-June 2022 for patients with any detected NF1 alteration and breast cancer diagnosis. NF1 synonymous alterations were excluded from this study. Statistics were conducted using a two-sided Fisher's exact test. Results: NF1 alterations were found in 895 patients with breast cancer over 1156 samples, typically in female patients (98.2%) diagnosed with breast carcinoma (99.4%). The average age of patients was 66 years old (23-93), with a median of 1.4 serial tests (1-19). The common nonsynonymous NF1 alterations are missense mutations (56.5%), nonsense mutations (23.5%), indels (22.3%), and aberrant splicing mutations (8.2%). There were significant differences in NF1 alteration frequency between younger (< 55 y/o) vs. older (≤55 y/o) patients, with older patients demonstrating an increase in NF1 alterations ($p < 0.0001$) across all mutation types except for splice mutations. There was also a significant difference in NF1 alterations between female vs. male patients, with male patients trending toward a higher frequency in NF1 missense alterations. Mutations affecting genes encoding the receptor tyrosine kinase (e.g., HER2) and the Ras-MAP kinase pathways (e.g., several RAS and RAF genes) co-occur with NF1 mutations. In contrast, there is no evidence of co-occurrence with mutations in the ESR1 gene, which encodes ER. The blood tumor mutational burden (bTMB) score was evaluable in 848 patients with an average score of 26.1 mut/Mb (range 1.16-447.7). In addition, mutations affecting genes controlling the cell cycle were also found to co-occur with NF1 mutations. Conclusions: Plasma-based liquid biopsy via G360 can efficiently identify NF1 alterations illustrating that such genetic alterations are common in this metastatic breast cancer cohort. Analysis of co-occurrent mutations supports our model that a key role of NF1 is to act as an ER transcriptional co-repressor, such that its loss is functionally redundant with acquiring ESR1 mutations. Oncogenic activation of the RTK-Ras pathways is needed for efficient progression to metastasis by additional mutations in this pathway. Mutational co-occurrence may also identify collaborating molecular events that collaborate with NF1 loss to promote treatment relapse and metastasis.

Disclosure(s):

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12/8/2022

5:00 PM - 6:15 PM

P5-05-04

Estrogen receptor 1 (ESR1) mutations in circulating tumor DNA (ctDNA) from patients with ER+/HER2- metastatic breast cancer (mBC) treated with lasofoxifene or fulvestrant in the ELAINE 1 study

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Introduction: Acquired ESR1 mutations (mutESR1) after long-term endocrine therapy drive treatment resistance, metastasis, and poor prognosis for patients (pts) with ER+/HER2- metastatic breast cancer (mBC). Lasofoxifene (LAS), a selective estrogen receptor modulator, alone or with a CDK4/6 inhibitor (CDK4/6i) reduced tumor growth better than fulvestrant (Fulv) in mutESR1 BC xenograft models. ELAINE 1 is a randomized trial of LAS vs Fulv in pts with mutESR1 and prior progression on aromatase inhibitor and CDK4/6i. Preliminary results (ESMO 2022) showed that LAS prolonged median progression-free survival (mPFS) compared with Fulv with a favorable safety profile. Here, we report changes in ESR1 ctDNA mutant allele frequency (MAF) from baseline to 8 wks and their associations with clinical benefit (CB) and mPFS.

Methods: ELAINE 1 pts were randomized to oral LAS 5 mg daily or IM Fulv 500 mg on days 1, 15, and 29, then every 4 wks, until disease progression or severe toxicity. ctDNA mutESR1 mutations (baseline and 8 wks) were assessed using the Sysmex Inostics OncoBeam or SafeSeq assays—which detect mutESR1 at low allele fractions. MAF changes from baseline to wk 8 were characterized as decreased (decrease in ESR1 MAF or fully cleared), increased (increase in MAF), or equivocal (polyclonal patients [>1 mutESR1] with some increasing and decreasing MAF trends); correlations with PFS and CB were explored. Efficacy measures included objective response rate (ORR), PFS, and CB at 24 wks (CB defined as response or stable disease ≥ 24 wks).

Results: 103 pts received LAS (n=52) or Fulv (n=51). Most common baseline ESR1 variants detected were D538G (56%), Y537S (39%), Y537N (29%), E380Q (22%); 56 (54%) pts were polyclonal. Of the 61 pts with evaluable baseline and wk 8 ctDNA, LAS decreased mutESR1 MAF in 29/35 pts (83% [11 complete clearance]) while Fulv decreased mutESR1 MAF in 16/26 pts (61.5% [6 complete clearance]) (Table).

mPFS with LAS was 8 and 4 mos for pts with decreased/cleared MAF and increased MAF, respectively, and with Fulv was 4.5 and 2.8 mos, respectively (Table). LAS decreased the common mutESR1 variants more frequently than Fulv (median relative change -87.1% vs -14.7%). In pts with decreased MAF, CB was observed in 16/29 LAS pts (55%) and 4/16 Fulv pts (25%). The predictiveness of ESR1 MAF clearance for CB was also explored. Of 11 pts with ESR1 MAF clearance taking LAS, 10 achieved CB, yielding a positive predictive value (PPV) of 90.9%. In contrast, 2/6 pts with ESR1 MAF clearance taking Fulv had CB for a PPV of 33.3%. Sensitivity for predicting CB based on direction of ESR1 MAF change was 94% with LAS and 80% with Fulv. In pts with Y537S MAF (n=33), LAS decreased Y537S in 13/15 (87%), with a median relative MAF decrease of 89%. In marked contrast, Fulv increased Y537S MAF in 11/18 pts (61%), corresponding to an MAF relative increase of 82%. LAS and Fulv resulted in complete clearance of Y537S MAF in 33% and 6% of pts, respectively.

Conclusion: Our data demonstrate that LAS more effectively decreased or cleared mutESR1 than Fulv. Further, mutESR1 clearance was associated with prolonged PFS and more CB in LAS but not Fulv pts, suggesting that LAS results in robust mutESR1 target engagement. Taken together, our data suggest mutESR1 as a potential liquid biomarker for predicting response to LAS in mutESR1, endocrine-resistant mBC pts.

Table. Change from baseline to week 8 in ESR1 MAF and clinical benefit at 24 weeks.

Clinical benefit at 24 weeks	Lasodoxifene (n=35)		Fulvestrant (n=26)	
	Decreased/ND MAF	Increased MAF	Decreased/ND MAF	Increased MAF
Yes	16 (45.7%)	1 (2.9%)	4 (15.4%)	1 (3.9%)
No	13 (37.1%)	5 (14.3%)	12 (46.2%)	9 (34.6%)
Sensitivity (%)	94.1 (95% CI, 69.2–99.7)		80.0 (95% CI, 29.9–98.9)	
Specificity (%)	27.8 (95% CI, 10.7–53.6)		42.9 (95% CI, 22.8–65.6)	
Median PFS (months)	Decreased/ND MAF	Increased MAF	Decreased/ND MAF	Increased MAF
	8 (95% CI, 4–9)	4 (95% CI, 2–6)	4.5 (95% CI, 3–10)	2.8 (95% CI, 0.5–6)

CI, confidence interval; MAF, mutant allele fraction; ND, none detected; PFS, progression-free survival.

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5:00 PM - 6:15 PM

P5-05-05

Monitoring for response and recurrence in neoadjuvant-treated hormone receptor-positive HER2-negative breast cancer by personalized circulating tumor DNA testing

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Background: The detection of circulating tumor DNA (ctDNA) may serve as an early predictor of response and recurrence. In this study, we used a tumor-informed ctDNA test to monitor clinical outcomes in patients with high-risk hormone receptor-positive HER2-negative (HR+HER2-) tumors who received neoadjuvant chemotherapy (NAC) on the I-SPY 2 trial (NCT01042379). Methods: We collected blood samples at pretreatment, during (at 3 and 12 weeks after initiation of paclitaxel-based treatment with or without an investigational drug), after NAC prior to surgery, 4 weeks after surgery, and annually until clinical diagnosis of recurrence. Cell-free DNA was isolated from plasma (N=329 samples) and ctDNA was detected using a personalized, tumor-informed multiplex polymerase chain reaction next generation sequencing-based test (Signatera™). All patients were at high risk for recurrence by MammaPrint. The response endpoints were pathologic complete response (pCR) and residual cancer burden (RCB), and the survival endpoint was event-free survival (EFS). Results: This analysis included 66 patients with HR+HER2- breast cancer who had blood samples collected before, during, after NAC and had at least one blood sample after surgery with sufficient plasma for analysis. 57.1% (32/56) had grade III disease; 72.4% (42/58) were node-positive; 36.2% (21/58) had T3/T4 disease; and 33.3% (22/66) were MammaPrint High 2. The percent ctDNA positivity rates at pretreatment, after NAC prior to surgery, and 4 weeks after surgery were 79.7% (47/59), 6.5% (4/62), and 2% (1/50), respectively. Significantly higher ctDNA positivity rates at pretreatment were observed in patients with larger tumors (95% in T3/T4 vs. 69% in T1/T2, Fisher's exact $p=0.0387$), higher grade tumors (94% in Grade III vs. 67% in Grade I/II, $p=0.0147$) and by MammaPrint score (100% in High 2 vs. 71% in High 1, $p=0.0052$). In this high-risk HR+/HER2- cohort, 10/66 (15.2%) achieved pCR/RCB 0, who were all ctDNA-negative at surgery. 56/66 (84.8%) had no-PCR, with RCB I (limited residual cancer), II (moderate) and III (extensive) in 7 (10.6%), 31 (47.0%) and 18 (27.3%), respectively. ctDNA-positivity after paclitaxel-based treatment was significantly associated with RCB II/III status (Fisher's exact $p=0.01$). All patients in this cohort with persistent ctDNA subsequently had RCB II or III at surgery. 47 patients had paired samples collected after NAC prior to surgery and at 4 weeks after surgery. Of the 47, 91.5% (43/47) were ctDNA-negative at both time points and 8.5% (4/47) were discordant; 1 was ctDNA-negative and later tested ctDNA-positive, while 3 were ctDNA-positive and later tested ctDNA-negative. 61/66 patients had EFS data with a median of 1.6 years of follow up (range: 0.6 to 5.6). 5 tested ctDNA-positive in at least one time point after surgery. Of these, 2 experienced a recurrence (one local relapse and one distant metastasis) and both tested positive at the time of recurrence. For the patient who developed a distant recurrence it was the only blood sample available at a follow-up time point; for the patient who developed a local recurrence, blood from two earlier follow-up time points had tested negative. To date, no recurrences have been observed in those whose test(s) after surgery were negative for ctDNA. Conclusions: The persistence of ctDNA during neoadjuvant therapy is associated with the extent of residual disease in a cohort of patients with HR+HER2- breast cancer in the I-SPY 2 trial and thus may be useful in identifying patients who are not having an optimal response to therapy. I-SPY 2.2 will test whether ctDNA has utility in redirecting therapy to improve surgical outcome and subsequent prognosis.

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ctDNA detection in seven different types of body liquids in patients with metastatic breast cancer

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Background. Liquid biopsies represent a less invasive alternative to tissue biopsy to characterize and possibly monitor the disease in patients with metastatic breast cancer. So far, blood remains the most frequently investigated body liquid in this context and the investigations mainly focus on the detection, quantification and characterization of the circulating tumor DNA (ctDNA). However, since blood might not capture the full disease profile, other sources of body liquids may have the potential to complement the information obtained from blood. The aims of the present study are therefore to assess whether: (i) ctDNA can be detected in different types of body liquids, and, (ii) the levels of ctDNA in a given liquid are associated with metastases in specific organs.

Patients and methods. Twelve patients from the post-mortem tissue donation program UPTIDER (NCT04531696) were included in this study. The receptor status of their primary tumor was: estrogen receptor negative, HER2 non-amplified (ER+/HER2-) (n=9), ER-/HER2- (n=2) and ER+/HER2+ (n=1). Median time between inclusion and death of the patient was 1.6 months (Interquartile range: [0.4-3.4]). Seven types of liquids were collected: blood, saliva, ascites, pleural fluid (PFL), cerebrospinal fluid (CSF), pericardial fluid and urine. Fluids were collected at study inclusion (blood, as well as saliva, urine, and ascites whenever possible) and at autopsy (except for saliva). In total, 108 liquid samples were collected and immediately centrifuged according to standard protocols. Cell free DNA (cfDNA) was extracted from the supernatant. All extracted cfDNA as well as germline DNA extracted from the 12 matched buffy coat samples underwent shallow whole genome sequencing. Log₂ ratios were computed with CNVkit, and co-segmented per patient using the copynumber R package. Purity and ploidy were assessed by ABSOLUTE. Associations between organ involvement and ctDNA yield were assessed by Wilcoxon rank-sum tests. Samples at study inclusion and at autopsy were considered together unless otherwise specified.

Results. At the sample level, ctDNA could be identified in 54% of the samples. At the patient level, the proportion of liquid types in which ctDNA was detected was highly variable (median: 58%, IQR: 34-77%, Table 1). CtDNA was detected in ascites of all patients when investigated, in 78% of PFL, 73% of CSF, 67% of blood and 37% of pericardial fluid. Only for one patient with invasive lobular carcinoma, ctDNA was detected in saliva and urine, the latter most likely explained by invasion of the bladder. Of note, in 4/12 patients ctDNA could not be identified in blood but was detected in at least one of the other fluids for 3 of these patients. At autopsy, ctDNA levels tended to be higher in PFL, ascites, and CSF in case of pleural, peritoneal, and central nervous system (CNS) metastases respectively, reaching statistical significance only for PFL. In CSF, two patients have CSF ctDNA detected with no documented involvement of the CNS. No brain autopsy was however performed for these patients.

Conclusion. We have shown that ctDNA can be detected in all 7 different body liquids that were investigated in this study. The ctDNA levels in a given liquid can be associated with the presence of metastases in specific organs. Since ctDNA was not detected in 4 of our patients in blood but detectable for 3 of them in other liquids, the evaluation of additional sources of body fluids should be further investigated in patients with metastatic breast cancer. These results therefore open new avenues for the clinical monitoring and characterization of the disease.

Table 1. Summary of ctDNA detection per liquid type at the patient level based on the 108 evaluated samples.

	Pt 2001	Pt 2002	Pt 2003	Pt 2004	Pt 2005	Pt 2006	Pt 2007	Pt 2008	Pt 2009	Pt 2010	Pt 2011	Pt 2012
Receptor status	ER-HER2-	ER-HER2-	ER+HER2+	ER+HER2-	ER+HER2-	ER+HER2-	ER+HER2-	ER+HER2-	ER+HER2-	ER+HER2-	ER+HER2-	ER+HER2-
Histo. type	NST	NST	ILC	Meta plastic	ILC	NST	NST	NST	NST	NST	ILC	ILC
Ascites	yes	yes	yes	NA	NA	yes	NA	yes	NA	yes	yes	yes
Blood	yes	yes	no	yes	no	yes	no	yes	yes	no	yes	yes
Cerebro-spinal fluid	yes	yes	NA	yes	yes	yes	no	no	yes	no	yes	yes
Pericardial fluid	yes	no	no	yes	no	yes	NA	no	no	no	no	yes
Pleural fluid	yes	yes	yes	NA	no	NA	no	yes	NA	yes	yes	yes
Saliva	NA	NA	NA	NA	no	no	no	no	NA	no	yes	NA
Urine	no	NA	no	no	no	no	no	no	no	no	yes	no
Nr of liquid types with ctDNA detected/ Total nr of liquids evaluated (%)	5/6 (86%)	4/5 (67%)	2/5 (40%)	3/4 (75%)	1/6 (17%)	4/6 (67%)	0/5 (0%)	3/7 (43%)	2/4 (50%)	2/7 (29%)	6/7 (86%)	5/6 (83%)

Histo.= Histological, ILC= Invasive lobular carcinoma, NA= not available, nr= number, NST= non-special type

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12/8/2022

5:00 PM - 6:15 PM

P5-05-07

Assessment of immune checkpoint expression on the peripheral blood mononuclear cells (PBMCs) of patients with breast cancer (BC)

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Background: Growing body of evidence highlights the role of the peripheral anti-tumor immune response in patients with solid tumors. Peripheral blood mononuclear cells (PBMCs) comprise all the key circulating immune cell subsets, and their analysis may inform on the peripheral anti-tumor immune response status in real-time. Programmed death-ligand 1 (PD-L1), toll-like receptor 4 (TLR4) and signal transducer and activator of transcription 3 (STAT3) hold a key role in the cancer-associated inflammation and tumor immune evasion. We herein aimed to investigate the distribution of these molecules on PBMCs and their prognostic value among patients with breast cancer (BC). Methods: Peripheral blood (PB) was obtained from patients with early (n=99) and metastatic (n=99) BC, prior to the initiation of adjuvant and first-line treatment, respectively. PBMCs were isolated through ficoll density gradient centrifugation and PBMC cytopspins were immunofluorescently stained using PD-L1, TLR4 and phosphorylated STAT3 (pSTAT3) antibodies. MDA.MB.231 BC cells served as controls to define the positivity of PBMCs for the respective markers via fluorescence microscopy. Results: PD-L1, TLR4 and pSTAT3 expression was identified on PBMCs of 27.8%, 27.1%, and 83.9% of all patients, respectively. The mean (\pm standard error of mean, SEM) percentage of positive PBMCs per patient was 13.8% \pm 1.8%, 10.5% \pm 1.6% and 37.1% \pm 1.9, respectively. A positive correlation was shown between the PD-L1pos, TLR4pos and pSTAT3pos PBMC proportions (PD-L1*TLR4; p=0.000, PD-L1*pSTAT3; p=0.001, TLR4*pSTAT3; p=0.002, Spearman's rho analysis). Patients with metastatic disease displayed increased TLR4pos PBMC percentages as compared to early disease (mean: 15.8% versus 5.2%; p=0.008, Mann Whitney U test). In the early BC setting, the detection of TLR4pos PBMCs was associated with reduced disease-free survival (DFS; median: not reached; p=0.020), while PD-L1pos PBMCs were correlated to shorter overall survival (OS; median: not reached; p=0.009). Early BC patients with PD-L1pos/TLR4pos PBMCs showed significantly reduced survival times (median DFS: not

reached; $p=0.016$; median OS: not reached; $p=0.004$, Kaplan Meier analysis). Conclusions: PD-L1, TLR4 and pSTAT3 molecules are frequently expressed on PBMCs of patients with BC and provide significant prognostic information for early-stage BC patients. The role of the immune-phenotyping of PBMCs as a source for biomarker discovery merits further investigation in BC.

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5:00 PM - 6:15 PM

P5-05-08

Dual ctDNA and tissue sequencing improves detection of actionable variants in breast cancer patients

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Background: Next-generation sequencing of circulating tumor DNA (ctDNA) and solid-tissue can identify clinically actionable genomic variants that may be used for both treatment selection and disease surveillance. Due to differences in tumor biology and assay design, ctDNA and solid biopsies may identify unique variants. Here, we investigate a real-world dataset of breast cancer patients to determine whether clinically actionable variant detection is enhanced by dual ctDNA and solid tissue testing. Methods: We used the deidentified Tempus Lens database to retrospectively analyze stage IV breast cancer patients with known hormonal subtype. Each patient had dual testing defined as Tempus xF (ctDNA) and Tempus xT (tumor tissue)—which resulted in clinical reports for both tests. Patients were further stratified according to the timing of ctDNA biopsy relative to tissue biopsy. Concurrent dual testing was defined as samples collected ≤ 30 days apart and longitudinal dual testing was defined as liquid > 30 days after solid. Variants were included in analyses if they met the limit of detection criteria of both assays. Clinical actionability was defined by indication-matched OncoKB Level 1-3. Fisher exact test was used to calculate significance. Results: Of the 1,341 breast cancer patients with dual ctDNA and tissue sequencing, at least one actionable variant was identified in 61% (n=823) of patients. In the subset of concurrent tested patients (n=782), 60% (n=473) had one or more actionable findings: 54% (n=257/473) of patients with actionable variants had perfectly concordant variants, 29% (n=136/473) had at least one unique variant detected only by solid tumor testing, and 20% (n=93/473) had at least one unique variant detected only by ctDNA testing. Similarly, in the longitudinal set (n=559), 63% (n=350) had one or more actionable findings: 34% (n=118/350) were concordant, 43% (n=150/350) were unique to solid, and 27% (n=96/350) were unique to ctDNA. When stratifying concurrent patients by OncoKB levels of evidence, 72% (n=98/136) of patients with variants unique in solid had at least one level 1-2 variant, while 39% (n=53/136) contained unique level 3 variants. Level 1-2 variants in PIK3CA were the most frequent variants seen uniquely in solid tumors, occurring in 54% (n=73/136) of patients. In contrast, in patients with unique ctDNA variants, 37% (n=34/93) of patients had at

least one level 1-2 variants and 72% (n=67/93) had level 3 variants. Level 3 variants in ESR1 were the most frequent variants seen uniquely in ctDNA, occurring in 57% (n=53/93) of patients. The proportion of concurrent patients with actionable variants found exclusively in ctDNA significantly differed by subtype (p=0.04): Luminal A (22%) and Luminal B (23%) contained the most patients with unique ctDNA variants. This ability to detect additional variants in ctDNA remained true even if profiling occurred over time. Indeed, in patients with ESR1 variants tested with ctDNA > 1 year after tissue, 78% (n=43/55) had ESR1 variants only detected in blood. Conclusions: We show that dual testing in breast cancer patients improves the identification of clinically actionable variants which may be missed by either ctDNA or solid tissue biopsy alone. Adoption of dual testing should be considered as standard practice to provide a comprehensive view of actionable molecular alterations.

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P5-05-09

Multianalyte liquid biopsy to aid the diagnostic workup of breast cancer

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Breast cancer (BC) affects 1 in every 8 women in the United States and is currently the most prevalent cancer worldwide. Precise staging at diagnosis and prognosis are essential components for the clinical management of BC patients. The liquid biopsy (LBx) has promising applications in cancer screening and early diagnosis ultimately leading to better survival results and less disease burden. In this study, we evaluated the feasibility of the high-definition single cell assay (HDSCA) LBx platform to stratify disease states (early- and late-stage BC) and normal donors using peripheral blood samples. In the HDSCA3.0 workflow, both common white blood cells (WBCs) and rare cells, including circulating tumor cells (CTCs), EMT and platelet-coated cells, plus acellular structures are identified and classified computationally from scanned immunofluorescent images. This comprehensive LBx approach provides a quantitative landscape view of each individual case. In a striking example of the insight provided by HDSCA, we compared LBx results for early-stage and late-stage BC patients with two independent cohorts of normal donors to show the utility of a blood draw as a source of biomarkers for early-stage cancer detection. As expected, CTCs were detected at a higher level in late-stage patients, compared to either the early-stage or normal donors. Surprisingly, however, we observed a significantly higher incidence of tumor-associated large extracellular vesicles (LEVs) in the early-stage patients, compared to the other two groups. A patient-level classification model was able to correctly classifying LBx profiles as normal, early, or late with LEV enumeration as the strongest predictor, followed by epi.CTC enumeration. We will present a reproducible LBx profile of rare cells and LEVs of early-stage disease compared to late-stage BC and normal donors with high accuracy, allowing for robust stratification. Our findings illustrate the feasibility of the LBx to assess early disease states prior to clinically defined metastasis, stratified from normal donors, highlighting the general consideration of the liquid biopsy for the diagnostic work-up and potentially screening.

Disclosure(s):

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P5-06-01

A Multi-center Clinical Study to Harvest and Characterize Circulating Tumor Cells from Patients with Metastatic Breast Cancer Using the Parsortix® PC1 System in support of FDA clearance

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Background: Circulating tumor cells (CTCs) captured from the blood of cancer patients may serve as a non-invasive surrogate source of tumor material to investigate tumor characteristics in real-time. However, the only FDA-cleared CTC assay is limited to the enumeration of surface marker-defined epithelial cells and not designed for further characterization of the CTCs identified. The Parsortix® PC1 system is a semi-automated microfluidic device capable of capturing and harvesting CTCs from peripheral blood based on cell size and deformability, making it cell-surface marker agnostic. Here, we demonstrate that the Parsortix® PC1 system enables the enrichment and capture of CTCs from the blood of patients with metastatic breast cancer (MBC) and their interrogation using evaluation techniques commonly available in clinical laboratories. Methods: As part of a multicenter clinical trial (NCT03427450), peripheral blood samples from 216 patients with MBC and 205 healthy volunteers (HVs) were prospectively collected at four different clinical sites located throughout the United States. Each subject provided two separate blood samples collected into K2EDTA Vacutainer® tubes to be processed using the Parsortix® PC1 system on the same day. The cells harvested from one of the blood samples collected from each subject by the Parsortix® PC1 system were deposited onto cytology slides using a cytocentrifugation method and stained with Wright-Giemsa reagents using an automated stainer. The stained slides were subjected to cytopathological evaluation by a board-certified pathologist to enumerate CTCs. As proof of principle, cells harvested from the second blood sample were evaluated using one of three additional techniques: molecular profiling by qRT-PCR, RNA sequencing, or cytogenetic analysis of HER2 amplification by FISH. Results: Cytologic examination identified one or more cells as a CTC in 48.5% (95% CI of 41.5 – 55.4%) of the 194 patients with MBC and 9.9% (95% CI of 6.4 – 14.9%) of the 192 HVs. The results from the qRT-PCR evaluation (102 HVs and 74 MBC patients) showed differential expression of cancer-related genes (KRT19, EPCAM, and TWIST1) in the patients with MBC compared to the HVs. Results from the RNA sequencing (53 HVs and 16 MBC patients) showed differential expression of several genes involved in the Kegg Cancer Pathway in the patients with MBC compared to the HVs. The results from the HER2 FISH evaluation (38 HVs and 101 MBC patients) showed that while the majority of the CTC identified had normal HER2/CEP17 ratios, detection of HER2 amplification was possible. Conclusions: The Parsortix PC1 system is capable of capturing and harvesting CTCs from the peripheral blood of patients with MBC. Harvested cells can be evaluated using standard orthogonal methodologies such as gene expression and FISH to identify and characterize

CTCs. Based in part on the above results, the FDA granted a De Novo classification request (DEN200062) for the Parsortix PC1 device in May of 2022.

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P5-06-02

Circulating tumor cells in metastatic breast cancer highlight potential role of copy number evolution in late-stage cancer mutational profile

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Background: Structural variation is a hallmark of breast cancer. Previous single-cell genomic analysis of 10 untreated early-stage primary TNBC tumors identified only one or two subclones per tumor, found that copy number variation (CNV) occurs early in the evolution of the tumor, and asserted that CNV changes do not contribute to genomic variation at later time points of a tumor's growth. This PCNE model (punctuated copy number evolution) is analogous to the big-bang theory of colorectal cancer. However, cancer exists in a dynamic environment, and systemic chemotherapy provides evolutionary pressure, making stasis quite unlikely. An investigation of late-stage cancers could shed light on CNV evolution. Methods: We performed a longitudinal, prospective observational study of over 130 patients with metastatic breast cancer, with regular follow-up and detailed treatment histories. CTCs were enumerated by CellSearch, and samples with >20 CTCs in 7.5ml of whole blood were further processed for single CTC isolation via DEPArray, single-cell library construction, and whole-genome sequencing. CNV counts for each cell were obtained using previously published binning methods (Ginkgo). Three mathematical models were used to evaluate the evolution of CNVs: a punctuated model, a gradual model, and a gradual-on-punctuated hybrid model. Results: In total, 150 patient-years of data were collected. Among samples with sufficient CTC counts for study inclusion, a total of nine patients and 376 cells were isolated for sequencing. A mean sequencing depth of 0.8x was achieved from each single cell. The degree of CNV heterogeneity varies from patient to patient. CNV changes occurred over time in a gradual manner on a background of punctuated changes. The adjusted R2 value for the punctuated model was 0.46, the adj R2 value for the gradual model was 0.76, and the hybrid model achieved an adj R2 of 0.99. Patient samples with large CNV heterogeneity across single cells tend to be from patients with longer treatment histories and from the last blood draw (i.e., the blood collection closest to patient's point of death). We also identified multiple whole-genome duplication (WGD) events from the same patient, in contrast to previous findings that WGD events are usually early clonal events in most instances. Finally, X loss events are among the most frequent chromosomal aberrations identified in CTCs (in up to 80% of CTCs in some patients), which supports previous literature on the loss of the Barr body in hastening metastatic spread. Discussion and Conclusion: In contrast to the previous study, our findings support a gradual-on-punctuated hybrid model, and this model can explain how copy number changes can be a source from which tumors gain resistance to systemic therapies. The model explains how CNV heterogeneities are seen in patients with longer treatment histories, suggesting that CNV continues to be a source of genetic variation at the metastatic stage of the disease course.

Disclosure(s):

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P5-06-03

Analyzing the results of liquid biopsy in the identification of ERBB2 amplified and HER2 expressing metastatic breast cancer: comparison and combination of cell and cell-free platforms

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Background Liquid biopsies are a non-invasive diagnostic approach for detecting circulating tumor cells (CTCs) or circulating tumor DNA (ctDNA) that may provide clinically actionable information for treatment decisions for metastatic breast cancer (MBC) patients when a conventional biopsy is otherwise infeasible. In addition, the development of quantitative, reproducible, and more sensitive HER2 assays is expected to enable the identification of patients with HER2-low MBC that may benefit from novel HER2-targeted therapies. Here we report a comprehensive liquid biopsy platform including immunofluorescent HER2 and ER quantitative protein expression in CTCs (ctcIF) coupled with the determination of ERBB2 amplification and the number of Large-scale State Transitions (LST) by single-cell CTC genomics (ctcDNA), and ctDNA alterations in plasma. Methods Blood samples were collected for cell-based and cell-free analysis from 62 patients with documented MBC and from 24 blood donors (HD) with no known cancer history. After isolation, nucleated cells were plated, and slides and plasma were bio-banked. CTCs were identified using Epic Sciences digital imaging and machine learning algorithms, and ctcIF enables quantitation of HER2 and ER protein expression. ctcDNA was analyzed by low-pass whole-genome sequencing (WGS), allowing detection of ERBB2 amplification (ERBB2amp) and quantification of large-scale state transitions (LST+) in individual CTCs. cfDNA from plasma was analyzed using a validated NGS panel (56 genes of interest) to detect ctDNA alterations. Results Within this cohort of 62 MBC patients, the presence of CTCs, ctcDNA (LST+) and ctDNA alterations were detected in 87%, 70%, and 59%, respectively, while no CTCs and no ctDNA alterations were detected in the HD

cohort, suggesting high specificity. ctcDNA genomics was more sensitive than ctDNA in detecting ERBB2amp in MBC patients (11%, and 2%, respectively). A variant allele frequency (VAF) of > 40%, which is required for detecting a two-fold ERBB2 amplification by ctDNA, was not present among 86% and 0% of MBC detected by the ctcDNA and ctDNA platforms, respectively, suggesting that the ctcDNA platform can identify ERBB2amp among patients with a low ctDNA fraction. HER2+ or ER+ expression by ctclF were detected in 37% and 58% of MBC patients, respectively. At the cellular level, across 62 patients, CTC with detectable ERBB2amp by ctcDNA had a higher median expression of HER2 protein by ctclF compared to CTC with ERBB2nonamp (1772 MFI vs 122.5 MFI, respectively; $p < 0.001$). Similarly, at the patient level, among patients with circulating ERBB2amp, HER2 protein was detected by ctclF in 100% of MBC patients ($p < 0.001$), suggesting a very high positive correlation between the presence of ctcDNA genomic ERBB2amp and ctclF HER2 protein expression. A liquid biopsy classification of HER2 status by combining the three platforms (ctclF, ctcDNA, and ctDNA) identified that among MBC, 11% were ERBB2amp, 26% were HER2 expressing (HER2+ and ERBB2nonamp), and 60% were HER2neg (HER2- and ERBB2nonamp). Combination models of the three individual platforms (ctclF, ctcDNA, and ctDNA) were able to provide potentially clinically actionable biomarker data (LST+ CTC, ERBB2amp CTC, HER2+ CTC, ER+ CTC and 1A+ SNVs) to 79% of MBC patients while retaining 100% specificity. Conclusions Here we reported a comprehensive liquid biopsy profile combining ctclF, ctcDNA, and ctDNA platforms with high sensitivity and specificity in determining clinically actionable HER2 and ER biomarker status that may impact therapeutic decision-making in late MBC patients. The comprehensive liquid biopsy platform's combined utility can aid biomarker profiling of MBC among often biologically heterogeneous tumor sites of metastatic disease and those inaccessible by conventional tissue biopsy.

Disclosure(s):

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P5-06-04

The prognostic value of c-MET monitoring by using c-MET-enriched circulating tumor cells in HR-positive HER2-negative metastatic breast cancer

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[Background] As the development of endocrine resistance and late recurrences are the major clinical concerns in hormone receptor (HR)-positive/HER2-negative metastatic breast cancer (MBC) patients, biomarkers to predict the occurrence of endocrine resistance or disease progression are crucial for improving patient outcomes. Aberrant HGF/c-MET signaling pathway has been reported to play a role in various cellular processes in cancer. Estrogen Receptor 1 (ESR1) mutations, encoding estrogen receptor α , are associated with endocrine resistance in HR+ breast cancer. PIK3CA hotspot mutations that induce hyperactivation of the PI3K are found in 30-40% of HR+ advanced breast cancers. In this context, we evaluated the prognostic values of c-MET-enriched CTC, ESR1 mutations, PIK3CA mutations, and cfDNA concentrations detected in the blood of HR+HER2- MBC patients. [Methods] MBC patients were prospectively enrolled during standard treatments at Samsung Medical Center (IRB No.2019-08-119). Circulating tumor cells (CTCs) were isolated using the GenoCTC® with c-MET-enriched or EpCAM-enriched CTC isolation kits (Genobio Corp., South Korea) from 4mL

of blood each. PIK3CA and ESR1 hotspot mutations were analyzed by droplet digital PCR kits (Gencurix Inc., South Korea). cfDNA concentrations were calculated using ESR1 gene copy numbers from plasma. To compare the proportion of c-MET overexpression between primary breast tumors and metastatic sites in HR+HER2- breast cancer patients, primary breast (n=358) and metastatic sites (n=27) were independently collected. c-MET expression was evaluated by an immunohistochemistry assay using an anti-total c-MET (SP44) antibody with a Ventana Discovery XY automated system according to the manufacturer's instruction. c-MET overexpression was defined if the staining was scored as 2+ or 3+. Progression-free survival (PFS) was defined as the time from blood draw to the first of either disease progression or death during standard therapy. [Results] Out of 93 patients with HR+ MBC, analysis was performed in 63 HR+HER2- MBC patients. Seventeen patients (27%) had one or more EpCAM-enriched CTCs, and fourteen patients (22%) had one or more c-MET-enriched CTCs detected in their blood. The median follow-up time and median time to censoring were 8.4 months and 18.7 months, respectively. According to the Kaplan-Meier survival analysis by log-rank test, c-MET-enriched CTCs, cfDNA concentrations, and ESR1 mutations were significantly associated with PFS ($p=0.0026$, 0.0064 , and 0.011 , respectively). However, PIK3CA mutations and EpCAM-enriched CTCs were not statistically significant with PFS ($p=0.38$ and 0.86 , respectively). Multivariate analysis showed that both c-MET-enriched CTCs (HR=3.5, $p=0.014$) and cfDNA concentrations (HR=2.2, $p=0.031$) were independent predictors for PFS in HR+HER2- MBC. The proportion of c-MET overexpression was significantly higher in metastatic sites (22.2%) than in primary breast tumors (4.7%) in HR+HER2- breast cancer patients ($p=0.00002$). As c-MET-enriched CTCs and cfDNA concentrations were independent predictors of disease progression, patients were divided into two groups depending on the result of c-MET-enriched CTCs and cfDNA concentration. When patients with low c-MET-enriched CTC and cfDNA concentrations were classified as a low-risk group and other patients into a high-risk group, the high-risk group had a shorter PFS than the low-risk group ($p=0.003$). [Conclusion] This study provided c-MET-enriched CTCs and cfDNA concentrations calculated by ESR1 copy numbers in patient blood were significant independent predictors of disease progression in HR+HER2- MBC. The poor prognosis in the c-MET-enriched CTC-high group and the difference in the c-MET overexpression rate between the primary breast and metastatic sites suggested the importance of monitoring c-MET-enriched CTCs in the blood of HR+HER2- MBC patients.

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P5-06-05

Whole-genome bisulfite sequencing of single circulating tumor cells identifies cellular methylation heterogeneity in metastatic breast cancer

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Background: Although different patterns and changes in DNA methylation play an important role in cancer progression and tumor subtype differentiation, methylation remains relatively less understood in the context of tumor heterogeneity. Intra-tumor heterogeneity influences chemotherapy response, resistance development, and metastatic progression, and can be identified with liquid biopsy, a non-invasive approach to monitor cancer progression and provide predictive information. In this study, we sequenced circulating tumor cells (CTCs) to interrogate whole-genome methylation at single-cell level and single-base resolution. Methods: We enumerated CTCs in 7.5ml of whole blood samples from over 130 metastatic breast cancer patients using CellSearch, and selected blood samples with more than 20 CTCs to be further processed by DEPArray. After single-cell library construction using the Swift Accel-NGS Adaptase Module, whole-genome bisulfite sequencing (WGBS) was performed. The sequencing data were then aligned to the reference genome, and the methylation information was extracted by Bismark. We compared methylation profiles between CTC and WBC samples from each patient to identify differentially methylated regions (DMRs) using Methylkit. Multiple-comparison was conducted by SMART2 to identify DMRs within CTCs. Heatmap was plotted based on the regional methylation rates of DMRs. CpG and genic annotations were performed by annotatr. The pathway and function enrichment analyses (KEGG and GO) were conducted using clusterProfiler. Genomic region-based enrichment was conducted using LOLA. t-SNE clustering was used to investigate intra-patient heterogeneity. Results: A total of 376 cells from nine patients that passed our selection criteria were isolated for WGBS. The mean sequencing depth of all single cells was 0.8x, and an average mapping rate of 54% was achieved. We first compared CTCs and WBCs, and observed a global hypo-methylation pattern in CTCs (average methylation rate 68.8% in CTCs vs. 76.7% in WBCs). Moreover, approximately 2,000 highly differentially methylated regions were found in each patient, with hundreds of hypo- or hyper-methylated genes related to these DMRs. Hypo-methylated DMRs showed genomic region-based enrichment in breast-, prostate-, and fibroblast-related region sets. Then, we investigated methylation heterogeneity within CTCs, where t-SNE clustering identified four different subsets in one representative patient. About 1,500 hypo-methylated DMRs were found, differentiating those four subgroups. KEGG pathway analysis indicated enrichment in the Rap1 signaling pathway and focal adhesion. GO enrichment analysis highlighted the regulation of GTPase activity and membrane potential. Conclusions: Our study identified differentially methylated regions in CTCs of metastatic breast cancer patients, and demonstrated intra-patient heterogeneity based on cellular methylation information. Future studies are warranted to validate our findings and explore their biological mechanisms and clinical relevance.

Disclosure(s):

Rui Luo, n/a: No financial relationships to disclose

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P5-06-06

TROP2 and HER2 expression by liquid biopsy in women with mTNBC

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Introduction A blood-based biopsy can inform the prognosis for MBC patients when conventional tissue biopsies are not feasible within often biologically heterogeneous sites of metastatic disease. Several anti-Trophoblast cell-surface antigen 2 (TROP2) and HER2 targeted therapies are now available, either as approved therapy options or in clinical trials for MBC patients. Tumor expression of TROP2 is prominent in metastatic cancers, such as HER2-negative MBC and TNBC, with limited treatment options. Technical feasibility data of blood-based TROP2 and HER2 immunofluorescence assays demonstrate the utility of the Epic Sciences platform for this cohort of metastatic TNBC (mTNBC) patients. Methods Cultured cancer cells (expressing TROP2, HER2, or neither) were added to Healthy Donor (HD) blood, creating the model system used in assay development studies. Blood from 11 confirmed mTNBC patients was collected to analyze this clinically relevant population. Immunofluorescence staining and image analysis were performed on replicate blood-based biopsy slides to assess expression for TROP2 and HER2. CTCs were identified and characterized using Epic Sciences digital imaging and machine learning algorithms. Results Three cancer cell lines of various TROP2 expression levels (HEK293, low; MDA-MB-231,

intermediate; and A431, high) exhibited immunofluorescence signal ranges of 168 MFI, 2147 MFI, and 26982 MFI, respectively. A fluorescence cutoff of 218 MFI was established following assay optimization to distinguish TROP2 positive CTCs based on a 95% confidence level. Within the cohort of 11 mTNBC patients, 100% of patients with mTNBC had detectable CTCs. 64% of mTNBC patients had TROP2 positivity (MFI, mean: 1328, range: 37-38281)). On the other hand, 0% of mTNBC patients had HER2 positivity (MFI, mean: 128, range: 40-361)). To date, studies with biomarker expression for these two drugs have been limited to tissue biopsy, which may not always yield contemporaneous sampling in the metastatic setting. These results offer a potential liquid biopsy test identifying pts more responsive to trop2 and her2 directed therapies. Discussion Here we report on a liquid biopsy profile combining protein expression of TROP2 and HER2. Blood-based assessment of TROP2 and HER2 expression is a potential marker for selecting MBC patients likely to respond to anti-TROP2 targeted therapies such as Sacituzumab, or Trastuzumab Deruxtecan has shown to improve survival in mTNBC in the ASCENT trial and DESTINY-04 studies. Recent data on the Destiny-04 trial, which allocated HER2 expressing MBC patients into T-DXd treatment, transformed the definition of TNBC. The development of quantitative, reproducible, and more sensitive immunofluorescence assays is becoming crucial for assigning patients whose disease continually evolves to targeted therapies by increasing clinical trial options. Analysis of the clinical utility of the blood-based cell analysis in guiding patient selection strategies for novel anti-TROP2, HER2, and other targeted therapies treatment in MBC is ongoing.

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5:00 PM - 6:15 PM

P5-07-01

Outcomes of multidisciplinary team approach and intensive patient education in young women with breast cancer to improve the rate of fertility preservation

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Background Young breast cancer patients of childbearing age often had to give up their opportunity as women or mothers for cancer treatment. As the survival rate of young breast cancer patients increases with advances in early detection and treatment of breast cancer, interest in issues such as fertility preservation, which have not been satisfied so far, is increasing. This study aims to report the experience of improvement of the fertility preservation rate through a multidisciplinary team approach and systematic patient education for young breast cancer patients. **Methods** Patients treated with multidisciplinary team approach including surgical, medical oncologist and fertility specialist were included for analysis. Patient were divided into two periods: before and after intensive patient education. Patient education included in-person counseling, hand-out materials, and audiovisual education about ovarian dysfunctions related to cancer treatment and fertility preservation methods. We compared the rate of fertility counseling, preservation between two periods. Also, effect of hormonal receptor status on fertility outcome with pregnancy and birth were analyzed. **Results** The rates of fertility counseling (39.4% to 58.1%), ovarian function preservation with gonadotropin releasing hormone antagonists (37.8% to 49.7%), and either embryo (0.9% to 5.6%) or oocyte preservation (0 to 7.5%) were significantly increased (all, $p < 0.001$) after intensive patient education. Pregnancy (9.5% vs 14.2%, $p=0.034$) and birth rate (7.7% vs 12.2%, $p=0.043$) were significantly higher with women with negative hormone receptor status. In hormone receptor positive patients, similar pregnancy rates were observed (13.3 ~ 15.4%) in patients who complete 5years of endocrine therapy, stopped endocrine therapy due to side effects, and received no endocrine therapy. Patients with any type of recurrence were not pregnant during follow up period. Patients who stopped endocrine therapy for child plan showed highest rate of pregnancy (56.0%). Multivariable analysis revealed intensive education were highly associated with improved fertility outcomes (OR 3.843 95% CI 2.781–5.311, $p < 0.001$) after adjusted for different stage and treatment modality. **Conclusion** Multidisciplinary team approach with intensive patient education of fertility preservation in young women breast cancer significantly improved fertility preservation attempt. Hormonal receptor status and recurrence were associated with impaired fertility outcomes

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P5-07-02

Embryo utilization in young breast cancer patients who have undergone egg harvesting for fertility preservation

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INTRODUCTION: Much progress has been made related to fertility preservation in women diagnosed with breast cancer. This includes heightened awareness of impaired fertility due to breast cancer treatment, increased referrals to fertility specialists and development of safe and expeditious means of egg harvesting. Nevertheless, there has been limited investigation of the ultimate issue in fertility preservation, namely the frequency with which women who have undergone egg harvesting actually pursue childbearing. We have retrospectively reviewed a single institution's experience with egg and embryo utilization among patients who expressly desired childbearing and underwent egg harvesting after a diagnosis of breast cancer. These issues have also been analyzed relative to race and insurance coverage. **METHODS:** In an IRB approved study, breast cancer patients treated in our institution between 2010 and 2020 were identified and their post-diagnosis fertility and childbearing history was reviewed. Inclusion criteria were age at presentation ≤ 45 years and diagnosis of either invasive breast cancer or ductal carcinoma in situ. Race (self-reported on clinic intake form) and insurance coverage data were analyzed. In cases of incomplete medical record data, we interviewed patients by telephone. **RESULTS:** 316 breast cancer patients of reproductive age were identified (average age at diagnosis = 39 years, range: 23 - 45). Of these, 168 patients (53%) were offered fertility referral and 118 (38%) saw a fertility specialist. 91 patients (29%) pursued egg harvesting followed by cryopreservation of eggs in 49 cases and embryos in 41 with 1 case unknown. Over an average of 5 years of follow-up (range: 2 - 12 years), 28 women (31% of those who pursued egg harvesting) utilized the egg or embryo to pursue childbearing. 17 underwent embryo transfer to themselves and 11 used surrogate carriers. To date, this has resulted in 20 childbirths from 24 pregnancies. Four pregnancies are currently ongoing and 1 woman is awaiting embryo transfer. Four patients who had undergone egg harvesting conceived without fertility intervention. Of the 55 Medicaid patients of reproductive age diagnosed with breast

cancer, only 8 (15%) met with a fertility specialist, 4 harvested eggs, and none pursued childbearing. HMO/PPO insured patients were significantly more likely than Medicaid patients to pursue egg harvesting and embryo utilization ($X^2 = 7.320$, $df = 2$, $p = 0.026$). Of 260 HMO/PPO insured patients, 110 (42%) met with a fertility expert, 87 harvested eggs and 28 pursued embryo transfer. Due to the small sample size of patients who utilized embryos in each racial subgroup, analysis did not yield statistically significant differences across groups ($p=0.067$). Nevertheless, apparent racial disparities exist. Our data reveal that 5 of 17 (29%) Asian patients and 22 of 62 (36%) White patients utilized embryos as opposed to Black patients (1/4 or 25%), Hispanic patients (0/4 or 0%) and those who identified their race as "other" (1/4 or 25%). CONCLUSIONS: These data demonstrate a low overall rate of cryopreserved egg and embryo utilization among women treated for breast cancer whose earlier pursuit of egg harvesting was evidence of a desire for childbearing. Furthermore, racial and insurance data demonstrate disparities in the pursuit of fertility treatment and utilization of preserved eggs and embryos. Further research will utilize interviews to analyze individual women's decision-making process relevant to such issues as hormone therapy utilization, concerns about breast cancer recurrence, progression of disease and restraints imposed by relationship status and finances. Given the disparity findings reported here, finances will likely emerge as a significant barrier to childbearing in future qualitative research.

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The Association Between Symptom Severity and Physical Function among Participants in I-SPY2

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Title. The Association Between Symptom Severity and Physical Function among Participants in I-SPY2 Background. Patient-reported outcomes (PROs) are increasingly recognized as a valuable component to understand treatment tolerability and toxicity among patients on clinical trials. We have implemented a system for monitoring patient reported outcomes (PROs), symptoms, and quality of life (QOL) using electronic PRO (ePRO) instruments for patients enrolled in the I-SPY2 trial. I-SPY2 is a phase II multi-site clinical trial evaluating the effect of novel neoadjuvant therapies for locally advanced breast cancer. We correlated patient demographic factors with symptoms, investigated the trajectory of symptoms throughout treatment, and sought to characterize symptoms associated with decline in physical function (PF). Methods. Our study population included 259 I-SPY2 patients that completed surveys on one of 9 study arms (including novel oral taxane/immunotherapy combinations, IV paclitaxel, checkpoint inhibitor+/- LAG3 inhibitor, and control IV paclitaxel +/- trastuzumab/pertuzumab). After the 12 week period of investigational agents, most patients received standard adriamycin and cyclophosphamide (AC). Symptom severity, frequency, and interference was assessed weekly using 33 items from the PRO-CTCAE item bank. PF was assessed using the NIH PROMIS instrument and was evaluated at baseline, inter-regimen (after 12 weeks of treatment), pre-surgery, and 1 and 6 months at follow-up. An odds ratio was used to assess univariate associations between age and race, and symptoms. Regularized multi-variate regression was used to evaluate early symptoms (prior to week 6) predictive of a clinically significant (>5 point T-score) decline in PF from baseline to post-treatment follow-up among all races and age groups. Results. Of 259 patients (mean age (SD) = 46.8 (13.6)), 160 (58%) were White, 13 (5%) were Asian, 26 (10%) were African American (AA), 25 (9.3%) were Hispanic, and 35 (13.5%) self-reported "Other". At baseline, AA patients had a higher severity of joint pain than White patients (OR = 14.9, $P < 0.05$). During study treatment with paclitaxel and/or novel agent within the first 12 weeks of treatment, AA patients and non-white (NW) patients were more likely to report severe vomiting than White patients (OR =13.22 and 12.72, $P < 0.05$ and $P < 0.03$ respectively). During treatment with AC, NW patients were more likely to report higher severity of neuropathy than White patients (OR = 5.43, $P < 0.03$). Among all patients, in analysis of early symptoms predictive of a clinically significant decline in PF between baseline and 1 month post treatment, predictors included high frequency of diarrhea, severity of itching, and severity of joint pain. Further analysis of symptom trajectories revealed that frequency of

diarrhea reported rose sharply between baseline and Cycle 2 with 9 patients (7%) reporting occasional or frequent diarrhea to 39 patients (28%) reporting occasional to almost constant diarrhea and remained stable at that proportion for the remainder of treatment. Frequency of diarrhea declined slightly during AC (17%) and dropped to baseline levels by follow-up. In contrast, severity of joint pain persisted post-treatment, rising consistently from baseline through follow-up with 3 patients (2%) reporting moderate to severe joint pain at baseline to 18 patients (35%) reporting moderate to severe joint pain at follow-up. Conclusion. Among I-SPY2 participants, when higher grade of diarrhea is persistent (or uncontrolled), it impacts physical function even after end of therapy. In some cases, race was also a determinant in symptom trajectory, although a higher enrollment of AA and NW patients will enable more robust estimates to be computed. While some of these early symptom predictors are transient and resolve by the time of follow-up, others persist long-term and contribute more directly towards impaired physical function at follow-up.

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P5-07-04

Evaluation of Treatment Choices at Baseline Among Breast Cancer Patients Based on the Frailty Status of the Patients

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Background

Previous studies have shown that the frailty scores aid in better patient assessment and in advising treatment strategies. The objective of this study is to evaluate the impact of frailty status on the treatment choices among breast cancer patients.

Methods

Patient Reported Outcomes Mobile Platform (PROmpt®), an application for remote patient reporting, was used by breast cancer patients for completing surveys between September 2020 and April 2021.

Out of 317 breast cancer patients, there were 84 women for whom frailty assessment was done at baseline based on age, Activities of Daily living (ADLS), Instrumental Activities of Daily living (IADLS) and comorbidities. Frailty status was stratified based on frailty score into fit (score=0), intermediate fit (score = 1) and frail (score >=2). Treatment choices at baseline were stratified into targeted and cytotoxic monotherapy, hormone therapy, and systemic combined therapy. Role of chemotherapy treatment as adjuvant or neoadjuvant therapy was also assessed. Descriptive analysis was performed to assess the association of frailty status on the treatment choices at baseline.

Results: Around 24% of breast cancer patients were below 50 years of age and 76% patients were at least 50 years of age or older. The majority of the study population was White (84.15%) and non-Hispanic and Latino's (63.09%). Around 61% of patients had early-stage breast cancer and around 36% of the patients had late-stage breast cancer.

The majority of fit patients (70.59%) and intermediate fit patients (81.82%) receive systemic combined therapy at baseline. Out of fit patients, 67.80 % patients received adjuvant or neoadjuvant therapy, while 44.44 % of the intermediate fit patients received adjuvant or neoadjuvant therapy.

Discussion/Conclusion

Results demonstrate the feasibility of gathering fitness and frailty data as part of routine breast cancer care. Overall, the treatment choices among fit, intermediate fit and frail groups of patients appear consistent, although adjuvant/neoadjuvant therapy is directionally higher in fit patients. This similarity in regimen choice may be due to sample size, as the number of frail and intermediate fit patients is relatively small when compared to the fit patients. Further exploration related to treatment choices is recommended in a study population with higher levels of patients assessed as frail for comparative evaluation.

Frailty Assessment and Treatment Choice

Frailty Category	Treatment Choices				Total
	Targeted monotherapy	Cytotoxic monotherapy	Hormone therapy	Systemic combined	
FIT	5 (7.35%)	3 (4.41%)	12 (17.65%)	48 (70.59%)	68
INTERMEDIATE FIT	1 (9.09%)	0 (0%)	1 (9.09%)	9 (81.82%)	11
FRAIL	0 (0%)	0 (0%)	1 (50%)	1 (50%)	2
TOTAL	6	3	14	58	81

Frequency Missing =3

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Improving Health-Related Quality of Life with Outpatient High-Dose Methotrexate Regimen Among Solid Tumor Oncology Patients with Intracranial Metastases: A Qualitative Study

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Introduction: Breast cancer patients with intracranial (IC) metastases including leptomeningeal metastasis (LM) confer poor prognosis. Upon disease progression with standard lines of therapy, high-dose intravenous methotrexate (HD IV MTX) is offered to patients given its effective CNS penetrance. HD IV MTX is commonly administered inpatient, requiring extended hospitalization, rigorous leucovorin rescue, IV hydration, and urine alkalinization. Currently, quality of life (QoL) aspects of inpatient v. outpatient regimens remain unknown. **Methods:** An outpatient MTX protocol with daily visits to outpatient infusion centers was institutionally developed. Study eligibility criteria included solid tumor diagnoses with IC±LM metastasis, disease progression on standard of care treatment, and transition from inpatient to outpatient regimen within the past 12 months. For eligible patients upon consent, qualitative semi-structured phone interviews were conducted with focus on physical functioning and symptom burden. Thematic analysis was utilized. **Results:** Of the 10 patients who were screened, three (breast=2, sarcoma=1) were eligible. Patient demographics included 2 Caucasians, 1 African American, mean age of 52 years, and s/p prior whole brain radiation. Among QoL measures, no differences in functional status were reported between the two regimens. Single sarcoma patient reported less nausea and emesis with the outpatient regimen. All patients agreed on convenience, autonomy, greater personal and family time, and stronger emotional support while undergoing the outpatient protocol. Despite honorable mentions of inpatient onsite staff and services, all patients reported higher QoL experienced with outpatient MTX protocol vs. inpatient. **Conclusions:** Interview analysis determined that patient autonomy and nonobligatory hospitalization are key outpatient MTX treatment hallmarks that greatly enhanced patient QoL. Despite the small preliminary patient pool, this study delineates the feasibility in development of an institutionalized patient-centered outpatient MTX protocol. Future clinical trials will additionally be dedicated in conducting a cost-effective analysis comparing both MTX regimens.

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P5-07-06

Prospective cohort of breast cancer patients exposed to a navigation program for timely access to referral services in Mexico

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Background: Patient navigation (PN) is an essential component of cancer care that reduces barriers and enhances the provision of comprehensive, patient-centered care. PN programs and evidence regarding their effectiveness in low- and middle-income countries are limited. This study aimed to assess whether a PN program for the systematic identification of breast cancer (BC) patients' medical and support needs facilitated referral and timely access to the specialty and supportive care services they required.

Methods: This prospective cohort included women ≥ 18 years with a recent BC diagnosis (≤ 3 months [m]), treated at Hospital Zambrano Hellion TecSalud in Mexico, and who provided signed informed consent to participate in the PN program from Apr-21 to Jul-22. Participants completed a series of target questions and validated questionnaires to systematically identify their health needs at baseline, 3 m and 6 m since diagnosis. Subsequently, the navigator had a face-to-face or remote meeting with each patient to inform them about the needs detected at each timepoint. According to these needs, the navigator provided referral to the required services. However, it was each patient's decision whether she attended to the recommended services. Patients' attendance to referrals provided at baseline and 3 m were assessed at 3 m and 6 m, respectively. Descriptive statistics were employed.

Results: During the analyzed period, 263 patients were invited to participate in the study. Of these, 161 (61%) agreed to participate, 57 (22%) agreed but did not complete any survey, and 45 (17%) denied participation. At the time of the analysis, 148, 119 and 86 patients had completed baseline, 3 m and 6 m navigation, respectively. Median time from BC diagnosis to the baseline navigation meeting post survey-completion was 46 days (12-90). Patients' median age at baseline was 48 years (24-88). Most had \geq high school education (93%), were unemployed (51%) and were married/in domestic partnership (73%). As for medical insurance, most had public (32%) or both public and private coverage (32%), while the rest had private

(26%) or no insurance (9%).

Patients' referrals according to their needs and the rate of attendance to those services are detailed in the Table. The main barriers that were qualitatively identified for non-attendance to referral services were time restrictions, patient-provider miscommunication, medical coverage limitations, and financial constraints.

Feedback regarding the PN program was provided in 72 cases. All respondents were very satisfied (97%) or satisfied (3%) with the program; affirmed the navigator had facilitated their referral to all (97%) or some (3%) of the services they believed they needed; and stated that the program aided to better cope with their illness (100%).

Conclusion: Patients experienced diverse health needs during their trajectory through BC, mainly in terms of psychological support, genetic counseling, maintenance of an adequate weight and access to support groups. However, a suboptimal proportion of patients received attention by the required services. This PN program effectively detected patients' needs and provided referrals to specific services. Moreover, patients were highly satisfied with the program and believed it aided their coping process. Yet, several barriers that hinder attendance to the referral services might exist and should be identified to enhance the provision of timely, comprehensive care.

Table. Patients' referral and attendance to specialty and supportive care services.

Referral services	Baseline		3 months		6 months
	Referred patients N=148 (100%)	Patients who attended (% of attendance)	Referred patients N=119 (100%)	Patients who attended (% of attendance)	Referred patients N=86 (100%)
Psychology	92 (62%)	48 (52%)	69 (58%)	37 (54%)	46 (53%)
Genetics	80 (54%)	56 (70%)	40 (34%)	28 (70%)	18 (21%)
Nutritionist	80 (54%)	20 (25%)	42 (35%)	17 (40%)	20 (23%)
Support groups	77 (52%)	54 (70%)	68 (57%)	62 (91%)	66 (77%)
Wigs	56 (38%)	44 (79%)	4 (3%)	4 (100%)	2 (2%)
Fertility preservation	37 (25%)	6 (16%)	NA	NA	0 (0%)
External prostheses	31 (21%)	3 (10%)	10 (8%)	2 (20%)	4 (5%)
Breast reconstruction	28 (19%)	21 (75%)	17 (14%)	13 (76%)	16 (19%)
Rehabilitation	24 (16%)	8 (33%)	21 (18%)	13 (62%)	22 (26%)
Psychiatry	6 (4%)	5 (83%)	7 (6%)	6 (86%)	4 (5%)
Pain clinic	4 (3%)	4 (100%)	3 (3%)	3 (100%)	2 (2%)
Geriatrics	4 (3%)	3 (75%)	4 (3%)	4 (100%)	2 (2%)
Palliative care	2 (1%)	2 (100%)	2 (2%)	2 (100%)	2 (2%)
Sexuality counseling	NA	NA	18 (15%)	0 (0%)	8 (9%)

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P5-07-07

Feasibility of a Whole-Food, Plant-Based Intervention Among Women with Metastatic Breast Cancer and its Effect on Patient-Reported Outcomes

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Background: Women diagnosed with breast cancer commonly gain weight during and after treatment; this obesity/weight change is associated with decreased quality of life (QOL) and other patient-reported outcomes (PROs) such as cognitive dysfunction. Whole-food, plant-based (WFPB) dietary interventions lead to weight loss and cardiometabolic improvements, but their feasibility among metastatic breast cancer patients and their effect on cancer-related PROs have not previously been studied.

Methods: Women with stage 4 breast cancer and stable disease were randomized 2:1 into: 1) a WFPB dietary intervention (N=21) or 2) usual care (N=11) for 8 weeks with assessments at baseline, 4 and 8 weeks. Our WFPB diet consisted of weekly educational visits and an ad libitum whole-food, plant-based diet. Three prepared meals a day were provided for the duration of the trial. The diet included fruits, vegetables, whole grains, legumes, nuts and seeds

and excluded meat, dairy, eggs, and added oils/solid fats. Effects of the WFPB diet on the outcomes were assessed by comparing marginal means by arm estimated at 8 weeks from the analysis of covariance model controlling for baseline.

Results: Of 32 subjects randomized, 20 intervention subjects and 10 control subjects completed all 3 assessments. Baseline and week 8 dietary intake among the intervention subjects is shown in table 1. Cognitive function, as measured by the Functional Assessment of Cancer Therapy – Cognitive Function (FACT-COG) questionnaire and a modified MD Anderson Symptom Inventory (MDASI), showed significant improvement within the intervention group as well as in comparison to the control group (Table 2). Overall quality of life, emotional and physical wellbeing, and breast cancer-specific symptoms, as measured by Functional Assessment of Cancer Therapy – Breast (FACT-B) questionnaire improved significantly within the intervention group. Mean fatigue was lower at 8 weeks within the intervention group as measured by the Brief Fatigue Inventory (BFI), but this did not reach statistical significance (p=0.10). When intervention subjects were asked, “On a scale from 1 to 10 [1 being “would not recommend” and 10 being “highly recommend”], how strongly would you recommend that other cancer patients be given this type of nutrition and support intervention if they were able and willing to participate?” participants’ mean score was 9.5.

Conclusion: Our WFPB intervention was feasible and acceptable, with high compliance despite asking subjects to make major changes in dietary intake. Clinically and statistically significant improvements in several PROs, including cognitive function, overall QOL, physical and emotional wellbeing were noted for those in the WFPB group. Given the benefits to QOL and PROs, longer studies are required to demonstrate durability of behavior changes and outcomes.

Table 1: Nutrient Intake of the Intervention Group (n=19*)

	Baseline	Week 8 Final	Percent Change	P-Value
Total grams (weight)	2702.8	3192.5	18.1%	0.03
Energy (kcal)	1733.2	1321.3	-23.8%	<.01
Fat (% of total kcal)	35.4	20.4	-42.4%	<.01
Carbohydrate (% of total kcal)	48.8	66.2	35.7%	<.01
Protein (% of total kcal)	14.8	12.6	-15.1%	<.02
% total protein provided by plant sources	46.5	95.7	105.8%	<.01
Dietary Cholesterol (mg)	210.3	7.5	-96.4%	<.01
Dietary Fiber (g/1000 kcal)	21.4	40.8	90.7%	<.01

*One participant was missing one three-day food record

Table 2. Patient-Reported Outcomes

	Intervention Group		Control Group		Between Group Difference	Between Group Effect Size	p value (between group)
	Baseline	Final	Baseline	Final			
FACT-COG	139.8	156.6*	146.4	145.1	16.1	0.46	0.04
Problems Remembering Things	3.4	2.0*	1.6	2.9	-1.8	-0.72	0.02
Problems Concentrating	3.0	1.9*	1.8	2.9	-1.5	-0.56	0.03
Problems Paying Attention	2.4	1.5*	1.8	2.8	-1.5	-0.58	0.05
FACT-B Total	100.9	111.0*	109.7	112.0	5.6	0.31	0.06
Physical Well Being	21.1	22.8*	22.6	22.1	1.7	0.36	0.09
Emotional Well Being	16.1	18.0*	18.1	16.9	2.2	0.55	0.02
Breast Cancer Subscale	25.7	28.9*	27.0	28.2	1.7	0.40	0.20
BFI	3.6	2.6	2.6	2.3	-0.1	-0.02	0.92

*p < 0.05 for within-group change

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P5-07-08

Evaluating the risk of cardiotoxicity associated with concurrent trastuzumab emtansine (TDM1) and radiation therapy in patients with early-stage HER2 positive breast cancer

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BACKGROUND:

HER2-positive breast cancers, which accounts for 20% of breast cancers, is associated with aggressive clinical behavior and inferior survival. The approval of HER2 targeted therapy has changed the landscape of this disease and has reduced disease recurrence by 50% and has improved survival by 33%. (1) However, cardiotoxicity is a well-recognized adverse event associated with HER2-targeted therapies. Adjuvant trastuzumab emtansine (TDM1) is the current standard of care for patients with residual breast cancer after neoadjuvant HER2-targeted therapy. TDM1 is associated with a risk of cardiotoxicity defined as a decline in left ventricular ejection fraction (LVEF). In a pooled analysis of data from seven metastatic breast cancer trials with TDM1, the incidence of cardiac events such as congestive heart failure (CHF), cardiac ischemia, cardiac arrhythmia or grade 1/2 LVEF drop was 3.37%.

Adjuvant breast radiation (RT) is routinely offered for patients at high risk for recurrence. Breast RT is also associated with long-term increased risk of cardiac disease more than 10 years after RT. The HERA trial which studied use of adjuvant trastuzumab showed that rates of cardiotoxicity were higher in patients receiving concurrent RT with trastuzumab (left sided > right sided breast cancer) compared to those who did not receive adjuvant RT, although not statistically significant. In the multivariate analysis, no treatment or baseline cardiovascular risk factors were strongly correlated with LVEF, but radiation therapy showed a borderline correlation (adjusted HR, 1.258; 95% CI, 1.00-1.58; P = .049).

The risk of cardiotoxicity with concurrent TDM1 and RT has not been well studied. With increasing use of TDM1 in the adjuvant setting, it is important to understand the cardiotoxic effects of combination therapy in early-stage breast cancer.

METHODS:

We undertook a review of our clinical database to identify patients who received adjuvant TDM1 with concurrent RT for Stage I-III breast cancer from 1/2020 to 01/2022. Clinical parameters including age, date of diagnosis, history of cardiac disorders, echocardiogram findings, radiation dose, final pathologic stage and molecular subtypes of cancer were extracted. All patients had ejection fraction to monitor cardiac fraction. Global longitudinal strain (GLS), which is a more sensitive and reproducible indicator of cardiac dysfunction than LVEF, was also collected, if available.

RESULTS:

Of 32 patients identified in our retrospective analysis, two patients (6%) developed a drop in ejection fraction post radiation. Median age of patients was 57y. Majority of the patients were Caucasian (44%) followed by Hispanic (28%). 19 (60%) patients had right sided breast cancers and 13(40%) patients had left sided cancers.

The mean pre-radiation ejection fraction was 60% and post radiation was 61%. Using paired t-testing, there was no statically significant difference in ejection fraction after radiation (p=0.343). Comparative GLS measurements were available for 16 patients and there was no statical difference with concurrent radiation (p=0.18). All patients tolerated radiation with mostly grade 2 skin dermatitis except four patients who had grade 3 skin dermatitis. One patient had to discontinue radiation early given grade 3 skin dermatitis.

CONCLUSION:

This institutional review of 32 patients suggests that adjuvant TDM1 with concurrent RT did not result in a significant change in ejection fraction or GLS. Most patients tolerated radiation without significant skin toxicities. One of the limitations of the study is the small sample size. A larger study should look at more broader conclusions; however this data has strong clinical implications.

Cardiac Parameters pre and post RT

Median age	57
Subtype of breast cancer	
HR+/HER2+	23 (72%)
HR-/HER2+	9 (28%)
Ethnicity	
Caucasian	14 (44%)
African American	3 (9%)
Hispanic	9 (28%)
Other	6 (19%)
Laterality of breast cancer	
Right	19 (60%)
Left	13 (40%)
History of Hypertension	
Yes	15 (47%)
No	17 (53%)
Radiation Dermatitis	
Grade 1	12 (38%)
Grade 2	16 (50%)
Grade 3	4 (12%)
Mean Ejection Fraction	
Pre-radiation	60%
Post-radiation	61%
P value	0.343

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P5-07-09

Fatigue in patients with locally advanced or metastatic breast cancer undergoing single-agent taxane-based chemotherapy: de novo versus relapsed

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Introduction: Fatigue is a debilitating and persistent condition of exhaustion that interferes with usual functioning. It is the most reported symptom across all cancer patients, and when related to the malignancy itself or to the neoplastic treatment, is referred to as cancer-related fatigue (CRF). Fatigue occurs in nearly all patients with metastatic breast cancer and is associated with poor clinical outcomes and worse quality-of-life. It is subjective and can be assessed from patient self-reports, such as the FACIT-Fatigue scale or Brief Fatigue Inventory, with no current gold-standard, which may lead to under reporting and lack of treatment intervention. Only since

2016, fatigue has been considered as a syndrome and included in the International Statistical Classification of Diseases, 10th edition, Clinical Modification (ICD-10-CM) according to specific criteria. The aim of this real-world data analysis was to describe the prevalence of fatigue, as reported by physicians using ICD-10-CM codes, in patients with locally advanced (Adv) or metastatic (Mtx) breast cancer (BC) undergoing single-agent taxane-based chemotherapy (CT), and to assess whether relapsed subjects had a higher prevalence versus those diagnosed de novo at an advanced stage.

Methods: Electronic health records (EHR) were analyzed from TriNetX, a global research network containing real-world data from approximately 150 million patients in 115 Health Care Organizations (72 in the United States and 42 in the European Union). Using ICD-10-CM codes and structured data only (no medical notes), subjects were identified with a diagnosis of Adv-Mtx BC who underwent CT with single-agent taxane in 2020, 2021 and 2022 (first quarter). After splitting the cohort based on “relapsed” (second- or further line treatment) vs “de novo” (first-line treatment), we assessed the prevalence of fatigue (any type, R53.x) and CRF (R53.0) within the first 3 months after initiation of taxanes.

Results: Among 379,880 BC patients under follow-up in 2021 across the 115 sites, 50,490 (13%) had Adv-Mtx BC, of whom 16,170 (32%) were diagnosed de novo and 34,330 (68%) experienced relapse. The proportion of patients undergoing single-agent taxane-based CT was 7.5% (1,220) and 13.4% (4,590), respectively. Almost one third (28%) of relapsed patients had previously received taxanes. The prevalence of fatigue (any type) and CRF was similar between the “de novo” and “relapsed” groups (24.6% vs 25.7% and 6.6% vs 5.4%, respectively). Overall, 27% and 21% of all fatigue was coded as CRF in the “de novo” and “relapsed” groups, respectively. No relevant differences were observed between 2020, 2021 and 2022 results.

Conclusions: This real-world analysis reveals that at least one in four patients with Adv-Mtx BC undergoing taxane based CT suffer from fatigue, independent of disease history and other factors. Fatigue is an unmet medical need in patients with BC, particularly in patients receiving taxanes.

Table. Fatigue prevalence (as per ICD-10-CM codes) within the first 3 months of single-agent taxane-based CT in patients with locally advanced or metastatic BC diagnosed “de novo” or relapsed in 2021

Table. Fatigue prevalence (as per ICD-10-CM codes) within the first 3 months of single-agent taxane-based CT in patients with locally advanced or metastatic BC diagnosed “de novo” or relapsed in 2021

Locally advanced or Metastatic BC patients undergoing Single-Agent Taxane-based CT (N=5,810)		FATIGUE PREVALENCE (within first 3 months)
De Novo diagnosis (1,220; 32%)	+ Any Fatigue (R53.x)	300 (24.6%)
	+ Cancer-related Fatigue (R53.0)	80 (6.6%)
Relapsed (4,590; 68%)	+ Any Fatigue (R53.x)	1,180 (25.7%)
	+ Cancer-related Fatigue (R53.0)	250 (5.4%)

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12/8/2022

5:00 PM - 6:15 PM

P5-07-10

Symptom and Functional Status for Individuals with Triple Negative Breast Cancer and Palliative Care Utilization: Findings from the Cancer Experience Registry

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Background: Triple negative breast cancer (TNBC) can spread quickly and has a higher rate of recurrence than other breast cancers. Due to TNBC's aggressive nature and treatment, patients can experience adverse symptoms and side effects. Palliative care (PC) is intended to improve health-related quality of life (HRQOL) for patients with serious disease at any stage of their illness. However, PC is often conflated with end-of-life care which can affect its rates of utilization. The goals of this study were to explore how TNBC patients characterize their HRQOL by time since diagnosis and describe the rate of utilization in the past year of PC providers for symptom and side effect management. Methods: Data was collected through Cancer Support Community's Cancer Experience Registry® (CER). From Jan 2015 to Aug 2021, 209 individuals with TNBC enrolled in the CER and completed the Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29 v2.0) profile measure. Five domains assess symptoms with higher scores corresponding to worse symptomology (depression, anxiety, pain interference, fatigue, and sleep disturbance) and two domains assess function with lower scores corresponding to worse functioning (physical and social). Scale scores were converted to standardized T scores and compared against the U.S. population (M=50, SD=10) and reference values for newly diagnosed patients with all types of breast cancer. We considered a group score difference of 3 points clinically meaningful. Moderate to severe impairments are reported as percentages of the sample that have PROMIS scores >1SD from M=50. Of the 209 TNBC patients, 66 (32%) participated after Nov 2018 and

answered newer survey items about utilization of PC providers in the past year. Results: Participants were mainly Non-Hispanic White (81%); resided in suburban/urban areas (84%); reported household income >\$40K (64%); Mean age=53y (SD=10; range 28-77). Median time since diagnosis was 2y. 25% reported advanced or metastatic disease; 41% were currently receiving treatment. TNBC patients reported elevated symptoms and deficits in functioning relative to the U.S. population (score difference>3) for all PROMIS subscales except depression (M=51.9) and social function (M=48.8). Fatigue and anxiety scores were highest (M=55.3 and M=56.2, respectively) exceeding the threshold for mild severity. About one-third of participants reported moderate to severe levels of symptom impairment for fatigue (36%), anxiety (36%), and pain interference (32%). Newly diagnosed participants reported higher levels of symptom severity and functional deficits which improved over time; however, survivors' PROMIS scores remained worse than the U.S population for fatigue and anxiety. Compared to reference values for breast cancer patients, newly diagnosed (< 2y) TNBC participants (n=83) reported elevated symptoms for fatigue, anxiety, and depression and worse social function (score differences, 4.0, 9.1, 5.3, and 3.9, respectively). In the past year, 69% saw an oncology provider for symptom and side effect support, 44% saw a primary care provider, and 9% a PC provider. Some participants sought care for symptom and side effect management from allied and psychosocial providers such as pharmacists (28%), counselors (25%), and physical therapists (24%). Conclusions: Among TNBC patients, we observed higher levels, on average, of fatigue, anxiety, and depression, and lower social function compared to reference values for breast cancer patients and the U.S. population. Symptom severity and functional deficits were highest among individuals newly diagnosed with TNBC suggesting the importance of incorporating PC into cancer care early in the disease course. TNBC patients and survivors most frequently rely on primary care and oncology care teams for management of symptoms. Future research should examine access barriers to PC providers.

Disclosure(s):

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12/8/2022

5:00 PM - 6:15 PM

P5-07-11

Referral patterns of metastatic breast cancer patients to Palliative Care team at a Cancer Center in Brazil

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Introduction: Breast cancer is the most common cancer in women and the leading cause of cancer-related death in women worldwide. The high prevalence of physical and psychosocial suffering among breast cancer patients and their families justifies the need for an early interdisciplinary approach by a palliative care team. The effectiveness of early palliative care for patients with advanced cancer has been demonstrated in many studies. Early referral to outpatient palliative care services improves symptom control, reduces suffering and improves quality of end-of-life care.

Aim: Evaluation of referral patterns of metastatic breast cancer patients to the outpatient embedded palliative care team.

Methods: We retrospectively retrieved data from electronic medical records of patients who were treated at a private community oncology practice in Brazil who died from metastatic breast cancer during the years of 2018 until 2021. We evaluated the patient's follow-up time by the palliative care team (follow-up > 12 weeks or not) and the year of referral to the service (pre-2020 vs 2020 and later) associated to the service referral type: Late referral (more than 8 weeks of metastatic diagnosis) or early referral. Each group was followed-up by cancer physicians and after referral was also followed-up by a palliative care multidisciplinary team who regularly evaluated cancer patients during their treatments at outpatient setting. During COVID-19 pandemic, some patients were evaluated by telemedicine appointments. We performed univariate comparisons analysis by Fisher's Exact Test. $p < 0.1$ was deemed as statistically significant.

Results: Of the 211 patients whose data were assessed, 99 patients were referred to Palliative Care team before 2020 and 112 patients after 2020. 13.1% of patients pre-2020 received early palliative care versus 33.9% of patients in the post-2020 referral group, resulting in a 3.37-fold odds of an early palliative care integration after 2020 (OR 3.37, CI95: 1.61 – 7.45; $p < 0.001$). Overall, 30.4% of longer follow-up patients were an early referral versus 19.3% of the shorter follow-up, resulting in an 82% greater chance (OR 1.82, CI: 0.92-3.63; $p < 0.1$) of prolonged assistance with early referral.

Conclusions: In this analysis, early palliative care integration for patients with metastatic breast cancer has increased after 2019 despite the COVID-19 pandemic, leading to prolonged time of accompaniment by the multidisciplinary palliative care team. This suggests that even in the face of this challenging moment, a mature and consolidated service is offered by the palliative care team. Also, according to previous data in literature, prematurely integration show signs of correlation with better quality of life and death, supporting early palliative care for this group of patients. However, further work is needed to examine the effect of this care model in our cohort.

Palliative Care Assistance by time-referral

Table: Palliative Care Assistance by time-referral			
Variables	Odds Ratio	95% CI	P-value
Prolongued Assistance	1.82	0.92-3.63	<0.1
Post-2020 referral	3.37	1.61-7.45	<0.001

Disclosure(s):

Sarah A. GOMES, MD: No financial relationships to disclose

Danielle N. Silva, SLP: No financial relationships to disclose

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5:00 PM - 6:15 PM

P5-07-12

Patient-Reported Symptom Burden in Women Undergoing Treatment for Early Stage and Metastatic Breast Cancer

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Background: Women undergoing treatment for breast cancer experience both disease- and treatment-related symptoms. Remote symptom management programs allow real time symptom documentation, earlier intervention, and opportunities to improve quality of life and decrease symptom burden. This study describes patient-reported outcomes (PROs) in women undergoing treatment for early stage and metastatic breast cancer.

Methods: Women with breast cancer using Carevive's remote symptom management (RSM) program completed weekly surveys to assess the presence of 14 common symptoms over 16 weeks. Symptoms assessed were anxiety, decreased appetite, fatigue, general pain, mouth sores, muscle pain, nausea, vomiting, numbness, sadness, shortness of breath, diarrhea, constipation, and insomnia. When a symptom was reported, additional questions were asked regarding symptom severity, frequency, and interference using the National Cancer Society's Patient Reported Outcomes-Common Terminology Criteria for Adverse Events (PRO-CTCAE). The PRO-CTCAE produced composite scores, which classified each symptom reporting event as mild, moderate-severe, or severe. A mild symptom classification generates an electronic care plan with recommendations for symptom management; moderate-severe and severe classifications trigger an alert to the care team. Descriptive analyses summarize PROs for early stage and metastatic patients. Symptom burden was assessed by calculating the frequency distribution of each patient's highest reported composite score for each symptom by month (Table 1).

Results: Between September 2020 and April 2022, 280 women enrolled in the RSM program; 201 of these women had complete staging information for analysis. 80% (n=160) had early stage (0-III) and 20% (n=41) had metastatic (IV) disease. 32% (n=64) were less than 50 years

old and 68% (n=137) were age 50 or older. 58% (n=116) were hormone receptor (HR) positive/HER2 negative, 22% (n=45) HR+ or -/HER2+ and 19% (n=39) HR-/HER2-. In Month 1, patients with metastatic disease most frequently reported moderate to severe symptoms for general pain (51%), nausea (32%), decreased appetite (22%), and diarrhea (29%). In Month 1, patients with early stage disease most frequently reported moderate to severe symptoms for general pain (32%) and diarrhea (28%). In Month 1, general pain was the most frequently reported symptom for both early stage (34%) and metastatic (51%) groups. In both groups over 16 weeks, nausea, diarrhea, and constipation were among the five most reported symptoms along with muscle pain for early stage patients and shortness of breath for metastatic patients. The frequency of all symptoms decreased over 16 weeks, but there remained cases of moderate-severe and severe symptom intensity through Week 16 for several symptoms. Conclusion: Women with metastatic and early stage breast cancer both report severe symptoms during treatment. Early stage patients may have different symptom profiles and unmet needs not captured by common PROs. Future work should further evaluate symptom profiles of early stage patients to understand how to best use PRO monitoring in the curative intent setting.

Percentage of Moderate-Severe and Severe Symptom Reports By Month and Symptom for Women with Early Stage and Metastatic Breast Cancer

Symptom	Early Stage				Metastatic			
	% MO1	% MO2	% MO3	% MO4	% MO1	% MO2	% MO3	% MO4
Anxiety	9	4	4	2	9	5	2	5
Decreased appetite	14	11	6	6	22	17	5	12
Fatigue	14	12	6	5	19	12	7	6
General Pain	32	23	19	15	51	27	20	17
Mouth sores	7	4	3	3	4	7	2	0
Muscle Pain	16	10	6	4	20	7	7	2
Nausea	22	18	16	9	32	20	15	12
Numbness	12	9	9	9	19	9	5	2
Sadness	5	2	2	1	5	7	0	0
Shortness of breath	11	10	8	6	24	15	0	4
Diarrhea	28	24	19	10	29	17	10	10
Constipation	26	15	13	6	22	10	7	7

MO=Month

Disclosure(s):

Tara Kaufmann, MD, MSCE: Carevive: Contracted Research (Ongoing)

Aaron Galaznik, MD: Carevive: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing); Medidata Solutions: Salary (Ongoing)

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12/8/2022

5:00 PM - 6:15 PM

P5-07-13

Effect of a 12 Week Virtual Supervised Exercise Program on Cardiorespiratory Fitness in Breast Cancer Patients Undergoing Chemotherapy: Results from the STRENGTH Trial

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Background: Chemotherapy (CTX) for breast cancer (BC) can have a detrimental effect on cardiorespiratory fitness (CRF), as measured by VO₂max. This decline may be attenuated by physical activity, which can also reduce mortality risk and improve quality of life (QoL) for patients (pts) with BC. During the COVID-19 pandemic, many have pivoted to home-based exercise routines, which have been shown to be safe and feasible for pts with BC receiving CTX. We conducted the STRENGTH Trial to evaluate the effect of a 12-week virtual supervised exercise program in BC pts receiving CTX on CRF. Methods: This is a single-center, prospective, single-arm study designed to evaluate the effect of a 12-week virtual supervised exercise training program on CRF in BC pts receiving CTX. Participants aged ≥18 years with stage I-IV BC who were planned to receive at least 12 weeks of CTX of investigator's choice were eligible for inclusion. Participants were asked to complete a total of 150 minutes (min) of moderate intensity physical activity/week, as a combination of a 45 min weekly virtual personal training session and workout classes streamed from the Peloton® Digital platform (i.e. walking, running, cardio, yoga, strength training, and cycling). The primary endpoint was the distance walked on a Six-Minute Walk Test (6MWT), an accepted surrogate marker for VO₂max, at the start and completion of the program. Secondary endpoints included assessment of QoL using the Functional Assessment of Cancer Therapy - General (FACT-G) and symptom assessment using the MD Anderson Symptom Inventory (MDASI) questionnaires at the beginning, middle and end of the study. Exploratory endpoints included treatment adherence, toxicities, completion and response. Results: 33 participants signed consent for the clinical trial and 2

withdrew voluntarily prior to beginning the program. 5 participants discontinued prematurely due to a diagnosis of COVID-19 (N=3) and pulmonary embolism (N=2) and were not included in the primary endpoint. One participant remains on study at this time. Median age 49 yrs; range 33-68. Mean BMI 29.55; range 18.1-46.5. 13 HR+/HER2-, 7 HR-/HER2-, 11 HER2+. 14 (45%) pts had Stage I, 11 (35%) pts had Stage 2, 5 (16%) pts had Stage 3, 1 (3%) pt had Stage 4. 23 pts (70%) received either an anthracycline or HER2-based therapy. 19 pts (61%) received neoadjuvant CTX on study, 11 pts (35%) received adjuvant CTX and 1 pt (3%) received treatment in metastatic setting. The average number of exercise min per week per participant was 123.2 min (95% CI, 104.1-142.2), with a relative dose intensity of 82%. In the pts that completed the study thus far (N=25), there was no statistically significant difference between the distance walked during the 6MWT at the start and end of the study (median difference= -10m, range: -129-150m, p= 0.67). There was no statistically significant difference in the FACT-G score at the start and end of the study (median difference= -1.0, range -17.83- 30.0, p=0.54). Pts scored higher on the MDASI (median difference= 0.33, range -1.55-4.62, p=0.04) at the end of the exercise program compared to the beginning. There were no new or unexpected treatment toxicities observed. Conclusion: Pts who participated in a 12-week virtual supervised exercise program during CTX for BC did not experience a statistically significant difference in the distance walked during the 6MWT between the beginning and end of the exercise program. Exercise may attenuate the decline in cardiorespiratory function that has historically been observed with CTX for BC. Some pts were not able to adhere to the recommended 150 min of exercise/week suggesting a potential need for modified exercise targets for pts with BC undergoing CTX. This study is limited by a small sample size and larger, randomized clinical trials are needed to further evaluate optimal exercise recommendations for patients with BC undergoing CTX in order to maintain and potentially, even improve, cardiorespiratory function.

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Eleonora Teplinsky, MD: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Eisai: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, May 1, 2021); Sermo: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 29, 2022)

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12/8/2022

5:00 PM - 6:15 PM

P5-07-14

A pilot study of novel approach of intraneural facilitation versus standard physical therapy for prevention of chemotherapy induced peripheral neuropathy

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Background Chemotherapy-induced peripheral neuropathy (CIPN) is a frequent side effect of commonly used chemotherapy (CT) regimens and often results in dose reduction or cessation of treatment which can adversely affect cancer outcomes. Treatment options for CIPN are limited and no standard approaches exist to prevent CIPN. A novel therapy, Intra-neural Facilitation (INF) has been developed by physical therapists at our institution's neuropathy treatment center as a preventative and treatment modality for CIPN. INF therapy involves physical maneuvers and systematic application of pressure to improve peripheral microvascular circulation to the endoneurial capillaries of the extremities. We conducted a randomized pilot study evaluating INF versus standard physical therapy (PT) maneuvers as a non-invasive treatment modality for preventing CIPN during participants' ongoing chemotherapy. This study was supported by an intramural (GRASP) grant and registered on [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT0327919) (NCT0327919). Methods Newly diagnosed patients with breast cancer stages I to III and CT naive gynecologic cancers without preexisting peripheral neuropathy planning to receive treatment with platinum-based compounds and/or taxanes were eligible for this study. Participants were randomized into two treatment groups. Group one received INF and group two received a standardized program of PT including muscle stretching and strengthening exercises. Each group received two (45-minute) treatments twice a week for six weeks under the supervision of trained physical therapists. Participants were evaluated at baseline, week 3, week 6, and 3 months after the date of initiation of chemotherapy. The use of neuropathy medications, CT dose reductions, and treatment discontinuation was compared between the two treatment groups. Vascular perfusion was also evaluated at the same intervals using ultrasound to measure volume flow and pulsatility of the popliteal and posterior tibial arteries. Participants completed a survey at the end of treatment evaluating the effectiveness and satisfaction of the intervention. Results 44 out of 104 patients screened met the eligibility criteria and were randomized to either of the two therapy modalities from July 2017 to June 2022. A total of 38 participants received the allocated intervention and were included in the analysis (n=20 in the INF arm and n=18 in the PT arm). CT dose reduction due to CIPN grade 2 or higher occurred in 6/18 (33%) and 4/20 (20%) participants who received standard PT and INF, respectively. 2/18 (11%) participants required discontinuation of CT prematurely due to CIPN in the standard PT arm when compared to 1/20 (5.0%) in the INF arm. Pharmacologic interventions were required to manage CIPN in 4/18 (22%) participants in the standard PT arm vs 2/20 (10%) in the INF arm at the end of CT. Participants reported more control over their health (95.2% INF arm vs. 83.3% PT arm) and decreased nerve discomfort (75% in the INF arm vs. 61.1% in the PT arm). Participants reported high levels of satisfaction overall at the end of each intervention (95% in the INF arm vs. 83% in the PT arm). Conclusion Our pilot study evaluated the feasibility and potential for INF therapy compared to standard PT for the prevention of CIPN during ongoing chemotherapy. Based on the patient satisfaction survey, the burden and satisfaction with the assigned therapy modality between the two arms were favorable overall. Our results showed that CT dose reduction and early cessation in addition to pharmacologic interventions for CIPN were numerically less prevalent in the INF arm compared to the standard PT arm; however, further studies are needed to validate these findings.

Disclosure(s):

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5:00 PM - 6:15 PM

P5-07-15

Impact of Integrative Therapies on Patients with Metastatic Breast Cancer

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Background: Integrative therapies are shown to support cancer patients' treatment plans, help with side effect management, and improve patients' quality of life ([1-9]). In 2017, the American Society of Clinical Oncology endorsed the Association of Integrative Oncology's Clinical Practice Guidelines highlighting their importance in breast cancer care. Recent studies suggest that more evidence is needed to bring attention to the role of integrative therapies in advanced breast cancer care [4, 7, 8, 10]. This analysis explores participants' experiences with a wellness program implemented by Unite for HER (UFH), a non-profit organization that delivers integrative therapies and support services such as whole food nutrition services, medical acupuncture, oncology massage therapy, counseling, reiki, meditation, yoga, and fitness classes to patients with breast, metastatic breast, and ovarian cancer. As of April 2022, there were over 1,700 women diagnosed with metastatic breast cancer (MBC) participating in UFH locally and nationally.

Methods: UFH members completed a survey about the impact of the UFH Wellness Program on the overall quality of life, including measures on side-effect management, OTC/prescription drug utilization rate, stress reduction, changes to wellness habits, and the social and emotional challenges associated with living with MBC. In total, 119 unique UFH members with MBC answered online surveys distributed by email in 2020 and 2021. Survey questions were designed to evaluate the impact of the UFH Wellness Program.

Descriptive analyses of survey questions and open-ended comments were conducted to

assess program impact.

Results: All respondents were MBC patients/survivors. No other demographic information was collected. While 2020 respondents received mostly in-person services for part of their program, all 2021 respondents received primarily virtual services due to the Covid-19 restrictions. Despite the inaccessibility of in-person services, the satisfaction levels with the wellness program did not drop significantly in 2021. More than two-thirds of respondents (80% in 2020, 67% in 2021) indicated that the therapies offered through UFH Wellness Program significantly improved the side effects of their treatment for MBC. Notably, more than a quarter of respondents (28% in 2020, 26% in 2021) specified that due to UFH integrative therapies they were able to reduce or eliminate one or more OTC/prescription drugs to manage side effects. At the same time, the majority reported experiencing reduced levels of stress after utilizing integrative therapies offered by UFH (93% in 2020, 81% in 2021), as well as improvements in their emotional wellbeing (95% in 2020, 83% in 2021), and quality of life during or after treatment for MBC (97% in 2020, 96% in 2021). Also, 86% of respondents in both years indicated that UFH services, such as nutrition counseling, cooking classes, and exercise classes, helped them adopt and maintain healthier habits in their life. Furthermore, a qualitative analysis of open-ended comments found that 1) respondents expressed deep gratitude and appreciation for UFH integrative therapies, 2) noted that they would otherwise not be able to access such therapies due to financial barriers, and 3) helped them feel better prepared to cope with the psychosocial aspects of their MBC experience.

Discussion: These results suggest that integrative therapies such as those offered by UFH can play a significant role in improving patients' outcomes by reducing stress and drug utilization to manage side effects and improving patients' well-being and quality of life during metastatic breast cancer treatment. These findings highlight the importance of choosing integrative oncology programs to support MBC patients' needs in managing the psychosocial and physical side effects of the disease.

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References

References:

1. Lyman, G.H., et al., *Integrative Therapies During and After Breast Cancer Treatment: ASCO Endorsement of the SIO Clinical Practice Guideline*. *Journal of Clinical Oncology*, 2018. **36**(25): p. 2647-2655.
2. Mao, J.J., et al., *Electroacupuncture for fatigue, sleep, and psychological distress in breast cancer patients with aromatase inhibitor-related arthralgia: A randomized trial*. *Cancer*, 2014. **120**(23): p. 3744-3751.
3. Hack, C.C., et al., *Self-reported Improvement in Side Effects and Quality of Life With Integrative Medicine in Breast Cancer Patients*. *Integrative cancer therapies*, 2018. **17**(3): p. 941-951.
4. Latte-Naor, S. and J.J. Mao, *Putting Integrative Oncology Into Practice: Concepts and Approaches*. *Journal of Oncology Practice*, 2019. **15**(1): p. 7-14.
5. Viscuse, P.V., et al., *Integrative medicine in cancer survivors*. *Current opinion in oncology*, 2017. **29**(4): p. 235-242.
6. Mehling, W.E., et al., *Symptom management with massage and acupuncture in postoperative cancer patients: a randomized controlled trial*. *J Pain Symptom Manage*, 2007. **33**(3): p. 258-66.
7. Rossi, C., et al., *A Model of an Integrative Approach to Breast Cancer Patients*. *Integrative Cancer Therapies*, 2021. **20**: p. 15347354211040826.
8. Magno, S., A. Filippone, and A. Scaldaferrì, *Evidence-based usefulness of integrative therapies in breast cancer*. *Translational Cancer Research*, 2018: p. S379-S389.
9. Chang, Y.Y., et al., *The Effects of a Mindfulness Meditation Program on Quality of Life in Cancer Outpatients: An Exploratory Study*. *Integr Cancer Ther*, 2018. **17**(2): p. 363-370.
10. Kida, K., et al., *Optimal Supportive Care for Patients With Metastatic Breast Cancer According to Their Disease Progression Phase*. *JCO Oncology Practice*, 2021. **17**(4): p. 177-183.

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12/8/2022

5:00 PM - 6:15 PM

P5-08-01

Pilot study of a patient-reported outcome (PRO) measurement strategy to determine impact of screening for minimal residual disease (MRD) in high-risk breast cancer survivors

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Background: Patients treated for early stage breast cancer (BC) have a 30% lifetime risk of developing metastatic disease. Numerous studies have demonstrated that dormant bone marrow disseminated tumor cells (DTCs) are independently associated with risk of recurrence and death, yet interventions targeting these cells are lacking. The PENN-SURMOUNT (Surveillance Markers of Utility for Recurrence after (Neo)adjuvant Therapy) Screening Study was launched in 2016 to screen high risk BC survivors for DTCs using bone marrow aspirate (BMA) and identify eligible DTC positive patients for clinical trials. Given the novelty of this approach, we concurrently developed and pilot tested a PRO measurement strategy to study how the screening method of BMA and disclosure of DTC results impacts early-stage BC patients. Methods: PENN-SURMOUNT is a single center prospective, longitudinal cohort study examining BM and blood biomarkers of MRD among patients within 5 years of BC diagnosis who have high risk criteria (positive axillary nodes, triple negative biology, ER+ with Oncotype Dx ≥ 25 and/or high risk Mammaprint, or pathologic residual disease after neoadjuvant chemotherapy). From May 2019 – August 2021, we recruited patients on SURMOUNT to complete PRO surveys at baseline (T0), after BMA (T1), and after disclosure of DTC results

(T2). Surveys were administered in paper form initially, then electronic form starting Feb 2021. PRO survey instruments were selected through literature review, followed by consensus among multidisciplinary clinical and research experts and patient advocates. PRO measures assess recurrence distress (Quality of Life in Adult Cancer Survivors, QLACS), illness intrusiveness (Illness Intrusiveness Ratings Scale, IIRS), and decision making (Decision Regret Scale). Additional survey items assess tolerability of the BMA and patients' risk perception and cognitive understanding after DTC results disclosure. Descriptive statistics summarize PRO survey compliance and responses at T0, T1, and T2 in the total population and the population who reported longitudinal data for T2. Results: 61 of 66 eligible patients on the SURMOUNT trial enrolled in the PRO pilot study and completed a baseline survey, of which 47 (77%) tested negative for DTCs. Mean completion rates were 0.92 at T0, 0.85 at T1, and 0.56 at T2. After electronic survey implementation, completion rates increased to 0.94 (T0), 0.97 (T1) and 0.81 (T2). At T0, 36 (59%) patients reported a high risk perception of developing BC recurrence at 5 years and 42 (69%) during their lifetime. Mean T0 recurrence distress using the QLACS subscale was 14.6 (SD 6.3) out of possible score 4-28, compared to an expected mean of 11.42 (SD 5.48) in a general survivorship population. Mean T0 illness intrusiveness was 27.3 (SD 13.9) out of possible score 13-91. At T1, approximately 85% of patients agreed that they correctly understood the purpose of the bone marrow procedure and what the procedure would entail. 44 (72%) of patients reported a maximum pain score ≤ 4 in the week post-procedure and 42 (69%) reported the BMA was same or better than expected tolerability. Exploratory subset analysis of patients with complete longitudinal data at T2 (n = 34) showed average scores of 13.4 (SD 6.0), 30.1 (SD 14.0), and 2.8 (SD 6.2) for recurrence distress, illness intrusive, and decision regret scores (scale 0-100), respectively. At T2, 26 (76%) of patients reported no decision regret for undergoing testing for DTCs; 27 (79%) reported feeling less anxious after DTC results disclosure. Conclusions: Participants of PENN-SURMOUNT perceived risk of recurrence as high. The BMA procedure was well-tolerated and better than expected among the majority of this cohort, and most did not regret having undergone BMA after DTC status disclosure. Longitudinal completion rates were low, limiting assessment of PROs at later time points, a major focus of future work in this setting.

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12/8/2022

5:00 PM - 6:15 PM

P5-08-04

Mammo-50: Mammographic surveillance in early breast cancer patients aged over 50 years – patient reported outcomes 3 years post diagnosis.

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Introduction: There is a lack of evidence or consensus on the optimum frequency and duration of mammographic surveillance and follow-up for breast cancer patients aged 50 years and older at diagnosis. Mammo-50 will provide clinicians with valuable, risk-adjusted information to guide their future practice and is due to report December 2023. Quality of life (QoL) was assessed in a sub-study of the main trial. **Methods:** A multi-centre, randomised controlled, phase III trial of annual mammography versus 2-yearly for conservation surgery and 3-yearly for mastectomy patients with an observational cohort to explore reasons for non-participation. The trial randomised 5235 women between April 2014 and September 2018 and a further 915 registered in the cohort; 90% of women agreed to participate in the QoL sub-study. QoL questionnaires were completed at trial entry (3 years post-surgery) and then annually for up to 10 years. The distress thermometer was used as a patient reported measure of distress and concerns throughout the trial. The trial team contacted the patient's clinical care team informing them of the reasons causing patients' high levels of distress. **Results:** A total of 4521 (74%) women completed the distress thermometer at baseline. Of these, 289 (6.4%) reported high levels of distress (score 8-10), 825 (18.2%) medium levels of distress (score 5-7), 2033 (45.0%) low levels of distress (1-4) and 1374 (30.4%) reported no distress. Levels of distress were similar across clinical characteristics including surgery type, disease type and ER status, but differed for hormone therapy use ($p=0.004$). Women who had stopped hormone therapy tended to have higher levels of distress than those who had never had hormone therapy or for whom hormone therapy was ongoing. The most common reasons for causing high levels of distress (score, 8-10) in the 289 patients were sleep problems and/or nightmares (135 (47%)), fatigue, exhaustion or extreme tiredness (132 (46%)), worry, fear or anxiety (111 (38%)), hot flushes (94 (33%)), pain (89 (31%)), memory or concentration (84 (29%)) and sadness or depression (84 (29%)) of patients. **Conclusions:** Within the Mammo-50 trial, 6.4% of women reported high levels of distress upon trial entry. A quarter of women reported high/medium levels of distress with sleep, fatigue, worry, hot flushes, memory and sadness/depression being the main concerns. Levels of distress were highest in those women who had stopped hormone therapy. These results have been fed back to the UK NCRI breast cancer symptom management group whose remit it is to identify and provide guidelines for supporting women with unmet needs. **Acknowledgement and disclaimer:** This study is funded by the NIHR HTA programme (project ref. 11/25/03). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

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12/8/2022

5:00 PM - 6:15 PM

P5-08-05

Conception and Pregnancy Among Young Breast Cancer Survivors

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Background: Breast cancer (BC) is the most common malignancy among women of reproductive age. Given limited data describing the conception and pregnancy experience of young BC survivors, we sought to explore these outcomes to inform counseling of women interested in future childbearing. Methods: Participants with stage 0-III BC in the Young Women's Breast Cancer Study (NCT01468246), a multi-center, prospective cohort of women diagnosed at age ≤ 40 from 2006-2016 who reported ≥ 1 live birth from a pregnancy after diagnosis were sent a survey with investigator-developed questions focused on their first post-diagnosis live birth. Women who had been diagnosed with BC during pregnancy were excluded from this analysis. The survey assessed conception, use of assisted reproductive technology (ART), pre-implantation genetic testing (PGT), endocrine therapy (ET), and peripartum complications. Summary statistics are presented. Results: 92/119 eligible women completed the survey (response rate: 77%). Median age at diagnosis was 32 (range:17-40) years and at delivery was 37 (range: 29-47) years. Median time from diagnosis to delivery was 58 months (range: 11-154). Most women had stage 2 BC (43%, 40/92); 68% received chemotherapy (63/92); about half (51%, 47/92) were nulligravida at diagnosis. Overall, 61% of pregnancies were conceived naturally (56/92) and 39% with ART (36/92): 32% by in-vitro fertilization (IVF, 29/92), 7% with fertility medications only (6/92), and 1 with intrauterine insemination. 38% of IVF pregnancies were conceived using products from fertility preservation prior to BC treatment (11/29). Among women who used ART, 74% attempted to conceive naturally (25/36) for a median of 9 (range: 2-48) months prior to pursuing ART. The most common reasons for pursuing ART include infertility following BC treatment (33%, 12/36) and expediting conception to resume treatment (17%, 6/36). 11% of those with known inherited pathologic variant mutations underwent PGT (2/19). Reasons for not pursuing PGT included belief in more effective cancer risk reduction in the future (29%, 5/17), not being offered PGT (24%, 4/17), high cost (12%, 2/17), no interest in IVF (12%, 2/17), acceptable odds for inheriting the mutation (24%, 4/17), and belief in other risk reduction strategies (18%, 3/17); 1 woman reported ethical concerns. Of 57 women who took ET pre-pregnancy (63%), nearly all (96%, 55/57) discontinued ET > 3 months prior to attempting to conceive; 1 discontinued after awareness of pregnancy. Of those who had received prior ET, 60% resumed ET (34/57) a median of 3 (range: 1-50) months after pregnancy. Among 23 women who did not resume, 13 (23%) had completed the recommended duration; the remaining 10 reported one or more of the following reasons: felt better while off (28%, 6/23), desire for another child (22%, 5/23), and desire to breastfeed (17%, 4/23). Median time to delivery was 39 (range: 28-42) weeks with 12% delivering preterm < 37 weeks (11/92). 47% had a Caesarean section (43/92), with prolonged labor the most common indication (33%, 14/43). Hypertensive disorders of pregnancy (HDP, 20%, 18/92), gestational diabetes (7%, 6/92), small for gestational age (7%, 6/92), and postpartum hemorrhage (5%, 5/92) were the most common obstetrical complications. 9% of women had newborns requiring NICU admission (8/92) and 9% had low birth weight (8/92). Conclusion: Among young BC survivors with a live birth following diagnosis, most conceived naturally, with the majority who used ART first attempting natural conception. There was limited use of PGT among mutation carriers with $\frac{1}{4}$ not having been offered testing. Patient reported peripartum complications appear consistent with population norms, though the relatively higher rate of HDP bears further research. Among those yet to complete their ET, a notable proportion did not resume following delivery. This novel data may help to inform the care of young breast cancer survivors pursuing pregnancy.

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5:00 PM - 6:15 PM

P5-08-06

Breastfeeding in Survivors of Early Breast Cancer

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Background: Breast cancer (BC) is the most common malignancy in women of reproductive age, and the incidence of the disease is rising in this population. Many of these women are interested in childbearing after their BC treatment and a substantial minority will go on to have a live birth. Some will also want to breastfeed. However, there is only limited information available regarding the experience of young BC survivors breastfeeding following treatment. Methods: Participants in the Young Women's Breast Cancer Study (YWS), a multi-center, prospective cohort study of women diagnosed with BC at age ≤ 40 years between 2006-2016, who reported at least one live birth following their diagnosis with stage 0-III BC were sent an additional survey including investigator-developed questions focused on breastfeeding after breast cancer treatment. Women who had been diagnosed with BC during pregnancy were excluded from this analysis. The survey assessed whether they breastfed, reasons for attempting and stopping breastfeeding, breastfeeding with the treated breast and untreated breast, and supports. Summary statistics, including medians and proportions, are presented. Results: Of 118 eligible women sent a survey, 92 completed the survey (78% response rate). Median age at diagnosis of BC was 32 (range: 17-40) years and at delivery was 37 (range: 29-47) years. 54% of women had attempted to breastfeed (50/92). Among those who had not, 93% noted a history of bilateral mastectomies (39/42). Additional reasons for not attempting to breastfeed included no interest regardless of BC history (5%, 2/42) and 1 woman underwent a unilateral mastectomy and did not think her supply would be sufficient. Among the women who did attempt breastfeeding, 68% had undergone lumpectomy and radiotherapy (34/50) with 85% of those women reporting that the treated breast did not produce milk (29/34). The 5 women who produced milk from the treated breast noted that the supply was substantially less than the untreated breast. To assist with breastfeeding, 76% used a pump only on the untreated breast (38/50) and 14% on both breasts (7/50). Women breastfed for a median of 5.5 (range: < 1-60) months and 64% were "somewhat"/"very much" satisfied with their ability to breastfeed (32/50). The most common reasons cited for stopping breastfeeding included having completed the planned duration (36%, 18/50), to start/resume endocrine therapy (22%, 11/50), and to resume breast imaging (8%, 4/50). Among patients who had not undergone a double mastectomy, 47% recalled receiving specific information about breastfeeding after a history of breast cancer (25/53), most commonly from the oncology team (56%, 14/25), lactation consultant (48%, 12/25), or online resources (44%, 11/25). Conclusion: In the largest series to date detailing the breastfeeding experiences of young BC survivors, approximately half of young BC survivors with a successful pregnancy attempted to breastfeed. Among those who had undergone prior lumpectomy and radiotherapy, women reported no milk production or only limited supply from the treated breast. Despite these limitations, most women who attempted to breastfeed were satisfied with their ability to do so. Specific resources to support the experience of breastfeeding in BC survivors are needed.

Disclosure(s):

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5:00 PM - 6:15 PM

P5-08-07

Dietary patterns among women with early-stage breast cancer from the Healthy Living Program

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Background: Diet is a modifiable risk factor for breast cancer risk and mortality. Current guidelines recommend a diet that provides a diverse array of nutrients, comprised predominantly of fruits/vegetables and whole grains, with limited added sugar. The Healthy Living Program (HLP) is a clinical program at Memorial Sloan Kettering Cancer Center for patients with early-stage breast cancer that offers longitudinal, personalized lifestyle management starting at the time of diagnosis. Here, we report dietary patterns among the HLP cohort and association with baseline body mass index (BMI). Methods: We included all patients enrolled in the HLP from September 2020-February 2022. At the time of enrollment, participants complete a survey containing the National Cancer Institute (NCI) Dietary Screener Questionnaire (DSQ), which consists of consumption frequency questions for 26 food items over the past month. Total daily intake equivalents are calculated for foods from every diet factor group according to standard NCI DSQ scoring as follows: 1) Total daily cup equivalents of fruits/vegetables, which includes fruit, fruit juice, salad, potatoes, beans, other vegetables, tomato sauce, salsa, and pizza; 2) Total daily ounce equivalents of whole grains, which includes cereal, whole grain bread, whole grain rice, and popcorn; 3) Total teaspoon (tsp) equivalents of added sugars from candy, doughnuts, cookies/cake/pie, cereal, ice cream, and sugar-sweetened beverages including soda, fruit drinks, and sugar/honey in coffee/tea. Adherence to recommended daily intake of fruits/vegetables, whole grains, and added sugars was assessed as per the 2020-2025 Dietary Guidelines, the American Institute for Cancer Research, and the World Health Organization guidelines. Patient and tumor characteristics were abstracted from medical records. Results: Among the 399 patients included, the median age at diagnosis was 58 and median baseline BMI was 26.1 kg/m². 45 patients had carcinoma in situ (11.3%), 296 had stage I disease (74.2%), 51 had stage II disease (12.8%), and 7 had stage III disease (1.8%). 316 had hormone-receptor positive disease (89.3%), 24 had HER2-positive disease (6.8%), and 26 had triple-negative disease (7.3%). 106 participants (27%) met the guideline recommendation of ≥ 4 -5 cup equivalents of fruits/vegetables daily and 3 participants (0.8%) met the guideline recommendation of ≥ 3 ounces equivalents of whole grains daily. All patients in the cohort met the guideline recommendation of < 6 tsp equivalents of added sugars daily. Only 2 patients (0.5%) met guidelines for all three diet factors. Baseline BMI was significantly higher among patients who did not meet the recommended fruit/vegetable intake than among those who did (26.9 kg/m² vs. 24.5 kg/m², $p=0.016$). There were no significant differences in BMI between those who did and did not adhere to the other diet factor guidelines and no significant association between tumor stage or histology and dietary guideline adherence. Conclusion: Most patients with early-stage breast cancer did not meet the recommended daily intake of fruits/vegetables or whole grains. Participants who did not meet the fruit and vegetable intake guideline had significantly higher BMI at diagnosis. These findings indicate that lifestyle assessment near the time of breast cancer diagnosis identifies patients that could benefit from personalized dietary interventions to optimize prognostic factors such as BMI.

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5:00 PM - 6:15 PM

P5-08-08

Ultrasound-guided injection with or without rehabilitation exercise in breast cancer survivors with sub-acromion-deltoid bursitis: a pilot randomized clinical study

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BACKGROUND: Due to the increasing overall survival of breast cancer (BC) patients, a growing interest has been raised in the current literature on disabling consequences of cancer and its treatment [1,2]. In particular, after radical surgery for BC, patients might frequently be affected by functional limitation of the shoulder joint, potentially related to the immobilization, surgical scar tensions, axillary web syndrome, subpectoral prostheses or expanders, or peripheral nerve damage [3]. In this scenario, several challenges are still open in the therapeutic approach to this disabling condition and the optimal management of shoulder dysfunction in breast cancer patients is far from being fully characterized. Therefore, the aim of this study was to assess the effects of a comprehensive rehabilitation program including ultrasound-guided injection of the sub-acromion deltoid bursa (SAD) followed by a rehabilitation exercise protocol in terms of feasibility, pain relief, upper limb function, quality of life, and safety. **METHODS:** In this study, we recruited consecutive breast cancer women referring to a Physical Medicine and Rehabilitation in Northern Italy and suffering from SAD bursitis in the absence of tendon lesions. Patients were assessed for eligibility and subsequently randomly assigned 1:1 to two groups. Group A received ultrasound-guided percutaneous injection of the SAD bursa (lidocaine and triamcinolone acetate) followed by a rehabilitation exercise program

of 5 sessions lasting 1 hour each., while Group B received ultrasound-guided percutaneous injection only. Patients were assessed at baseline (T0), after a week (T1), and after 3 months (T2). The outcomes were numerical pain rating scale (NPRS), handgrip strength (HGS) test, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), the Oxford Shoulder Score (OSS), Global Perceived Effect (GPE), and safety. RESULTS: Thirty-seven patients were enrolled and randomly assigned to Group A (n=19; mean age: 56.05 ± 10.30 years; body mass index (BMI): 23.58 ± 2.79 kg/m²) and Group B (n=18; mean age: 58.39 ± 12.09 years; BMI: 22.72 ± 3.16 kg/m²). No major or minor adverse events were reported after this multidisciplinary intervention. Statistically significant within-group differences were found in both groups in terms of NPRS after the treatment (p < 0.05) and after the follow-up (p < 0.05). The between-group analysis showed significant differences in pain intensity (NRS: 2.16 ± 1.39 vs 4.78 ± 1.77; p < 0.05), isometric muscle strength (25.11 ± 3.20 vs 20.33 ± 4.92; p < 0.001), shoulder function (OSS: 17.00 ± 3.27 vs 33.11 ± 6.47; p < 0.0001), and EORTC QLQ-C30 (Functional subscale: 88.74 ± 7.71 vs 77.67 ± 13.64; p=0.017; Symptom subscale: 11.43 ± 8.56 vs 19.61 ± 13.72; p=0.048; Global Health subscale: 79.36 ± 13.72 vs 70.56 ± 8.26; p=0.022) of the after the follow-up. However, no significant differences (p > 0.05) were reported at T1. CONCLUSION: Our findings showed that a comprehensive rehabilitation approach including ultrasound-guided injection combined with rehabilitation exercise might be safe, well-tolerated, and effective in breast cancer patients with SAD bursitis. These data emphasized the positive role of an interdisciplinary rehabilitation management in pain management and improving overall well-being of breast cancer patients. Further studies with larger samples and longer follow-ups are needed to confirm our data. REFERENCES: 1. Nardin S et al. Breast Cancer Survivorship, Quality of Life, and Late Toxicities. *Front Oncol* 2020, 10, 864. 2. D'Egidio V et al. Counseling interventions delivered in women with breast cancer to improve health-related quality of life: a systematic review. *Qual Life Res* 2017, 26, 2573-2592, doi:10.1007/s11136-017-1613-6. 3. Hidding JT et al. Treatment related impairments in arm and shoulder in patients with breast cancer: a systematic review. *PLoS One*. 2014 May 9;9(5):e96748.

Disclosure(s):

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P5-08-09

Does Breast Inflammation Contribute to Lymphedema Risk in Patients Treated with Axillary Lymph Node Dissection?

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Background

Chronic inflammatory responses initiated by lymphatic injury play a key role in the pathophysiology of secondary lymphedema. However, it is unclear if baseline inflammation or ethnic/racial variability in inflammatory responses increase lymphedema risk. Crown-like structures of the breast (CLS-B), consisting of macrophages engulfing necrotic adipocytes, are a marker of systemic inflammation and have been implicated in the pathogenesis of breast cancer, but their role in lymphedema development is unknown. Here we determine whether baseline differences in inflammation, characterized by the presence of CLS-B, contributed to lymphedema risk in a diverse cohort of patients treated with ALND.

Methods

Patients ≥ 18 years undergoing ALND were enrolled in a prospective lymphedema screening study. Body mass index (BMI) and volumetric arm measurements (perometer) were performed at baseline, postoperatively, and every 6 months. Breast tissue obtained at definitive surgery was assessed for CLS-B with CD-68 IHC stain in non-tumor breast tissue. Inflammation severity was determined by number of CLS-B/cm², with the median used to differentiate between mild and severe inflammation. Lymphedema was defined as a relative arm volume change of $\geq 10\%$. Lymphedema incidence was assessed using competing risk analysis and compared between patients with and without CLS-B. Uni- and multivariable analysis was

performed to identify factors associated with lymphedema development.

Results

Between 11/2016-03/2020, 304 ALND patients were enrolled; 281 had at least 6 months of follow-up and were included in the study. Eleven percent self-identified as Asian, 20% Black, 6% Hispanic, and 60% White. Median age was 48 years; median BMI was 26.3 kg/m², with higher BMI observed in Black and Hispanic women compared to Asian and White women ($p < 0.001$). Overall, 54% had CLS-B, with severe inflammation (> 0.4 CLS-B/cm²) identified in 71 (25%) patients. CLS-B presence correlated with BMI (36% [BMI < 25], 63% [BMI 25-30], 70% [BMI > 30], $p < 0.001$) and varied across racial/ethnic groups, with a higher prevalence in Black and Hispanic women (68% [Black], 69% [Hispanic] vs 59% [Asian], 46% [White], $p = 0.03$) (Table). Inflammation severity did not differ by race/ethnicity ($p = 0.11$). At 2.1 years median follow-up (IQR 1.6-3.1), 66 women developed lymphedema, with a 2-year lymphedema rate of 21.3% (95% CI 16.4-26.8). Lymphedema incidence was higher among Black and Hispanic women, compared to Asian and White women (2-year rate: 33.8% [Black], 31% [Hispanic], 17.4% [Asian], 18.2% [White], $p = 0.002$), and was higher among women with CLS-B (2-year rate: 28.2% [CLS-B] vs 12.9% [no CLS-B], $p = 0.02$). On multivariable analysis, Black race (White [referent]: HR 2.85, 95% CI 1.4-5.8; $p = 0.03$), receipt of NAC (upfront surgery [referent]: HR 2.46, 95% CI 1.04-5.8, $p = 0.04$) and older age (HR 1.03, 95% CI 1.01-1.06 per 1-year increase; $p = 0.009$) were independently associated with lymphedema development, while CLS-B was not (HR 1.37, 95% CI 0.81-2.34, $p = 0.2$).

Conclusions

In a prospective cohort of patients treated with ALND, Black race, receipt of NAC, and increasing age, but not CLS-B, were independently associated with lymphedema risk. However, the higher CLS-B prevalence in Black women suggests that they may have a propensity for increased inflammation, which may in part be contributing to the higher lymphedema risk observed, but is likely not the only inflammatory mechanism that modulates risk.

Table. Clinical characteristics of study cohort stratified by the presence of CLS-B

Characteristic	Overall (n = 275)*	Patients with CLS-B (n = 149)	Patients without CLS-B (n = 126)	P value
Age, years	48 (40, 57)	49 (42, 57)	46 (39, 56)	0.2
BMI, kg/m ²	26.3 (22.5, 31.1)	28.7 (24.2, 32.3)	23.4 (21.1, 29.3)	< 0.001
Race/Ethnicity				0.03
Asian	29 (11%)	17 (11%)	12 (10%)	
Black	57 (21%)	39 (26%)	18 (14%)	
Hispanic	16 (6%)	11 (7%)	5 (4%)	
White	164 (60%)	76 (51%)	88 (70%)	
cT stage [#]				0.007
1	57 (21%)	39 (26%)	18 (14%)	
2	125 (45%)	54 (36%)	71 (56%)	
3	44 (16%)	28 (19%)	16 (13%)	
4	44 (16%)	24 (16%)	20 (16%)	
cN stage				0.9
0	72 (26%)	37 (25%)	35 (28%)	
1	180 (66%)	99 (66%)	81 (64%)	
2	6 (2%)	4 (3%)	2 (2%)	
3	17 (6%)	9 (6%)	8 (6%)	
Histology				0.11
Ductal	232 (84%)	121 (81%)	111 (88%)	
Lobular	35 (13%)	21 (14%)	14 (11%)	
Other	8 (3%)	7 (5%)	1 (1%)	
Receptor subtype				0.10
HR+/HER2-	185 (67%)	100 (67%)	85 (67%)	
HER2+	55 (20%)	25 (17%)	30 (24%)	
HR-/HER2-	35 (13%)	24 (16%)	11 (9%)	
Neoadjuvant chemotherapy				0.2
Yes	194 (71%)	110 (74%)	84 (67%)	
No	81 (29%)	39 (26%)	42 (33%)	
Type of breast surgery				0.7
Lumpectomy	69 (25%)	39 (26%)	30 (24%)	
Mastectomy	206 (75%)	110 (74%)	96 (76%)	
Breast pCR [#]	22 (11%)	11 (10%)	11 (13%)	0.5
Total No. LNs removed	18 (13, 23)	18 (14, 23)	18 (13, 22)	0.2
Total No. positive LNs	2 (1, 5)	2 (1, 5)	2 (1, 6)	0.8
RT done	259 (94%)	143 (96%)	116 (92%)	0.2
Nodal RT	254 (92%)	139 (93%)	115 (91%)	0.5

Frequency (column percent) reported for categorical variables and median (IQR) reported for continuous variables
*CLS-B unknown in 6 cases
[#]cTx, n = 5
[#]Denominator includes only women treated with NAC (n = 194)
Abbreviations: CLS-B crown-like structures of the breast; BMI body mass index; HR hormone receptor; HER2 human epidermal growth factor receptor 2; pCR pathologic complete response; LN lymph nodes; RT radiotherapy

Disclosure(s):

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5:00 PM - 6:15 PM

P5-08-10

Safety and Tolerability of Paxman Scalp Cooling at Lower Temperatures to Improve Efficacy with Anthracycline Chemotherapy

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Background: Chemotherapy induced alopecia is one of the most distressing side effects of cancer therapy since it is a constant reminder of the underlying malignancy. Anthracycline chemotherapy induces total alopecia. Although scalp cooling devices have been used to prevent this alopecia, there is still a need to improve efficacy with anthracycline therapy. This study was performed to evaluate if the Paxman Scalp Cooling System is safe, tolerable, and more efficacious at lower temperatures.

Objectives: The primary end point is to assess the safety and tolerability of the Paxman Scalp Cooling System at lower temperatures (-7.5 Celsius and -10 Celsius), defined as the ability of patients to undergo scalp cooling without any DLTs during the treatment period. The secondary end point is successful hair preservation assessed using the Common Terminology Criteria for Adverse Events version 4.0 scale (grade 0 [no hair loss] or grade 1 [< 50% hair loss not requiring a wig] were considered to have hair preservation) after anthracycline chemotherapy.

Methods: 34 women with stage I-III breast cancer who were receiving anthracycline-based neoadjuvant or adjuvant therapy were enrolled on study. The first 7 patients received scalp cooling at -7.5 Celsius and the subsequent 27 patients received scalp cooling at -10 Celsius. Patients completed safety and tolerability assessments at each visit. In addition, participants

had standardized scalp photography to assess the superior, vertex and frontal scalp views, trichoscopic assessments, alopecia grading and completed PROs (CADS, Tolerability, Change in scalp coverage).

Results: Thirty-four women (56% White, 18% Black, 8% Asian, 18% other) with a mean age of 44 (range 20-68) were enrolled on this IRB-approved pilot study. Seventy-four percent received ddAC-T, 18% received ddAC-THP and 8% received ddAC/Pembro-T/Carbo/Pembro. Twenty-six patients were evaluable for the DLT end point. Three patients are still on study and five patients left the study before completion (2 due to lack of efficacy, 1 shaved her head, 1 was removed from study due to hospitalization for sepsis and 1 patient changed her mind and never started scalp cooling). There were no DLTs in any patient throughout the study. Both the -7.5 and -10 Celsius temperatures were found to be tolerable with no difference in tolerability. The most common reported AEs were headaches 48%, discomfort 13%, scalp pain 9.7%, dizziness 9.6%, scalp coldness 6%, feeling cold 3% and lightheadedness 3%. Twenty-nine percent of patients reported that scalp cooling triggered a headache and the average level of pain was mild. Only 16% of patients reported pain killer use due to scalp cooling, which effectively resolved headaches or discomfort. Sixty-one percent of patients reported hair preservation at the primary end point. Hair regrowth was reported in patients after they experienced grade 2 alopecia and while still on study. More detailed data on hair preservation will be forthcoming once all of the photos and trichoscopic measures are assessed.

Conclusions: Paxman Scalp Cooling System is safe, tolerable and even more efficacious at lower temperatures. The -10 Celsius is more efficacious and as tolerable as -7.5 in patients being treated with anthracycline therapy. When using the Paxman Scalp Cooling System in patients being treated with anthracycline therapy, you should consider performing scalp cooling at lower temperatures

Table 1: Demographics

Table 1: Demographics Patient Characteristics (All)		
	N=34 Mean= 44 Median= 44.5 Range (20-68)	%
Age		
Ethnicity		
Hispanic/Latino	10	29%
Not Hispanic/Latino	24	71%
Race		
Black or African American	6	18%
White	19	56%
Asian	3	8%
Other	6	18%
Paxman Temperature		
-7.5	7	21%
-10	27	79%
Evaluable for DLT		
Yes	26	76%
No	5	15%
Pending	3	9%
Evaluable for Primary Endpoint		
Yes	20	59%
No	9	26%
Pending	5	15%
Adjuvant vs Neoadjuvant		
Adjuvant	11	32%
Neoadjuvant	23	68%
Stage		
I	11	32%
II	20	59%
III	3	9%
Chemotherapy Type		
ddAC-T	25	74%
ddAC-THP	6	18%
ddAC-T Carbo Pembro	3	8%

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Shari B. Goldfarb, MD: Ms. Medicine LLC: Consulting Fees (e.g., advisory boards) (Ongoing); NanOlogy: Consulting Fees (e.g., advisory boards) (Ongoing); Paxman Cooling LTD: grant recipient (Ongoing); Revision Skincare: Consulting Fees (e.g., advisory boards) (Ongoing); Sermonix Pharmaceuticals LLC: Consulting Fees (e.g., advisory boards) (Ongoing); Spectrum Pharmaceuticals: Consulting Fees (e.g., advisory boards) (Ongoing); Sprout Pharmaceuticals: Grant Recipient (Ongoing)

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Jinae Park, BA MPH: No financial relationships to disclose
Monica Fornier, MD: No financial relationships to disclose
Mario Lacouture, MD: Apricity Health: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Azitra, Inc: Consulting Fees (e.g., advisory boards) (Ongoing); Bicara Therapeutics, Inc: Consulting Fees (e.g., advisory boards) (Ongoing); Bristol-Myers Squibb: Consulting Fees (e.g., advisory boards) (Ongoing); Deciphera: Consulting Fees (e.g., advisory boards) (Ongoing); DelMar Pharmaceuticals, Inc: Consulting Fees (e.g., advisory boards) (Ongoing); Egg au Carré: Consulting Fees (e.g., advisory boards) (Ongoing); Hoth Therapeutics, Inc: Consulting Fees (e.g., advisory boards) (Ongoing); Innovaderm Research Inc.: Consulting Fees (e.g., advisory boards) (Ongoing); Johnson & Johnson: Consulting Fees (e.g., advisory boards) (Ongoing); Kyowa Hakko Kirin Pharma: Consulting Fees (e.g., advisory boards) (Ongoing); La Roche-Posay: Consulting Fees (e.g., advisory boards) (Ongoing); Loxo Oncology: Consulting Fees (e.g., advisory boards) (Ongoing); Lutris Pharma Ltd.: Consulting Fees (e.g., advisory boards) (Ongoing); Menlo Therapeutics Inc.: Consulting Fees (e.g., advisory boards) (Ongoing); Nanology LLC: Consulting Fees (e.g., advisory boards) (Ongoing); NKMax America, Inc.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Novartis Pharmaceuticals Corporation: Consulting Fees (e.g., advisory boards) (Ongoing); Novocure: Consulting Fees (e.g., advisory boards) (Ongoing); Oncoderm LLC: Consulting Fees (e.g., advisory boards) (Ongoing); OnQuality Pharmaceuticals Ltd.: Consulting Fees (e.g., advisory boards) (Ongoing); QED Therapeutics, Inc.: Consulting Fees (e.g., advisory boards) (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing); Sol-Gel Technologies Ltd.: Consulting Fees (e.g., advisory boards) (Ongoing); TWi Biotechnology, Inc.: Consulting Fees (e.g., advisory boards) (Ongoing); Varsona Pharmaceuticals, LLC: Consulting Fees (e.g., advisory boards) (Ongoing); WebMD: Consulting Fees (e.g., advisory boards) (Ongoing); Wolters Kluwer: Consulting Fees (e.g., advisory boards) (Ongoing)

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P5-08-11

Objective Comparison of Post-operative Activity after Sentinel Lymph Node Biopsy versus Axillary Lymph Node Dissection Using Wearable Activity Monitors – The ‘BRACELET’ Study

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Introduction Axillary de-escalation is driven by both a desire to minimize injury and a growing awareness of the oncological safety of axillary conservation. However, the evidence of the impact of axillary procedures is largely subjective and based on patient questionnaires. Sensing technologies such as Wearable Activity Monitors (WAM) can acquire functional postoperative data, enabling objective analysis of patients' physical activity (PA) levels. This technology implementation would help surgeons better comprehend the post-operative recovery phase and provide individualized interventions for patients. We aimed to use WAMs in order to investigate differences in physical recovery between axillary lymph node dissection (ALND) and sentinel lymph node biopsy (SLNB) – with a hypothesis that the ALND group has slower recovery compared to SLNB. Methods A single centre, prospective non-randomized observational study was conducted from September 2019 to May 2022. Consecutive patients undergoing breast and axillary surgery were identified from theatre lists. Patients with movement disorders or upper limb impairment and those using mobility devices or aids were excluded. Eligible consented patients wore WAMs (AX3, Axivity, UK – triaxial accelerometer) on both wrists at least one day pre- and up to two weeks post-operatively. The Mann-Whitney U test and the Wilcoxon Signed Rank Test were performed to analyze the PA levels between arms and surgeries. Patient demographics and potential confounders such as concomitant breast/reconstruction surgery were recorded. Results A total of 53 patients were recruited. Greater PA level was observed in the control arm compared to the surgically treated side in both SLNB and ALND groups in week 1 (SLNB: 69.6% vs 61.1%, $p=0.006$; ALND: 75.3% vs 60.4%, $p<0.001$) and 2 (SLNB: 77.6% vs 71.1%, $p=0.113$; ALND: 81.9% vs 70.2%, $p<0.001$) respectively. When comparing activities of the surgically treated side only, the ALND patients

had significantly lower PA level compared to SLNB group in post-operative day 7-9 (65.4% vs 72.5%, $p=0.035$). Subgroup analysis was performed to compare surgically treated side of 'Mastectomy Only and SLNB' versus 'Mastectomy Only and ALND'. PA level was significantly lower in the latter than the former in week 2 (78.5% vs 83.5%, $p=0.027$). There were no significant differences in demographics between the 2 groups. Conclusion ALND consistently results in decreased PA level compared to SLNB. The findings also demonstrate the longitudinal impact of SLNB, which impacts PA levels, even up to 2 weeks after surgery. Monitoring recovery objectively after breast cancer surgery provides patients and surgeons with more information about the likely outcomes of their treatment and may help them choose the best option, particularly where oncological outcomes are equivocal. This information could also be used to improve outcomes by identifying vulnerable patients who would benefit from early exercise intervention, encouraging physical activity, and keeping track of individualised PA that could be added to the feedback rehabilitation care plan.

Disclosure(s):

Nur Amalina Che Bakri, MBChB BMedSc (Hons) MPhil: No financial relationships to disclose

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Lifestyle factors and patient-reported outcome measures using the European Organisation for Research and Treatment of Cancer survivorship questionnaire in early breast cancer patients attending for surveillance imaging.

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Background An increasing number of patients survive their early breast cancer (EBC) but may experience longer term impact on their quality of life (QoL) arising from their diagnosis and treatment. Survivors are also at risk of other possibly life-shortening chronic diseases due to concomitant risk factors (smoking, drinking >14 units of alcohol/week, and low exercise levels). Little is known about the lifestyle factors and long-term challenges facing EBC survivors. We report the initial results of a questionnaire (containing patient-reported outcomes measures (PROMS), and lifestyle factor questions) completed by EBC survivors at the Royal Marsden hospital (RMH), UK. **Methods** We prospectively identified a patient cohort of patients (October 2021 to June 2022) with stage I-III EBC who had completed their curative treatment (endocrine treatment (ET) may be ongoing) and who were attending for their annual surveillance breast imaging at years 1, 2, 4, and >5 years. Patients completed PROMS (using EORTC (European Organisation for Research and Treatment of Cancer) QLQ-SURV100 and -BR23) and questionnaires regarding smoking, alcohol, and exercise levels (via the International Physical Activity Questionnaire (IPAQ)). Patient, clinical, disease and treatment characteristics were recorded and the EORTC and IPAQ questionnaires were analysed according to the EORTC and IPAQ analysis manuals. Results Data are available for 187 women at the time of this

analysis (it is anticipated data will be available for 350 at the time of SABCS 2022). Patients were attending for their year 1 (N=66, 35.3%), 2 (N=43, 23%), 4 (N=43), or >5 years (N=35, 18.7%) imaging post-surgery. 62 (86.6%) patients were Eastern Cooperative Oncology Group Performance Status 0-1, and 31 (16.6%) had >2 of other comorbidities. 123 patients (65.8%) were post-, 16 (8.6%) peri-, and 48 (25.7%) premenopausal. 178 (95.2%) underwent primary surgery. Of those patients undergoing surgery, 19 (10.2%) had a mastectomy, and 168 (89.8%) breast conserving surgery. All patients had axillary surgery: 26 (13.9%) axillary dissection, and 158 (84.5%) sentinel lymph node biopsy. 166 patients (88.8%) received adjuvant ET and for most patients (N= 149, 79.7%) this was ongoing at time of analysis. 31.6% (N= 59) had prior exposure to cardiotoxic treatment. Risk groups for other chronic health conditions could be identified: 92 (49.2%) patients had a BMI of >25, 5 (4.2%) were current smokers, and 16 (13.6%) were classified as at-risk drinking. Patients reported that their physical function was affected following their diagnosis and treatment, with 51 (27.3%) having trouble running short distances and 52 (27.8%) taking a long walk carrying a heavy backpack. Nonetheless all patients (N=118 available for IPAQ analysis) had moderate (N=61, 51.7%), or high-level (N= 58, 49.2%) levels of exercise. 85 patients (45.5%) had pain in the past week, and 101 patients (54%) were dissatisfied with the appearance of their body. Most patients (N=152, 81.3%) estimated their overall QoL in the last week as very good (5-7) (scale 1-7, with 7 being excellent). QLQ-BR23 symptom scales were compared between patient groups. Patients who had chemotherapy suffered ongoing from hair loss (52.6% vs 45.2%) than chemo-naïve patients. There were no major differences between groups who received ET and those ET naïve. Conclusions We were able to identify groups of patients at risk for other comorbidities and cancers. We could also highlight groups of EBC survivors with a higher level of QoL concerns. PROMS should be routinely assessed in EBC survivors to better address subgroups at higher risk, inform consultations, and treatment decisions.

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P5-08-13

Frequency of low bone mineral density in young women with breast cancer and associated factors

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Background: Young women with breast cancer (YWBC) may experience bone mineral density (BMD) loss due to the effects of cancer treatment on estrogen levels. Studies assessing BMD in breast cancer (BC) patients have had a limited representation of young women. This study

aimed to analyze the frequency of low BMD and its associated factors in this specific age group.

Methods: This retrospective, multicenter study included women ≤ 40 years diagnosed with stage 0-III BC, treated with chemotherapy (CT) and/or endocrine therapy (ET) between 2010-2020, and with no documented bone metastases during follow-up. The protocol was conducted in 5 BC referral centers in Mexico. Demographic, clinical and treatment data were collected, as well as bone dual-energy X-ray absorptiometry (DEXA) results. Low BMD was defined as T-score < -1.0 or Z-score ≤ -2.0 at the lumbar spine (L1-L4) or femoral neck.

The frequency of low BMD was analyzed with descriptive statistics. Binary logistic regression using complete case analysis was conducted to calculate odds ratios (OR) and 95% confidence intervals (95%CI) of experiencing low BMD according to demographic, clinical and therapeutic factors.

Results: In total, 716 YWBC met inclusion criteria. Median age at BC diagnosis was 36 years (21-40); 708 (99%) women were premenopausal at diagnosis. Most were married (355; 50%), had higher education (381; 53%), were unemployed (433; 61%), and were non-smokers (552; 77%). Body mass index (BMI) was < 18.5 kg/m² (underweight) and ≥ 25.0 kg/m² (overweight/obese) in 14 (2%) and 392 (58%) cases, respectively. The most common BC subtype was hormone receptor (HR) positive/HER2 negative (371; 52%), followed by triple negative (168; 24%), HR positive/HER2 positive (122; 17%) and HR negative/HER2 positive (55; 8%). Patients were mostly diagnosed with stage II (346; 48%) or III (276; 39%) disease. As for treatment, CT in 667 (93%), ET in 468 (65%), anti-HER2 therapy in 168 (24%), and radiotherapy was administered in 562 (79%) cases.

DEXA scans were documented in 213/716 (30%) patients. In total, 286 DEXA results were available. The time elapsed from the start of the first systemic treatment to the DEXA result was 0-12 months in 42 cases (15%); 13-36 months in 103 (36%); 37-60 months in 72 (25%); and >60 months in 69 (24%). Overall, 133/213 patients (62%; 95%CI 56-69%) had at least one low BMD report after the start of CT or ET. T-scores and Z-scores in each period are detailed in the Table. No fractures were recorded in any case after BC diagnosis. The only variable associated with at least one low BMD result was BMI ≥ 25.0 kg/m² (OR, 1.88; 95%CI, 1.04-3.40). The described demographic, clinical and treatment factors were not significantly associated with low BMD.

Conclusion: This study showed a suboptimal frequency of bone DEXA monitoring in YWBC. A considerable proportion of YWBC experienced low BMD after initiation of CT and/or ET; and a significant association was found between obesity/overweight at BC diagnosis and subsequent low BMD. These data reflect the importance of requesting DEXA scans in young patients on a regular basis and promoting the maintenance of an adequate body weight, in line with international recommendations. Further studies evaluating the degree of BMD loss and its determinants would contribute to establish the optimal periodicity to monitor BMD in relation to BC therapy, allow timely offering of interventions to reduce bone morbidity, as well as improve the quality and life and survivorship of this young group of patients.

Table. DEXA T-scores and Z-scores.

Months since start of systemic therapy	N	T-score ≥-1.0	T-score -1.0 to -2.5	T-score ≤-2.5	N	Z-score >-2.0	Z-score ≤-2.0	Overall low BMD
0 – 12	42	50%	45%	5%	17	82%	18%	50%
13 – 36	103	46%	49%	6%	27	78%	22%	55%
37 – 60	72	26%	61%	13%	27	81%	19%	74%
>60	69	32%	59%	9%	40	95%	5%	68%

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Fernanda Mesa-Chavez, n/a: No financial relationships to disclose

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Cynthia Villarreal-Garza, n/a: AstraZeneca: Contracted Research (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Myriad Genetics: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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Blockade of CD47/Thrombospondin-1 signaling increases glycolytic metabolism as a protective mechanism against chemotherapy-associated cardiac injury in a model of Triple-Negative Breast Cancer.

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Due to advances in diagnosis and treatment, cancer-related mortality has decreased, and by the year 2030, there will be 22 million cancer survivors in the United States. This success comes with an increased incidence of serious adverse effects, mainly in the cardiovascular system. While new treatment modalities are emerging for Triple-negative breast cancer (TNBC), most current strategies include anthracycline-based regimens to manage disease. Therefore, novel strategies are needed to overcome anthracycline-induced cardiotoxicities in this patient population. Activation of the TSP1/CD47 signaling axis is implicated in the progression of heart failure, with reported increases in TSP1 levels following myocardial infarction. Therefore, we examined the potential of CD47 blockade as a strategy to prevent cardiac injury as a consequence of cancer chemotherapy. Our data in a syngeneic orthotopic breast cancer model shows that blockade of CD47 using an in vivo anti-sense phosphodiesterase morpholino (PMO) preserved ejection fraction, fractional shortening, and cardiac output when compared to DOX treatment while preserving oncologic efficacy of chemotherapy. To determine a potential mechanism of cardioprotection, hearts of control and CD47 PMO-treated mice were subjected to RNA sequencing. Gene set enrichment analysis (GSEA) showed significant positive enrichment for metabolic pathways including pyruvate metabolism (NES= 2.3 , p< 0.002), and oxidative phosphorylation (NES=2.0, p< 0.01). During cardiac insult, metabolic flexibility of cardiomyocytes results in metabolic reprogramming from fatty acid oxidation to a glycolytic mechanism to overcome injury. Thus, DOX-associated

cardiotoxicity may be mediated by an increase in TSP1 and a decrease in glycolysis, leading to the inability to overcome acute cellular stress. In vitro cellular bioenergetics, analysis revealed that TSP1 caused a dose-dependent reduction in glycolytic flux and glycolytic capacity in cardiac myoblast. This, coupled with preserved cardiac viability of cardiac cells treated with CD47 PMO in the presence of DOX, suggests that TSP1 may act through CD47 to prevent cardiac cell metabolic reprogramming needed to overcome injury. Furthermore, anti-sense experiments with siRNAs to Glut-4 and Hexokinase-II showed that the protection conferred by CD47 is mediated by activating these proteins. Therefore our studies suggest that the TSP1/CD47 axis may be central to the interplay of metabolism to preserve cardiac tissue integrity; thus, targeting this pathway may prevent the onset of chronic cardiac disease due to chemotherapy in cancer patients.

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5:00 PM - 6:15 PM

P5-08-15

Reducing Rates of Chronic Breast Cancer Related Lymphedema with Screening & Early Intervention: An Update of Recent Data

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Background: Breast cancer related lymphedema (BCRL) represents a dreaded complication of breast cancer treatment that can lead to morbidity, diminished quality of life, and psychosocial harm and is associated with increased costs. Increasingly, data has supported the concept of prospective BCRL surveillance coupled with early intervention to mitigate these effects.

Methods: We performed a systematic review of the literature searching for published randomized and prospective data evaluating prospective BCRL surveillance with early intervention. Results: We identified 12 studies (2,907 patients) including 4 randomized trials (1,203 patients) and 8 prospective studies (1,704 patients). Randomized data consistently demonstrate that early intervention reduces rates of progression to chronic BCRL with multiple paradigms and diagnostic modalities utilized; the strongest data in the review comes from the randomized PREVENT trial which demonstrated early detection with bioimpedance spectroscopy (BIS), coupled with a compression garment applied for 12 hours a day over 4 weeks, significantly reduced the rate of chronic BCRL compared to tape measurement.

Conclusions: Current data support the role of prospective BCRL surveillance with early detection and intervention to reduce rates of chronic BCRL. Breast cancer patients at risk for BCRL should undergo prospective surveillance as part of survivorship. Given the level 1 data demonstrating that BIS is superior to conventional tape measure, it should be included as the standard BCRL diagnostic modality unless an equally effective modality is employed.

Disclosure(s):

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5:00 PM - 6:15 PM

P5-08-16

"It's like Coming Home": A Qualitative Evaluation of Project Life a Virtual Wellness Community for People Living with Metastatic Breast Cancer

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Background: Project Life is a virtual wellness house led by people living with metastatic breast cancer (MBC) for people with MBC. Through the organization's targeted programming and curated content, Project Life promotes key dimensions of wellness: physical, emotional, social, spiritual, and financial. Project Life was created to fill the gaps in survivorship care for people with MBC specifically. The objective of this study was to qualitatively evaluate members' experiences with Project Life, understanding the impact of the organization and potential areas for future growth. Methods: From March 2022 to May 2022, we conducted semi-structured qualitative interviews virtually with members of the Project Life wellness community. The study design and primary objectives were designed in direct collaboration with Project Life leadership. A study flyer was distributed by e-mail and social media to the Project Life community. Participants were eligible if they self-identified as having MBC, were a member of the Project Life community and could complete the interview in English. Participants were asked a series of questions about how they heard about the organization, the types of programming they have participated in, the greatest benefits of Project Life, and areas for future growth and improvement. Interview transcripts were transcribed verbatim and analyzed. We then analyzed transcripts with phronetic iterative analysis, to uncover contextually grounded, emergent themes through synthetic coding. Results: We interviewed 36 women with MBC who were members of the Project Life Wellness Community in Spring 2022. Overall, 22% of participants identified as people of color, including Black, Latina and Asian women. In terms of age, 8 participants were 30-45, 15 were 46-59, and 13 were 60+. The overwhelming majority heard about Project Life through social media, with only one participant indicating they learned about the organization from their cancer center. Many participants stated that they wished cancer centers connected patients to external MBC support organizations like Project Life. The most commonly utilized Project Life programs included healing circles, legal clinics, cooking classes, and therapeutic art. Many participants endorsed having improvements in quality of life from being engaged with Project Life through MBC-specific curated content and the strong sense of community. Several participants indicated the appeal of participating in an organization that was developed by people with MBC for people with MBC. Additional suggestions for content

included finding information about clinical trials and increasing caregiver programming. Suggested opportunities for growth included programming across time zones, facilitating geographic connections, and partnering with other MBC advocacy organizations. Conclusions: Patient-led and curated virtual communities are filling substantial gaps in survivorship care for individuals with metastatic breast cancer. Through its virtual format, the Project Life wellness community has a widespread reach and offers a promising model for intentionally curated metastatic survivorship care. The unique virtual format of Project Life should spark creativity in how quality survivorship care for people with MBC can be delivered. Healthcare settings including cancer centers can play a larger role in connecting people with MBC to external support organizations to better ensure survivorship needs are being holistically met.

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5:00 PM - 6:15 PM

P5-08-17

Monitoring for cardiotoxicity in early breast cancer: an Australian experience

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Background Breast cancer is the most commonly diagnosed cancer in Australia. Patient outcomes continue to improve with current 10 year survival of 86%. Given this, greater focus is needed to minimise potential long term toxicities of prescribed therapies. Anthracyclines and HER2 targeted therapies are commonly prescribed agents for high risk early breast cancers and are associated with acute and long term cardiotoxicity. Despite this, screening of cardiotoxicity in Australian patients receiving these therapies remains variable due to a lack of endorsed national screening guidelines. We conducted a retrospective review of screening procedures for cardiotoxicity in 2 major oncology centres in metropolitan Sydney and compared the findings to current international recommendations from ASCO/ESMO guidelines. Methods Patients were included if they received doxorubicin, epirubicin or trastuzumab with neoadjuvant or adjuvant intent during 2021. Baseline patient and tumour characteristics including cardiovascular risk factors were reviewed. Baseline ECG, transthoracic echocardiogram (TTE) or cardiac biomarkers (cardiac troponin or brain natriuretic peptide) were recorded, as well as frequency of serial monitoring and incidence of cardiotoxicity and cardiology referrals. Results 111 patients receiving initial curative therapy were included of which 45 received anthracycline therapy without trastuzumab. 66 received trastuzumab of which 34 also received anthracycline. 38 patients were aged greater than 60 and 31 had 2 or more cardiovascular risk factors. Of the patients receiving anthracycline only, 96% had a baseline TTE. All patients receiving trastuzumab only had a baseline TTE and of the 34 patients who received anthracycline and trastuzumab 3 did not undergo baseline TTE but underwent one prior to commencing trastuzumab. 3 patients total had a baseline ECG. No patients had baseline biomarkers measured. Only 5 patients had biomarkers measured at 1 year and all 5 had developed grade 1 heart failure on treatment. These 5 patients were referred for cardiology review and 2 required an interruption of trastuzumab. All patients receiving trastuzumab underwent 3 monthly TTEs on treatment. Of the 35 patients now more than 1 year post treatment completion, only 3 patients had a TTE at 12 months. No patients referred to cardiology have reached 12 months post treatment. Discussion International guidelines recommend screening to identify and treat early cardiotoxicity and prevent long term morbidity. ASCO and ESMO guidelines both recommend patients receiving anthracycline undertake a TTE at baseline and at 6-12 months after completing therapy. Both recommend 3 monthly TTEs for patients receiving trastuzumab. The ESMO guidelines recommend a baseline ECG and consideration of further TTE at 2 years post therapy. For high risk patients the ASCO guidelines discuss offering routine TTEs during treatment. The ESMO guidelines recommend measurement of cardiac biomarkers for patients receiving anthracycline prior to each cycle and routine monitoring can be considered for patients receiving anti HER2 therapy. The ASCO guidelines reserve use of cardiac biomarkers

for patients who develop signs or symptoms of cardiac dysfunction. Our study demonstrates that while baseline cardiac assessment is well performed a personalised approach to cardiac monitoring during curative therapy is not. These were unexpected findings given both treatment units are located in well resourced areas of Sydney. An outcome of this study has been the development of a cardio-oncology group within our oncology and cardiology departments. This has led to the development of new clinical guidelines to screen and manage high risk breast cancer patients receiving cardiotoxic therapies. This has empowered patients, care coordinators and physicians to proactively manage cardiac risks from therapy and we hope these institutional guidelines will be adopted nationally.

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Brendan Kirwin, MBBS: No financial relationships to disclose

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5:00 PM - 6:15 PM

P5-08-18

A novel free-to-use software for upper limb volume quantification in breast cancer related lymphedema: implementing cutting-edge technology in the individualized therapeutic approaches of breast cancer survivors

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BACKGROUND: Breast cancer related lymphedema (BCRL) is a detrimental condition affecting a growing number of breast cancer (BC) survivors worldwide [1]. Effective screening programs and early diagnosis are mandatory in the clinical management of this disabling condition and limb volume assessment plays a crucial role [1]. However, a reproducible volumetric assessment is still challenging in clinical practice. In this scenario, augmented reality tools have been recently proposed for volumetric quantification of BCRL [2]. Despite the advantages in safety and time effectiveness, the integration of these devices in clinical practice is affected by several barriers, and free-to-use software for volume quantification are still lacking [3]. Therefore, the aim of this study was to develop and validate a free-to-use software for volume quantification of BCRL in order to overcome barriers to technology implementation in the complex management of BC patients. **METHODS:** A cohort of mixed-gender young adults was assessed by tridimensional laser scanning, centimetric method, and water displacement method. The upper limb volume measures were saved and processed using a software package composed of three programs (Edit 3D, Slice 3D, Cut 3D). The novel software package was specifically developed and freely released on the online site <https://mn-visions.gitbook.io/software-kit-for-3dls-limb-volume-quantification/>. In addition, hand volume has been assessed two groups (experimental group and optimization group). Digital volume quantification algorithms have been specifically designed using the gift wrapping (GW) or cubic

tessellation (TE) method. The novel software package was subsequently used to assess a small pilot sample of BCRL patients. The upper limb volumes were analyzed to assess linear regression and correlation, level of agreement, and consistency between the different methods. RESULTS: Forty upper limb volumes of 20 participants were assessed in the present study. The linear regression analysis showed a statistically significant correlation between laser scanning method and centimetric method ($R^2= 0.99$, $p < 0.0001$). A high level of agreement was reported (R^2 interval from 0.93 to 0.97, r ranged from 0.965 to 0.984) between the centimetric method and the novel software package. Hand volume has been assessed in 5 subjects (experimental group). The optimization group ($n: 4$) demonstrated that the hand volumes calculated from digital method (tessellation method) show a high correlation with the values obtained with water displacement ($\rho = 0.83$; $p < 0.05$). Preliminary data from BCRL women were recently assessed ($n:3$) and suggested a high correlation between LS3D and centimetric method ($R^2= 0.96$). CONCLUSION: Our data underlined promising results for the implementation in clinical setting of the three programs Edit 3D, Slice 3D, Cut 3D for the upper limb volume quantification. In addition, significant correlations between water displacement method (gold standard) and hand digital volume method were highlighted, suggesting intriguing implications in a precise quantification of hand volume in clinical setting. These findings might provide advantages in reproducibility between different operators enhancing data sharing between different centers. Future data on BCRL patients are needed to confirm the role of this novel free-to-use software in the rehabilitation management of breast cancer survivors. REFERENCES: 1. Heller DR et al. Prevention Is Key: Importance of Early Recognition and Referral in Combating Breast Cancer-Related Lymphedema. *Journal of Oncology Practice* 2019;15:263–4. 2. Invernizzi M et al. Integrating Augmented Reality Tools in Breast Cancer Related Lymphedema Prognostication and Diagnosis. *J Vis Exp.* 2020 6;(156). 3. Kassamani YW et al. Diagnostic Criteria for Breast Cancer-Related Lymphedema of the Upper Extremity: The Need for Universal Agreement. *Ann Surg Oncol.* 2022;29(2):989-1002

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P5-09-01

Neoadjuvant hormonal therapy plus palbociclib versus hormonal therapy plus placebo in women with operable, hormone sensitive and HER2-negative primary breast cancer

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Background: Early biologic response to endocrine therapy, such as changes in Ki67 labeling index (LI), has been suggested to predict long-term outcomes in hormone sensitive breast cancer. The addition of a CDK4/6 inhibitor to endocrine therapy has been shown to augment biological response in breast cancer. Pre-operative Endocrine Prognostic Index (PEPI) scores, generated based on post-treatment Ki67 LI, have been shown to predict patient outcomes.

EndoPredict® is a multigene assay that predicts the risk of distant recurrence in patients with operable estrogen receptor (ER)-positive HER2-negative breast cancer. This study was conducted to evaluate the efficacy of the neoadjuvant endocrine therapy plus palbociclib versus neoadjuvant endocrine therapy plus placebo. Patients and Methods: This is a phase III randomized, double-blind study of neoadjuvant hormonal therapy plus palbociclib versus neoadjuvant hormonal therapy plus placebo in untreated pre/peri- and post-menopausal women with operable, hormone receptor-positive (ER and/or progesterone receptor), HER2-negative breast cancer. The other major inclusion criteria included tumor size $\geq 15\text{mm}$, T1c-3N0-1, Ki67 LI $\geq 14\%$ by central assessment, and no previous history of radiotherapy or systemic therapy for breast cancer. Patients were randomly assigned 1:1 to receive 16 weeks of hormonal therapy plus palbociclib or hormonal therapy plus placebo. Hormonal therapy consisted of letrozole for post-menopausal patients and tamoxifen plus LH-RH agonist for pre/peri-menopausal patients. The co-primary endpoints included PEPI score and EPclin Risk Score, a score combining EndoPredict® molecular score with clinical factors. These scores were sequentially analyzed on a modified intent-to-treat basis according to the gatekeeping procedure: if statistical significance was detected on the PEPI score, the statistical significance of EPclin Risk Score would be assessed. The sample size was 100 patients in each arm, which was calculated with $< 5\%$ type I error rate (two sided) and 80% power. Results: Between 16 July 2019 – 7 July 2021, 141 eligible patients were randomized from 25 participating institutes in Japan, Korea, Taiwan, Hong Kong and Australia. One hundred twenty-six patients completed the treatment duration and surgical samples were collected to evaluate endpoints. All randomized patients were evaluable for safety assessment. Randomization was well-balanced in terms of age, menopausal status and cancer stage. The proportion of patients who had a low, moderate, or high PEPI score was 15.2%, 50.0% and 34.8% in the hormonal therapy plus palbociclib arm and 13.3%, 55.0% and 31.7% in the hormonal therapy plus placebo arm, respectively. There was no statistically significant difference in PEPI score between two arms (one-sided p-value=0.563). The proportion of patients who had a high risk EPclin Risk Score seemed lower in the palbociclib arm than in the placebo arm (62.1% vs 68.3%) although hypothesis testing was not performed on EPclin Risk Score because statistical significance was not detected on the PEPI score. No new safety signals were found in the study. Permanent discontinuation from the study in association with adverse events was reported for 7 (9.7%) patients in the hormonal therapy plus palbociclib arm and for 0 patients in the hormonal therapy plus placebo arm. Conclusions: The addition of palbociclib to neoadjuvant hormonal therapy did not improve efficacy measured by PEPI score. In palbociclib arm, the rate of patients who had a high risk EPclin Risk Score after treatment was lower than in placebo arm. Translational researches are ongoing to analyze molecular changes by treatments. The role of chemotherapy after neoadjuvant therapy is under investigation. Clinical trial identification: NCT03969121 Funding: Pfizer Inc.

Disclosure(s):

Takayuki Ueno, MD,PhD: Astra Zeneca: lecture (Ongoing); Chugai Pharmaceutical: lecture (Ongoing); Eisai Co.Ltd: lecture (Ongoing); Novartis Pharma KK: lecture (Ongoing)

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5:00 PM - 6:15 PM

P5-09-02

Impact of neoadjuvant endocrine therapy on tumor transcriptome in patients with early-stage breast cancer from the FLEX trial

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BACKGROUND: Neoadjuvant Endocrine Therapy (NET) is seldom used in breast cancer management except in patients with several comorbidities or in elderly patients in which chemotherapy is not an option. Clinical response with NET is not typically achieved until after several months of treatment. In the NET setting, reduction of Ki67 (< 10%) after 2-4 weeks has

been used as a predictor of positive response, but studies such as ALTERNATE have questioned this association. It remains uncertain whether a single gene or protein can adequately predict outcomes or inform how NET alters a variety of cancer genes and global tumor biology. This study evaluated the effect of short-term NET on the tumor genomics of patients with early-stage breast cancer (EBC) by comparing whole transcriptome gene expression changes in matched pre- and post-NET tumor samples. METHODS: In this single-institution FLEX substudy performed at Johns Hopkins, patients (n=30) with matched pre- and post-treatment specimens who received at least two weeks of NET between 2019 – 2021 were included. Premenopausal and male patients with breast cancer received Tamoxifen (n=10) and postmenopausal women received either Letrozole (n=10) or Exemestane (n=10). Limma R package was used for quantile normalization and differential gene expression analysis. Significant differentially expressed genes (DEGs) had a false discovery rate of < 0.05 and >2-fold change. Pathway enrichment analysis was performed using Reactome. For patients with available clinical information, changes in immunohistochemistry (IHC) between pre- and post-NET were quantified using absolute values, and the median percent change was reported, with significance assessed using the Wilcoxon test. The observational FLEX trial (NCT03053193) enrolls patients with EBC who have MammaPrint (MP) with or without Blueprint testing and consent to clinically annotated full transcriptome data collection. MammaPrint classifies tumors as having a Low Risk (LR) or High Risk (HR) of distant recurrence. Blueprint is a molecular subtyping assay, and together with MammaPrint, tumors are classified as Luminal A-Type (MP LR), Luminal B-Type (MP HR), HER2-Type, or Basal-Type. RESULTS: Transcriptional profiles between pre- and post-NET samples were distinct with short-term NET inducing 774 DEGs. The majority of significant DEGs (n=748) such as MGAT1, IQGAP3, and PRC1, which are associated with tumor aggressiveness and metastasis, were downregulated in post-NET samples. Upregulated genes in post-NET tumors, such as FOS, JUN, and EGR1, are involved in estrogen signaling and NF-κB pathways and are associated with better outcomes. Among the 30 patients, 7 (6 Luminal B and 1 Basal) remained MP HR and 16 remained MP LR (Luminal A) pre- and post-NET, 1 changed from LR (Luminal A) pre-NET to HR (Luminal B) post-NET, and 6 changed from HR (Luminal B) pre-NET to LR post-NET (Luminal A). The median percent change by IHC in matched pre- and post-NET tissue was 2.5% for estrogen receptor (ER) (range: 0-50%; p=0.750), 22% for progesterone receptor (PR) (range: 0-81%; p=0.097), and 9% for Ki67 (range: 0-43%; p=0.026). CONCLUSIONS: In this study, significant gene expression changes were discovered within a shorter timeframe than when clinical responses are usually observed in the NET setting. This could indicate biological complexity and diverse response pathways, which may be more informative when combined with a single IHC biomarker (ER/PR/Ki67). Results from this study should be confirmed using a larger cohort. Future studies will determine the significance of these DEGs and their impact on outcomes, and will further define gene expression changes by endocrine therapy type (tamoxifen versus aromatase inhibitors). ACKNOWLEDGMENTS: We would like to thank Lynn and Robert Downing for their generous support of our study.

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P5-09-03

Real World Data on Neoadjuvant Endocrine Treatment and Ki67 Assessment in ER+/HER2- Breast Cancer. Results from a Single-Institution Prospective Cohort Study

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Purpose: Neoadjuvant endocrine treatment (NET) has become a useful tool for the downstaging of luminal-like breast cancers in postmenopausal patients. It enables us to increase breast conserving surgery (BCS) rates and provides an opportunity for assessing in vivo NET effectiveness and studying any biological changes that may act as valid biomarkers. The purpose of this study was to evaluate the effectiveness of NET as well as to assess the role of Ki67 proliferation rate changes as an indicator of endocrine responsiveness.

Methods: From June 2016 to January 2022, a single-institution cohort of patients treated with NET and further surgery was evaluated. In patients with Ki67 \geq 10%, a second core biopsy was performed after four weeks. Information regarding histopathological and clinical changes, as well as surgical management, was gathered.

Results: A total of 168 estrogen receptor positive (ER+)/HER2 negative patients were included. The median age at diagnosis was 69.5 years old (IQR: 16.0). The median treatment duration was 5.0 months (IQR: 4.0). Median maximum size in the surgical sample was 44.0% smaller than pretreatment size measured by ultrasound ($p < .0001$), showing an inverse linear relationship with treatment duration. Median pretreatment Ki67 expression was 20.0% (IQR: 18.0) and was reduced to 5.0% (IQR: 8.0) after four weeks, and to 2.0% (IQR: 7.25) in the surgical sample ($p < 0.0001$). Other significant downgrading changes were observed with respect to tumor grade ($p < 0.0001$) and progesterone receptor (PR) expression ($p < 0.0001$). BCS was performed on 145 patients (86.3%). One case of pathological complete response was recorded. A larger Ki67 fold-change after four weeks was significantly related to a PEPI score

of 0 ($p < 0.002$). No differences were observed between luminal A- and B-like tumors with regard to fold-change and PEPI score. No treatment abandonment was produced during the study.

Conclusions: In our cohort, NET has proven effective for tumor size and Ki67 downstaging. This results in a higher rate of conservative surgery, aids in therapeutic decision-making, provides prognostic information, and constitutes a safe and well-tolerated approach

Biological changes after NET

Differences	Pre-Net / Pathological	Pre-Net / Intermedial	Intermedial / Pathological
Size (p)	<0.0001	<0.0001	<0.0001
Estrogen Receptor Expression (p)	<0.05	ns	ns
Progesterin Receptor Expression (p)	<0.0001	<0.0001	<0.005
Ki67 (p)	<0.0001	<0.0001	ns
Histological Grade	<0.0001	<0.0001	<0.0001

Patient and tumor characteristics

n=168 (100%)	
Clinical Stage	(n/%)
IA	66 (39.3)
IIA	70 (41.7)
IIB	24 (14.3)
IIIA	8 (4.8)
Clinical N stage	(n/%)
cN0	94(81.7)
cN1	21(18.3)
Histological type	(n/%)
Ductal	125 (74.4)
Lobular	31 (18.5)
Other	12(7.1)
Histological grade	(n/%)
G1	31 (18.5)
G2	112(66.7)
G3	25 (14.9)
Size (mm)	25(18)
Pre-NET ER expression (%)	100(0)
Pre-NET PR expression (%)	70.0 (80)
Pre-NET Ki67 (%)	20.0(18)

Disclosure(s):

Covadonga Marti, MD PhD: No financial relationships to disclose

Laura Frias, MD: No financial relationships to disclose

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5:00 PM - 6:15 PM

P5-09-04

Efficacy of neoadjuvant endocrine therapy compared with neoadjuvant chemotherapy in pre-menopausal patients with hormone-responsive and HER2-negative, lymph node-negative breast cancer.

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Background: Neoadjuvant endocrine therapy (NET) has demonstrated efficacy in post-menopausal patients with hormone-responsive and her2-negative breast cancer. This trial was designed to compare the efficacy of neoadjuvant chemotherapy (NCT) with NET in pre-menopausal patients with hormone-responsive, her2-negative and lymph node-negative breast cancer.

Materials and Methods: In this prospective, randomised study, pre-menopausal patients with hormone-responsive, her2-negative and lymph node-negative breast cancer were recruited. Enrolled patients were randomly assigned (1:1) to receive either NCT or NET with goserelin and tamoxifen, followed by goserelin and anastrozole. The primary purpose was to evaluate the non-inferiority of NET compared to NCT using clinical response, assessed by ultrasound.

Results: A total of 68 patients were assigned to receive NCT (n = 31) or NET (n = 37). The clinical response rate was 16.1% for NCT and 35.1% for NET (estimated difference 19%, 95%CI: -1.1%-39.1%, non-inferior p = 0.002). Rates of breast-conserving surgery were similar between NCT and NET (90.3% vs 83.8%, p=0.494).

Conclusions: The clinical response rate of NET is non-inferior to NCT in pre-menopausal patients with hormone-responsive, HER2-negative, lymph node-negative breast cancer.

Summary of ultrasound clinical response

	Chemotherapy N=31	Endocrine therapy N=37	Non-inferior p
WHO criteria			0.002
uCR+uPR	5 (16.1%)	13 (35.1%)	
uSD+uPD	26 (83.9%)	24 (64.9%)	
RECIST criteria			<0.001
uCR+uPR	5(16.1%)	15(40.5%)	
uSD+uPD	26(83.9%)	22(59.5%)	

The breast surgery and MP grading system

	Chemotherapy N=31	Endocrine therapy N=37	p
Breast surgery			0.494
BCS	28(90.3%)	31(83.8%)	
mastectomy	3(9.7%)	6(16.2%)	
MP grading system			0.445
Grade 1-2	9(29.0%)	14(37.8%)	
Grade 3-5*	22(71.0%)	23(62.2%)	

Disclosure(s):

chongshan gu, n/a: No financial relationships to disclose
yingjian he, n/a: No financial relationships to disclose
jinfeng li, n/a: No financial relationships to disclose
tianfeng wang, n/a: No financial relationships to disclose
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P5-09-05

A phase II, single-arm study of histone deacetylases inhibitor Tucidinostat and Exemestane as neoadjuvant therapy in patients with hormone receptor positive HER2 negative breast cancer (NeoTEE trial)

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Background: Tucidinostat (formerly known as chidamide) plus exemestane is approved for postmenopausal patients with advanced, hormone receptor-positive breast cancer. We evaluated the efficacy and safety of tucidinostat plus exemestane as the neoadjuvant strategy in hormone receptor-positive early breast cancer patients. Methods: NeoTEE is an open-label, single-center, phase II study. Patients with HR-positive, HER2-negative and stage II/III breast cancer were enrolled at the First Affiliated Hospital of Sun Yat-sen University. Eligible patients received 25 mg oral exemestane once daily for 2 weeks followed by 30 mg oral tucidinostat twice weekly in combination with 25mg oral exemestane once daily for 24 weeks. GnRHa was used for premenopausal patients. Endpoints assessed here included objective response rate (ORR), complete cell cycle arrest (CCCA, Ki-67 \leq 2.7%) at surgery, disease control rate (DCR), pathological complete remission (pCR) and safety. Results: Between July 2020 and July 2022, 26 patients were enrolled, of whom 24 were evaluable for response per RECIST 1.1 criteria. Partial response (PR) was observed in 18 patients, with an ORR of 75% (18/24). The DCR was 100%. Of the 14 patients with surgery, one patient achieved pCR and 8 patients were exempt from postoperative adjuvant chemotherapy. CCCA at surgery was 64.3% (9/14). The follow-up remains ongoing and updated results will be presented thereafter. Most adverse events (AEs) were grade 1 or 2. Grade 3 AEs occurred in 8 of 26 patients, the most common were neutropenia 19.2%, leukopenia 7.7%, anemia 3.8%, ALT increased 3.8%, pneumonitis 3.8%. Only 1 patient experienced grade 4 neutropenia. Grade 3/4 neutropenia recovered after dose

reduction or discontinuation of tucidinostat. No patient received G-CSF. Conclusions: Tucidinostat combined with exemestane was well tolerated and demonstrated meaningful responses in neoadjuvant setting for women with early HR+/HER2- breast cancer. Further investigation is warranted. Clinical trial information: NCT04465097.

Disclosure(s):

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P5-10-01

Phase 2 study of anlotinib combined with taxanes and lobaplatin in the neoadjuvant treatment of triple-negative breast cancer: efficacy, safety and biomarker analysis from the SWH-B006 (neoALTALL) trial

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Background: Anlotinib, a novel multi-target tyrosine kinase inhibitor that effectively inhibits VEGFR, PDGFR, FGFR, c-KIT, c-MET, and RET, monotherapy has been proven effective in HER-2 negative metastatic breast cancer, but its efficacy in early-stage triple-negative breast cancer (TNBC) is unknown. This phase 2 study aims to evaluate the efficacy and safety of adding anlotinib to neoadjuvant chemotherapy in patients (pts) with primary TNBC.

Methods: Pts with clinical stage II/III TNBC were to be treated with 5 cycles of anlotinib (12mg, d1-14, q3w) plus 6 cycles of taxanes (docetaxel 75 mg/m² or nab-paclitaxel 125 mg/m², d1 and d8, q3w) and lobaplatin (30 mg/m², d1, q3w), followed by surgery. The primary endpoint was pathological complete response (pCR) in the breast and axilla (tpCR; ypT0/is ypN0) and the secondary endpoints include pCR in the breast (bpCR; ypT0/is), event-free survival (EFS), invasive disease-free survival (iDFS), overall survival (OS), and safety. Exploratory study included biomarker analysis and efficacy comparison based on FUSCC classification (IHC-based).

Results: From Jan 2021 to Feb 2022, a total of 24 pts were enrolled. The median age was 50 years (range, 26-64), 54% were postmenopausal, 75% were nodal involved, 29% had stage III, and 79% were Ki-67 high ($\geq 30\%$). At the data cut off time of 30th Jun 2022, all 24 pts received at least one dose of study treatment and underwent surgery. Overall, 21 pts received five courses of anlotinib. Two pts discontinued anlotinib for safety reason, and one pt discontinued anlotinib due to missed dose in cycle 4. After surgery, 14 out of 24 pts achieved a tpCR (58.3%; 95% CI, 36.6%–77.9%), and the bpCR rate was also 58.3% (14/24). Of the 18 pts with the node-positive disease at diagnosis, 15/18 (83.3%) became ypN0. Based on the FUSCC IHC-based subtypes, the tpCR rates were 66.7% (6/9) for BLIS subtype, 80% (4/5) for IM subtype and 0% (0/4) for LAR subtype, respectively. Next-generation sequencing revealed that the most commonly mutated genes in these pts were TP53 (19/21, 90.5%), MYC (7/21, 33.3%), BRCA1 (5/21, 23.8%), PIK3CA (4/21, 19.0%), BCL2L1 (4/21, 19.0%), and RB1 (3/21, 14.3%).

Subgroup analysis showed that the tpCR were 71.4% (5/7) and 42.9% (6/14) in MYC-amplified and wild-type pts, respectively, and 80% (4/5) and 43.8% (7/16) in BRCA1-mutated and wild-type pts, respectively. All of 24 pts in the safety population showed at least one treatment emergent adverse events (TEAEs). Grade 3 or 4 TEAEs occurred in 14 pts (58.3%), and the most common events were leucopenia (29.2%; n=7), neutropenia (29.2%; n=7), thrombocytopenia (20.8%; n=5), anemia (16.7%; n=4), hypertension (12.5%; n=3), and oral mucositis (8.3%; n=2), respectively. No treatment-related deaths occurred.

Conclusions: The addition of anlotinib to neoadjuvant chemotherapy showed manageable toxicity and promising antitumor activity for pts with early-stage TNBC. The study is still ongoing, and the enrollment has been completed. Clinical trial information:

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Corresponding author: Dr. Xiaowei Qi, qxw9908@foxmail.com. Department of Breast and Thyroid Surgery, Southwest Hospital, Army Medical University, Chongqing.

<i>Efficacy endpoint</i>	<i>pCR</i>	
	<i>Frequency</i>	<i>95% CI</i>
All patients (N=24)		
tpCR (ypT0/is, ypN0)	14/24 (58.3%)	36.6%–77.9%
bpCR (ypT0/is)	14/24 (58.3%)	36.6%–77.9%
Lymph node positive (N=18)		
apCR (ypN0)	15/18 (83.3%)	58.6%–96.4%
FUSCC IHC-based subtypes (N=18)		
BLIS subtype	6/9 (66.7%)	29.9%–92.5%
IM subtype	4/5 (80.0%)	28.4%–99.5%
LAR subtype	0/4 (0%)	0.00%–60.2%
Biomarker analysis (N=21)		
MYC amplification	5/7 (71.4%)	28.0%–96.3%
BRCA1 mutation	4/5 (80.0%)	28.4%–99.5%

Disclosure(s):

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Jing Liu, n/a: No financial relationships to disclose

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P5-11-01

Epithelial-Mesenchymal Plasticity is Regulated by Inflammatory Signaling Networks Coupled to Cell Morphology

Presenting Author(s) and Co-Author(s):

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Purpose: During development and homeostatic processes such as wound repair, certain cells undergo a remarkable process where they radically transform in cell shape and state, from epithelial to mesenchymal cells. This ability is referred to as 'Epithelial-Mesenchymal Plasticity' (EMP), triggered by both mechanical (i.e. loss of cell-cell contact) and soluble cues (i.e. TGF β), and is absolutely essential in both embryonic and adult organisms. Dysregulation of EMP also occurs in cancer; where tumor cells undergo EMP to become metastatic, stem-like, and drug resistant. Critically, increased EMP correlates with increased cancer severity. However, it is largely a black box as to how EMP is regulated and how epithelial cells sense physical, geometrical, and soluble cues in their environment to assume a mesenchymal fate. This work inferred that cell shape is a determinant of not only fates – but of long-term outcomes. That is, we provide mechanistic explanations between cell context, environment, and cancer severity. In this work, we investigated how mechanical and soluble cues are coupled to the dynamics of signaling pathways that regulate transcriptional and post-transcriptional events that underpin EMP. Especially with regards to mechanical cues, we attempt to unlock the 'black box' as to how changes in adhesion, ECM (Extracellular Matrix) stiffness, and environment geometry are coupled to the transcriptional events that drive EMP. Results: We show that changes in cell and nuclear shape result from the actions of the cytoskeleton and important drivers of EMP in upregulating 'interlocking' networks that promote EMP-driving inflammation and suppressing insulin signaling. Using a combination of cell biology, proteomics, and new statistical methods, we provide a systems biology model demonstrating: Cell shape \rightarrow MT bound Kinesin-1 activity and nuclear shape \rightarrow inflammation (IKK, JNK), insulin signaling (IRS), and YAP/TAZ \rightarrow EMP. Our work connects observable changes in phenotype to causal changes in signaling network architecture and cell fates. We used an integrative -omic approach to analyze tumors from breast cancer patients. We identified a novel tumor suppressor – JAM3 – whose loss is associated with altered nuclear shape in vivo, inhibiting JAM3 in cells, or stimulation with canonical EMP inducer TGF β to promote EMP, and thus changes the organization of microtubules and alters nuclear shape. During EMP we observe there is upregulation of a pro-inflammatory, insulin resistant, signaling network that is predictive of mesenchymal states across cancer. EMP following JAM3 depletion and/or TGF β stimulation is rescued by inhibition of Kinesin-1 motors. This rescue is explained by changes in inflammatory and insulin signaling. We show that while Kinesin-1 activity is responsible for upregulation in canonical signalling and network 'hubs', changes in nuclear shape upregulate 'effectors' of these hubs. Thus, microtubules and nuclei differentially regulate different parts of 'interlocking' networks. Conclusions: This work has integrated image-omics, comprehensive global proteomics, and quantitative cell biology to provide a mechanistic –and systems-level understanding of how epithelial cells differentiate into mesenchymal forms during disease development and progression. This work is of major significance for three reasons. First, it shows how cell shape can mechanistically regulate cell fates on an unprecedented systems-level. Second, we identify an EMP network that is conserved across cancers and may indeed be conserved across both normal and diseased mesenchymal cells. Indeed, we speculate that different types of diseased

cells may all share the same network. Finally, we introduce the concept of interlocking networks – where hubs and effectors are regulated by different cellular components. Our work has been extensively validated, using chemical and genetic approaches and in vivo model of in human breast cancer.

Disclosure(s):

Zheng Yin, PhD: No financial relationships to disclose

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P5-11-03

Knockdown of TMEM45A regulates malignant progression of triple-negative breast cancer by inhibiting TGF- β /Smad signaling pathway-mediated EMT

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Objectives: The incidence of breast cancer has jumped to first place in the global malignant tumor. As an essential component of the TMEM family, TMEM45A is abnormally highly expressed in some malignant tumors, and plays a role in promoting and regulating the occurrence and development of tumors. This study analyzed the expression of TMEM45A in breast cancer tissues and breast cancer cell lines, and explored the relationship with clinical subtypes. To examine the effects of TMEM45A on TNBC cell proliferation, migration, invasion and other biological functions, and to preliminarily clarify the molecular mechanism of TMEM45A regulating the epithelial-mesenchymal transition of TNBC cell lines. Methods: 1. Download and analyze the TCGA database, analyze the difference in the expression of TMEM45A in normal breast tissue and different subtypes of breast cancer tissue, and detect the protein expression level of TMEM45A in 8 pairs of cancer tissues and adjacent tissues by western blot experiment. 2. Detection of TMEM45A protein expression in normal breast epithelial cell line MCF10A and five breast cancer cell lines (MCF-7, MDA-MB-231, BT-549, MDA-MB-468, SK-BR-3) by western blot experiment. 3. Using small interfering RNA technology to down-regulate the protein expression levels of MDA-MB-231 and BT-549 TNBC cell lines with relatively high TMEM45A expression. The changes in cell proliferation ability were detected by CCK8 assay and clone formation assay, and the changes in cell migration ability and invasion ability were detected by wound healing assay and transwell assay, respectively. 4. After down-regulating TMEM45A in two TNBC cell lines, the expression changes of epithelial cell phenotype marker E-cadherin, mesenchymal phenotype marker N-cadherin, Vimentin, and critical molecules in TGF- β /Smad signal transduction pathway (TGF β 1, Smad2, Smad3, p-Smad2, p-Smad3) were detected by western blot experiment. Results: 1. Based on the TCGA database, the results showed that the expression level of TMEM45A mRNA in breast cancer was significantly higher than in normal breast tissue. The expression level of TMEM45A mRNA in any breast cancer subtype was higher than that in normal breast tissue, and it was the highest in the TNBC subtype. In the results of western blot experiments of clinical breast cancer specimens, the expression of TMEM45A in breast cancer tissues was significantly higher than that in the corresponding adjacent tissues, which further confirmed the reliability of the results of the TCGA database. 2. In normal breast epithelial cell line MCF10A and five breast cancer cell lines, MCF10A has the lowest expression level of TMEM45A protein. Among the five breast cancer cell lines, MDA-MB-231 had the highest expression of TMEM45A, followed by BT-549. 3. CCK8 assay, clone formation assay, wound healing assay and transwell assay showed that down-regulating TMEM45A protein levels in the two TNBC cell lines could significantly reduce cell proliferation, migration and invasion abilities. 4. After down-regulating TMEM45A protein levels in two TNBC cell lines, EMT-related indicators E-cadherin protein expression levels increased, N-cadherin and Vimentin protein expressions decreased, and the expression levels of essential protein molecules Smad2 and Smad3 in the TGF- β /Smad signal transduction pathway did not change significantly, while p-Smad2, p-Smad3 and TGF- β 1 protein

expressions decreased. Conclusions: TMEM45A is relatively highly expressed in breast cancer tissues and cell lines, especially in the subtype of TNBC. Down-regulation of TMEM45A expression can inhibit the proliferation, migration and invasion of TNBC cell lines. Mechanistically, TMEM45A may reverse EMT by inhibiting the activity of the TGF- β /Smad pathway.

Disclosure(s):

Yingkun Xu, n/a: No financial relationships to disclose

Shengchun Liu, n/a: No financial relationships to disclose

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5:00 PM - 6:15 PM

P5-11-04

Differentially expressed genes and their pathways in breast cancer patients with mesenchymal CTC.

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Background: Circulating tumor cells (CTC) with phenotype of epithelial-mesenchymal transition (CTC_EMT) represent novel subpopulation of CTC associated with inferior outcome in primary breast cancer (PBC). However, molecular characterization of primary tumors associated with this CTC subpopulation is lacking. The aim of this study was to identify signaling pathways associated with presence of CTC_EMT in PBC patients using a comprehensive genomics approach. Methods: This translational study included 17 patients with PBC and 5 donors of normal breast tissue. CTC_EMT were detected before surgery by quantitative RT-PCR assay for expression of epithelial-mesenchymal transition (EMT) genes (TWIST1, SNAIL1, SLUG, ZEB1). Total RNA was extracted, in parallel, from fresh frozen primary tumor and whole-transcriptome profiles were obtained using RNA sequencing and additionally mRNAs profiles by microarray. Genes expressions were further validated by qRT-PCR. Results: Analyzing RNA sequencing and microarray data, we found set of genes differentially expressed in absence or presence of CTC_EMT in PBC. We identified 157 genes differentially expressed in CTC_EMT phenotype compared to patients with non-detectable CTC. Namely, keratin family is represented by genes KRT5, KRT14, KRT17. Gene ontologies related to membrane structure

or communication and immunology appears to be involved in CTC-related processes, pathways related to cell junction and various signaling pathways including PI3K and Ras-signaling appear to be significant in processes leading to CTC EMT presence. Conclusions: We suspect multiple genes of having a role in primary tumour processes leading to CTC EMT production in breast cancer patients. Data suggest, that PI3K & Ras-signalling and pathways related to cell junction are the key pathways for changes inside of primary tumour tissue between CTC EMT and CTC-phenotype of breast cancer patients. We propose, additional study with single-cell resolution is needed for better understanding of the processes.

Disclosure(s):

Michal Mego, n/a: No financial relationships to disclose

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P5-12-01

MUTYH In A Cancer Population

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Draft Proposal

Title: MUTYH In A Cancer Population

Author: Linda Ann Smith

Background:

Germline genetic testing has become a critical quality point in caring for breast cancer patients and high risk patients. Originally testing panels were extremely limited, but now expanded hereditary cancer testing panels are more common and have raised the question of other genes being linked to cancer risk. In this cohort, we examine the prevalence of the gene mutation MUTYH in a high risk population tested with expanded panels.

Method:

Patient data was obtained from an IRB-approved multi-center longitudinal, observational study, in which 2276 patients underwent expanded (>9 gene) germline genetic testing and also contributed personal and family history of cancer information. The average age in this cohort was 58.58 years old, with 2197 (96.53%) Female and 1762 (77.43%) with a personal cancer diagnosis and 1625 (71.40%) with a family history of cancer. Germline genetic tests were lab agnostic and tested an average of 73.2 genes (1214 or 53% tested with 85 gene panel) and a range of 9-85 genes tested.

Results:

Overall, the patients had a 16.70% positivity rate for pathogenic germline result of genetic test, with 42 (1.85%) reporting a Monoallelic MUTYH pathogenic variant (PV) result. Of those reporting a MUTYH PV, the average age was 58.48, with 40 (95.24%) females and 35 (83.33%) with a personal cancer diagnosis and 32 (76.19%) with a family history of cancer. Those patients with and without a personal and family history of cancer were compared, and found that a personal history of cancer has a very significant difference in MUTYH PV rate ($9.56e-6$) while family history of cancer does not have a significant difference (0.496). In the patients with a MUTYH PV and a diagnosis of cancer, 31 (88.57%) had a breast cancer diagnosis and only 1 (2.86%) had a colorectal cancer diagnosis - 73.81% and 2.38% of all MUTYH carriers. Of the 32 patients who had information about their family cancer diagnoses, there were 27 patients with multiple diagnoses and only 5 with a single family diagnosis, with 116 total family members with reported diagnosis. There were 44 breast cancer diagnoses in 23 of the MUTYH PV carriers' families, which is 71.88% of all patients with family cancer information and 54.76% of all MUTYH PV carriers. There were 6 colorectal cancer diagnoses in 6 of the MUTYH PV carriers' families, which is 18.75% of all patients with family cancer information and 14.29% of all MUTYH PV carriers.

Conclusions:

Our findings match with other reported cancer cohorts (on the order of 1-2%, Thompson et al). Monoallelic MUTYH has a significant association with both personal history of cancer. These findings suggest that patients with a personal and or family history of cancer should consider expanded gene panel testing which includes MUTYH.

Requested Data 7/13 - MUTYH carrier personal and family history of cancer

PHxC Summary Mutation Carriers			
Cancer Dx	Number Dx	% PHxC Subjects	% MUTYH Subjects
Breast	31	88.57%	73.81%
Melanoma	9	25.71%	21.43%
Lung	1	2.86%	2.38%
Thyroid Cancer	1	2.86%	2.38%
basal cell	1	2.86%	2.38%
Colorectal	1	2.86%	2.38%
Total Cancers	44		
Total Patients with MUTYH and Cancer	35		
Total Patients with MUTYH	42		

FHxC Summary Mutation Carriers			
Family Cancer Dx	N Family Members	Rate of subjects with FHx and MUTYH reporting FHxC (#FHxC/#FHxCSubjects)	Rate of subjects with MUTYH reporting FHxC (#FHxC/#Subjects)
Breast (23 unique Subj)	44	2.0952381	1.04761905
Prostate	16	0.76190476	0.38095238
Pancreatic	7	0.33333333	0.16666667
Melanoma	6	0.28571429	0.14285714
Colorectal (6 unique subj)	6	0.28571429	0.14285714
Lung	6	0.28571429	0.14285714
Ovarian/Fallopian/Peritoneal	6	0.28571429	0.14285714

Disclosure(s):

Linda Ann Smith, MD: No financial relationships to disclose

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5:00 PM - 6:15 PM

P5-12-02

Germline variants detected by next-generation sequencing-based multigene panel testing in patients with suspected hereditary breast cancer at a University Hospital in Japan

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Background: The usefulness of prophylactic surgery and surveillance for hereditary breast cancer has been demonstrated, and germline testing for BRCA1 and BRCA2 had been covered by insurance since 2020 in Japan. In addition to BRCA1 and BRCA2, several other genes are also associated with an increased risk of developing breast cancer, such as PALB2, ATM, BARD1, CHEK2, PTEN, and TP53. Next-generation sequencing-enabled multigene panel testing provides information about these gene variants at the same time, and at a low cost. Although germline testing of BRCA1 and BRCA2 has become widespread in Japan, multi-panel gene testing for germline variants has been conducted only in a limited number of facilities, partly due to the difficulty associated with dealing with the gene variant information obtained from the test. The aim of this study was to clarify the current status of multigene panel testing in our institute, and reveal the characteristics of the variants detected in patients with, or predisposed to, hereditary breast cancer. **Methods:** This retrospective study included 37 individuals who underwent next-generation sequencing-based multigene panel testing in order to investigate any inherited genetic variants due to a suspicion of hereditary breast cancer. Eighteen patients had a diagnosis of breast cancer with a family history of breast and/or ovarian cancer, nine patients had a diagnosis of breast cancer without family history of breast or ovarian cancer, and 10 patients had a family history of breast cancer but had not developed breast cancer themselves. **Results:** Utilizing multigene panel testing, at least one alteration was found in 24 genes, and a total of 39 variants were found in the 37 patients. Of these 37 patients, nine (24.3%) had a pathogenic/likely pathogenic variant with or without other variants of uncertain significance (VUS), 15 (40.5%) had VUS, and 13 (35.1%) had negative genetic test results. Among the nine patients with pathogenic/likely pathogenic variants, seven had variants in either BRCA1 or BRCA2 (one BRCA1 pathogenic variant, five BRCA2 pathogenic variants, and one BRCA2 likely pathogenic variant), while the remaining positive results were attributed to other genes (one MLH1 pathogenic variant, and one SDHB pathogenic variant). VUS included BRCA1 and BRCA2, as well as other breast cancer-associated genes, such as ATM (n=2), CDH1 (n=2), NF1 (n=2), PALB2 (n=1), CHEK2 (n=1), NBN (n=1), and RAD51D (n=1). VUS also included other cancer syndrome-related genes, such as MLH1 (n=2), MUTYH (n=2), APC (n=1), and RET (n=1). **Conclusion:** Multigene panel tests in our institute revealed pathogenic/likely pathogenic variants in 24.3% of individuals who suspected hereditary breast

cancer. As expected, multigene panel tests also revealed more VUS than pathogenic variants and 40.5% individuals were detected with VUS, which included many genes associated with hereditary breast cancer and other cancer syndromes, in addition to BRCA1 and BRCA2. Individuals with VUS will need to cope with new information if the interpretation of the variant changes in the future. We need to be aware of the characteristics and limitations of this type of panel testing, and to properly utilize the test results and information obtained for good quality patient care.

Disclosure(s):

Yusa Atake, Medical Doctor: No financial relationships to disclose

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12/8/2022

5:00 PM - 6:15 PM

P5-12-03

Intratumor heterogeneity and intrinsic immune activation are associated with response to chemotherapy in BRCA-related breast cancers

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Background Breast cancers in women with a germline BRCA1/2 mutation (gBRCAm) have homologous recombination deficiency (HRD) and are sensitive to therapies causing double-

strand DNA breaks. In TBCRC 031 (INFORM), both neoadjuvant cisplatin and doxorubicin/cyclophosphamide (“AC”) in gBRCAm carriers resulted in a complete pathologic response in 18% and 26% respectively in patients with newly diagnosed HER2–negative breast cancer. Herein, we describe molecular features from tumor whole exome (WES) and transcriptome sequencing (RNAseq) associated with response. Methods TBCRC 031 (the INFORM Trial - NCT01670500) was a randomized phase II neoadjuvant trial comparing the efficacy of cisplatin versus AC in gBRCAm carriers with stage I-III HER2–negative breast cancer. Of 118 patients enrolled, 92 patients provided fresh frozen research biopsies, collected prior to chemotherapy initiation, which were subjected to WES and RNAseq. Variants were called using GATK best practices and intratumoral heterogeneity was inferred from mutations and variant allele frequencies using Mutant Allele Tumor Heterogeneity (MATH) scores. Mutational Signature 3 (Sig3) and Genomic Instability Score (GIS) were calculated with SigMA and scarHRD, respectively. RNAseq data were utilized to perform differential gene expression and functional analyses, while cellular deconvolution was performed with CIBERSORTx trained against breast cancer single cell data. Patients were grouped according to their residual cancer burden (RCB) as responders (RCB-0 or 1), or non-responders (RCB-2 or 3). P-values ≤ 0.05 were considered statistically significant and when appropriate, adjustment for multiple testing was performed using a false discovery rate $\leq 5\%$. Results Of the 92 patients with gBRCAm, 59 (64%) had triple-negative and 33 (36%) were hormone-receptor positive HER2-negative breast cancer, 40 (43%) were classified as responders and 52 (57%) as non-responders. WES analysis revealed that indices of HRD were high (Sig3 exposure predominant and GIS ≥ 42) across most samples irrespective of receptor status and not significantly different among responders and non-responders. In contrast, responders exhibited lower levels of intratumor heterogeneity than non-responders (median MATH 42.9 vs. 33.5, $p = 0.01$). 223 genes were differentially expressed between responders and non-responders following control for tumor hormone receptor status, BRCA1/2 mutation, and menopausal status. Pathways identified as significantly enriched in upregulated genes were indicative of intrinsic immune activation in responders (e.g., T-cell activation, immune response-signaling, and regulation of leukocyte activation). Cellular deconvolution of the tumor microenvironment confirmed that responders presented a higher proportion of T-cells ($p = 0.025$) and myeloid cells ($p = 0.003$) in the tumor samples, while perivascular-like cells were enriched in non-responders ($p = 0.034$). Conclusion In this analysis of the largest cohort of treatment-naïve gBRCAm breast cancer to date, we found that response to cytotoxic chemotherapy is associated with a transcriptional program of intrinsic immune activation and an increased population of intratumoral T-cells and myeloid cells. Lower levels of intratumor heterogeneity and higher immune activation were associated with response to chemotherapy gBRCAm carriers while HRD scores were not.

Disclosure(s):

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12/8/2022

5:00 PM - 6:15 PM

P5-12-05

Gestation and breast cancer in women with mutations in DNA repair genes: Is there any relationship?

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Introduction: Women carrying mutations in reparative genes frequently ask about the safety of pregnancy or the use of fertility-promoting techniques. The evidence on gestation and breast cancer (BC), specifically in mutated BRCA, provides contradictory results^{1,3}. On the one hand, there are studies that support the protective nature of pregnancy, while others show that gestation is a factor that promotes it¹. Likewise, some point to differences in the association according to the type of mutation, BRCA1 or BRCA2².

Objectives: To prove whether there is a relationship between pregnancy and BC in patients with mutations in DNA repair genes and to establish a solid knowledge base for counseling these patients in clinical practice.

Patients and methods: We conducted an analytical, observational and retrospective study of 259 women with mutations in DNA repair genes, whether they had developed cancer or not, with different gestational histories in the Medical Oncology Service. The genes studied were: BRCA1 and 2, MUTYH, hMSH2,

hMSH6,RAD51C,APC,CHECK2,ATM,PALB2,PTEN,BRIP1,ATM+RAD51D,BRCA1+NTHL1,CDKN2A,TP53,NF1,RAD51D.

Results: The proportion of patients who develop cancer in the pregnant group is 46.9%. pregnant women is 46.9%, compared to 37.3% in nulliparous women ($\chi^2 = 1.839$, $p = 0.171$). We observed that the diagnosis of BC occurred before the age of 40 years in 40% of pregnant women, compared to 30% in nulliparous women. Likewise, we observed that from the third pregnancy onwards, the percentage of women suffering from BC is higher, with a peak in the fourth pregnancy (68.8% vs. 31.3%) ($p = 0.135$) and that 51.3% of women whose first pregnancy was before the age of 30 years developed BC, compared to 38.6% in those whose first pregnancy was at a later age ($X^2 = 4.16$, $p = 0.041$). Finally, we observed that 80% of breast cancers developed after 10 years from the first birth.

Conclusions: Considering our results, we cannot affirm that at present there is an association between gestation and BC in women with mutation in genes involved in DNA repair.

Table: Cross table between cancer (Yes/No) and pregnancy (Yes/No)

		Pregnancy		
		Yes	No	
Breast cancer	Yes	Count	90	25
		%	46.9%	37.3%
	No	Count	102	42
		%	53.1%	62.7%
	Totally	Count	192	67
		%	100%	100%

Disclosure(s):

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12/8/2022

5:00 PM - 6:15 PM

P5-12-06

Comprehensive analysis of DNA damage repair gene germline mutations in Chinese breast cancer patients

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Background: Germline DNA damage repair (DDR) mutations has been associated with increased cancer risk, PARP inhibitor therapeutic opportunity for breast cancer (BC) patients. However, the profile of germline mutations in BC covering comprehensive DDR genes remains unclear.

Methods: A total of 341 women with breast cancer who tested 102 germline related genes (including 50 DDR genes) between April 2021 to May 2022 in Guangdong Provincial People's Hospital were identified. Variants were classified into pathogenic, likely pathogenic, variant of uncertain significance (VUS), likely benign and benign groups according to the ACMG/AMP Standards and Guidelines. We defined pathogenic and likely pathogenic variants as deleterious mutations.

Results: The median age of 341 breast cancer patients was 48 (range, 20-89) at the first diagnosis of BC. A total of 47 patients (13.78%) carried 53 deleterious germline variants in 21 cancer predisposition genes, 16 of which were DDR genes. DDR deleterious mutations were detected in genes including BRCA2 (n=18), BRCA1(n=7), FANCA (n=4), PMS2 (n=4), PALB2(n=2), RECQL4(n=2), PALB2 (n=2), etc. The younger age at diagnosis (less than 40-year-old) were significantly associated with deleterious mutations in DDR pathway(P=0.02). At least one VUS was identified in 238 (69.79%) patients. The top 5 DDR VUS genes were FANCM (n=21), ATM (n=20), RAD54L (n=17), FANCD2 (n=15) and ATR (n=14). Breast or ovarian cancer family history were significantly correlated with VUS germline mutations in DDR pathway(P=0.039). Interesting, we found that patients with pCR efficacy of neoadjuvant therapy were more likely to have VUS mutations in DDR pathway (table 1).

Conclusion: We provided a comprehensive view of germline DDR gene mutations in BC patients and also analyzed the association between clinical characteristics and germline DDR mutation status. DDR mutations are prevalent in Chinese BC patients. Patients with younger and breast or ovarian cancer family history were more likely to carry DDR alterations. Moreover, patients with higher frequency of DDR VUS mutations may benefit from neoadjuvant therapy.

Table 1

Table 1. Clinicopathological characteristics between germline mutation carriers and non-carriers.

Characteristics	DDR pathway genes			DDR pathway genes		
	P/LP mutation non-carriers	P/LP mutation carriers	P-value	VUS mutation non-carriers	VUS mutation carriers	P-value
Age at diagnosis (year)			0.02			0.1166
<=40	2(50.00%)	11(25.58%)		18(30.00%)	37(20.79%)	
40-60	1(25.00%)	32(74.42%)		33(55.00%)	124(69.66%)	
>60	1(25.00%)	0(0.00%)		9(15.00%)	17(9.55%)	
Family history of breast or ovarian cancer			1			0.0398
Yes	0(0.00%)	6(13.95%)		0(0.00%)	14(7.87%)	
No	0(0.00%)	23(53.49%)		31(51.67%)	91(51.12%)	
Efficacy of Neoadjuvant			1			0.3575
pCR	0(0.00%)	4(9.30%)		1(1.67%)	11(6.18%)	
non-pCR	0(0.00%)	2(4.65%)		5(8.33%)	13(7.30%)	

Clinicopathological characteristics between germline mutation carriers and non-carriers

Disclosure(s):

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P5-12-07

Polygenic Risk Score in a cohort of 105 Breast Cancer patients previously tested with a multi gene panel for hereditary cancer.

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AIM: Most patients tested by a 44-gene panel for hereditary cancer (HerediGene), even though they had a strong family history, have a negative result or a finding in a low-risk gene. This creates a question about the risk for these individuals to develop breast cancer. The Polygenic Risk Score is a tool used to identify and calculate the lifetime risk of developing breast cancer and thus we are investigating whether it can be used in our cohort of patients to identify this risk. PATIENTS AND METHODS: Among 111 patients analyzed with a 44-gene hereditary cancer panel, we were able to produce the Polygenic Risk Score for 105 of them. All the patients were diagnosed with breast cancer, and they all had a strong family history. We analyzed the ability of the PRS to identify the risk of the patients in combination with the findings of the 44-gene panel. RESULTS: Overall, 74% of patients with a family history had a negative PRS (with a cut-off of 20%). Among the BRCA positive patients all of them had a positive PRS and among all the high-risk gene positive cases, 70% had a positive PRS. On the other hand, among the low-risk genes and the negative cases 18.5% had a positive PRS. There is a positive correlation between the findings from the NGS panel analysis and the PRS. CONCLUSION: Our analysis shows that PRS is correlated to the findings of the 44-gene NGS panel having the majority of the PRS positive patients carry high risk mutations. In addition to this, in 18.5% of the patients with low-risk findings or negative result from the 44-gene panel, the PRS was positive which can explain the outcome of the patient since breast cancer had developed. This is an indication that the combination of PRS with the findings from the 44-gene panel can identify individuals with a higher risk of developing breast cancer.

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TUMOR PROGRESSION MODEL IN BREAST CANCER WITH BRAIN METASTASIS

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INTRODUCTION: Breast cancer are the main cause of related deaths cancer among women, corresponding to 25% of new cases each year. When diagnosed at early stages, it has an overall five-year survival rate of up to 90%. However, in more advanced stages, survival is reduced to about 24%, with 90% of women in stage IV dying as a result of complications related to metastases. Considering that brain metastasis is an unfavorable prognostic site, and the identification of genetic-molecular profiles in primary tumors and in metastatic sites are a subject poorly described in the literature, we understand that the identification of mutational profiles may contribute to elucidate the genetic-molecular mechanisms associated with tumor progression. **AIM:** The aim of this study was to identify clonal and subclonal driver mutations that lead to evolution of metastatic clones from a breast cancer progression model. **MATERIAL AND METHODS:** For tumor progression model, automated extraction of DNA from buffy coat and paraffin samples of breast tumors and paired brain metastases (n=9) was performed. In the present work, we used a subclonal reconstruction model based on the combination of machine learning and population genetics concepts. This proposal is based on the frequency spectrum of each somatic mutation (SNVs or indels), considering VAF (Variant Allele Frequency - ratio of mapped reads of the mutant allele) in relation to the coverage of variant locus, as known as CCF (Cancer Cell Fraction). CCF is defined as the proportion of neoplastic cells that have a certain set of mutations and then is normalized considering the sample purity and the segments with changes in number of DNA copies (Copy Number Alterations). Then, a statistical model based on finite Dirichlet mixtures with mixed distributions is applied. In this model, Beta components capture clonal expansions and population genetics concepts were applied to mutant alleles in each population considering principles of cancer evolution. Finally, confidence was computed using both parametric and non-parametric bootstraps. The functions for building the model are implemented at <https://caravagnalab.github.io/mobster/>, and for visualization and construction of graphs, packages in R statistical-mathematical environment were used, such as ggplot2, sads, cli, clisymbols, cowplot, crayon, ctree, dndscv, dplyr, magrittr, reshape2, and tidyr. **RESULTS:** With this model was possible to identify the distribution of clones according to somatic alterations in patients with breast cancer and brain metastasis. It was possible to observe common patterns, such as alterations of the SF3B1 gene as a common ancestral clone in both conditions and the frequency of the AKT1 gene in a subclonal condition. Other genes relevant to breast cancer carcinogenesis, such as PIK3CA and TP53, are found in a

different clonal hierarchical pattern between the two conditions. CONCLUSION: This data suggests a model of clonal evolution capable to identify which drivers clones and subclones are involved in the metastatic process.

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P5-13-03

Real-world clinico-genomic data reveal differences in genomic landscape associated with CDK4/6 inhibitors in HR+/HER2- breast cancer

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Purpose: Studies based on data from routine clinical practice (real-world data, RWD) benefit from larger patient numbers and are more representative of patient diversity than clinical trial studies. When combined with comprehensive genomic profiling (CGP), RWD may uncover the impact of therapies and patient characteristics on tumor genomic landscape. Here we aimed at assessing the feasibility of using RWD to identify changes in the prevalence of genomic alterations upon treatment and proposed a methodology to address RWD inherent caveats. Experimental Design: To explore associations between tumor genomics and treatment chosen by physicians, we evaluated data from 5323 patients with metastatic hormone receptor-positive HER2-negative (HR+/HER2-) breast cancers from a nationwide real-world clinico-genomic database, originating from approximately 280 US cancer clinics (~800 sites of care). To perform our comparisons, we defined groups based on the therapy administered in the metastatic setting and the timing of the CGP relative to treatment. We used bootstrapping to estimate the significance of the effect and stratified analyses to assess the impact of potential confounders such as the site of the collected samples or disease history. Results: ESR1 alteration prevalence increased from 5.6% (CI: 2.8-8.9) pre-treatment to 21.4% (CI: 13.3-29.6) following aromatase inhibitor. Yet, it was significantly less than the prevalence following treatments including CDK4/6 inhibitors (CDK4/6i; 37.1% [CI: 27.8-46.4]; P=0.006). Further, exposure to CDK4/6i led to an increase in FGFR1 and TP53 alterations as well as genes of the cell cycle (FDR < 0.2). Overall, we found that more pathways were likely to be altered in a given tumor following AI+CDK4/6i than after AI alone (P=0.02). In particular, alterations of the MAPK pathway were not exclusive to ESR1 alterations in the post-AI+CDK4/6i group compared to AI only, suggesting that MAPK pathway alterations alone may not overcome CDK4/6i-based treatments. Differences following exposure to CDK4/6i were retained in samples taken after the second-line treatment. Stratified analyses confirmed that these results are independent of exposure to adjuvant therapy or treatment duration and showed that ESR1 mutations occurred in both primary and metastatic samples. Conclusions: Analysis of EHR-derived clinical data linked to CGP results from routine care can replicate associations previously observed in clinical trials and uncover unknown changes in tumor genomic landscape. Bootstrapping and stratified analysis reinforced our confidence in the results and thus allowed us to identify that CDK4/6i exposure led to a different – more altered – genomic landscape in HR+/HER2- breast cancer patients. This finding can inform design of clinical trials post-CDK4/6i and may help guide treatment choice for late stage patients. Thus, our work demonstrates the feasibility of leveraging real-world clinico-genomic data for translational research in oncology and leads the way for analyses including a more diverse patient population.

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P5-13-04

Clonal evolution of mammary epithelial cells into breast cancers

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[Introduction] Proliferative lesions in the breast have been implicated in the development of breast cancer. Previous studies showed that some proliferative lesions and adjacent breast cancers shared common genetic alterations, suggesting that these originated from the same ancestral cell. However, the clonal structure of normal epithelia and their clonal history during evolution to cancer are poorly understood. In this study, we analyzed genetic profiles of normal epithelia and proliferative lesions in the cancer-borne breast to illustrate the clonal evolution of cancer from a normal epithelial cell. [Methods] Single cell-derived organoids (n=47) were established from breast milk of 4 healthy women aged 22–36 and normal breast tissue of 15 breast cancer patients aged 29–83 to evaluate somatic mutation rate in normal epithelial cells. Multiple normal lobules and proliferative lesions together with cancer lesions were collected using laser-capture micro-dissection (LCM) from fresh frozen (n=3) or formalin-fixed paraffin-embedded (n=5) surgical specimens in 9 premenopausal breast cancer patients. Somatic mutations and copy number alterations were evaluated using whole-genome sequencing. [Results] The mutation profile of single cell-derived organoids suggests that somatic mutations accumulate in normal mammary epithelial cells at a constant rate of 19.4/genome/year before menopause, and the mutation rate decreases to 6.9/genome/year after menopause. Parity was negatively associated with mutation number (-49.3 per life birth). In total, we analyzed 143 LCM samples, including those from 72 normal lobules, 43 proliferative lesions, and 19 non-invasive and 9 invasive cancer samples. Five cases showed a large expansion of proliferative lesions sharing a substantial number of somatic mutations with cancer. These lesions expanded over a distance of 35-90 mm, sharing tens to hundreds of mutations including those in breast cancer-related driver genes, such as PIK3CA, AKT1, GATA3, CBFB and PTEN, while harboring private mutations or copy number alterations of their own. Of interest, the cancers in 4 out of these 5 cases was luminal-A type invasive ductal carcinoma or ER-positive HER2-negative ductal carcinoma in situ, and characterized in common by the presence of der(1;16), concurrent whole-arm 1q gain and 16q loss, in both cancer and proliferative lesions. Phylogenetic analysis adapted with the mutation rate in normal cells predicted that der(1;16) had been acquired between puberty and early 20's, and the common ancestors of non-cancerous and cancerous lesions emerged by early 30's, >10 years earlier than at the time of cancer diagnosis. By contrast, analysis of non-cancerous lobules unrelated to cancer showed that der(1;16)-negative non-cancer clones that had emerged after puberty stayed within a single lobule or spatially confined to adjacent lobules and rarely expanded to a large area as observed for those carrying der(1;16), even if the clones had acquired mutations in driver genes such as PIK3CA and PIK3R1, which highlighted the role of der(1;16) in wide clonal expansion. [Conclusions] Our results suggest that in some breast cancer cases, particularly in those with der(1;16), a highly recurrent translocation accounting for the major subset of Luminal A breast cancer, the clones with the founder driver alterations expanded macroscopically long before the onset of cancer, in which further clonal evolutions recursively occur multi-focally, giving rise to multiple proliferative lesions and ultimately, invasive cancers. Our findings provide new insight into the early development of breast cancer.

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P5-13-05

Profiling of APOBEC3 dysregulation in breast cancer

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DNA of many breast tumors is barraged by C-to-T/G mutations within TCW (W:T,A). These mutations are attributed to the aberrant expression and activity of APOBEC3 enzymes. They have been shown to account for many driver mutations in genes such as PIK3CA, ERBB2, and PPP2R1A, however their precise source and also their roles in tumor development, evolution, and patient survival are debated. Currently, quantification of APOBEC3 expression changes in tumor cells is confounded by the ubiquitous expression of these enzymes in immune infiltrating cells. In this study, we used a novel quantitative biology approach to determine the expression profiles of APOBEC3 enzymes in breast tumor and tumor microenvironment cells from >1,000 patients. We combined diverse datasets including tumor/matched normal RNAseqs, tumor somatic mutations, cell line RNAseqs and mutations, estimates of tumor purities and immune cell compositions, and expression of purified cell populations to show that in breast cancer there is only a single APOBEC3 dysregulation process. This process is subtype-independent and is represented by APOBEC3B upregulation and extreme APOBEC3C downregulation. Compared to all other tumor types, breast tumors are affected the most by this process.

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Overexpression of somatic mutation in NSDHL promotes breast cancer cell migration and tumor growth

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Background: We had identified somatic mutations of the NAD(P) Dependent Steroid Dehydrogenase-Like (NSDHL) gene from breast tumors of patients with distant metastasis using whole-exome sequencing. This study aimed to investigate the function of NSDHL mutants in breast cancer. Methods: ER-positive and tamoxifen-resistant human breast cancer cell line (ZR75-1) and mouse macrophage cell line (RAW264,7) were used. GFP-tagged NSDHL mutants were generated by subcloning the mutant NDHL into a lentiviral vector yielding an in-frame fusion of 3' to GFP. ZR75-1 cells expressing the GFP-tagged NSDHL mutants were selected by puromycin with subsequent FACS analysis. The following experiments were performed: western blot, immunofluorescence staining, qRT-PCR, CellTiter-Glo assay, cell cycle assay, transwell migration assay, wound healing assay, tumor spheroid formation assay, and total cellular cholesterol measurement. An orthotopic breast tumor mouse model by injection of ZR75.1 cells into mammary gland fat pad was used in vivo. Results: Four novel NSDHL somatic mutations were discovered in the breast tumor tissues of patients. While total cholesterol levels in NSDHL mutant-transduced cells did not significantly increase, they were notably higher in wild-type NSDHL-transduced cells than in parent ZR75-1 cells. When compared to the parent and wild-type NSDHL-transduced cells, there was a minor increase in growth rate and a large increase in migratory capacities in NSDHL mutant-transduced cells ($P < 0.05$). The size of tumor spheroids is significantly larger in NSDHL mutant-transduced cells than in wild-type NSDHL-transduced cells. Both EGFR expression and epithelial to mesenchymal transition (EMT) markers were higher in NSDHL mutant-transduced cells than in parent and wild-type NSDHL-transduced cells. The NSDHL mutant-transduced cells' conditioned media

promoted the migratory ability and M2 polarization of RAW264.7 cells. In an orthotopic xenograft mouse model, NSDHL mutant-transduced cells were shown to promote tumor growth better than parent and wild-type NSDHL-transduced cells, suggesting that somatic mutation of the NSDHL contributes to the malignant progression of breast cancer cells. Conclusion: The present data indicate that breast cancer cells harboring somatic mutants of the NSDHL gene seem to display more aggressive behavior by gaining biological worse phenotype both in vitro and in vivo. More investigation is required into the mechanisms behind the function and accumulation of mutant NSDHL proteins to speed the development of therapies for patients with breast cancer harboring mutant NSDHL.

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Transcriptomic insights into lobular breast cancer biology: a retrospective analysis of the MINDACT clinical trial

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Background: Invasive lobular carcinoma (ILC) represents the second most common subtype of breast cancer after invasive breast cancer of no special type (NST). In this retrospective analysis of the MINDACT trial, we aimed at identifying/refining the transcriptomic differences between: 1) estrogen receptor positive/HER2-negative (ER+/HER2-) ILC versus ER+/HER2-NST, 2) classic and non-classic ER+/HER2- ILC, and, 3) recurring and non-recurring ER+/HER2- ILC in the subgroup of patients with a low clinical and low genomic (cL/gL) risk (as defined by a modified version of Adjuvant Online! and the 70-gene signature). Patients and methods: Central pathology review was performed for histological subtype, grade and Ki67 (G.V.) for 5929/6693 (88.6%) of the patients included in the MINDACT trial (NCT00433589). Analysis of transcriptomic data adjusted for age and grade was performed using the R/Bioconductor package 'limma' to identify differentially expressed genes (DEGs). DEGs having absolute log-fold change (logFC) ≥ 0.2 and FDR-adjusted p-value (q-value) < 0.05 were

considered. Gene set enrichment analyses (GSEA) of MSigDB hallmark gene sets were performed. Adjusted Cox regression models were used to evaluate the association of these hallmarks with disease free survival (DFS) and distant recurrence free survival (DRFS). Results: After central pathological review, 464 patients with ER+/HER2- ILC and 3798 patients with ER+/HER2- NST were identified. Patients with ILC were significantly older at diagnosis, had larger tumors, less axillary nodal involvement, more grade 2 tumors than patients with NST. At the transcriptomic level, we observed a high number of DEGs between these 2 subgroups, confirming their distinct phenotype. CDH1, the gene coding for E-cadherin, was as expected the most highly overexpressed gene in NST versus ILC. We further observed an increased expression of leptin (LEP), leptin receptor (LEPR), lipoprotein lipase (LPL), and the fatty acid transporter CD36 in ILC. This could suggest that ILC relied on increased lipid uptake thanks to the increased contact of ILC tumor cells with the adipocytes. IGF1 was also overexpressed in ILC versus NST, as a potential consequence of high LEP and high LEPR expression. Differences were also evident with regard to the extracellular matrix (ECM), with many collagens, matrix metalloproteinases (MMPs) and other key enzymes (e.g. LOXL1) being differentially expressed. We confirmed a decreased ER-signaling and increased PI3K/Akt signaling in ILC versus NST. Out of the 464 ER+/HER2- ILC tumors, 253 (55%) were classic ILC and 211 (45%) non-classic ILC. There were more grade 3 tumors, more highly proliferative tumors and more nodal involvement in patients with non-classic versus classic ILC. At the transcriptomic level, differences were subtler than the differences seen above. Still, a significant enrichment of the hallmarks related to cell cycle in the non-classic ILC, and of the hallmarks related to epithelial-to-mesenchymal transition, hypoxia, adipogenesis and IL6/JAK/STAT3 signaling in classic ILC was observed. Finally, 216/464 patients with ER+/HER2- ILC (47%) were assigned to the cL/gL risk group and did not receive chemotherapy. 28/216 of these patients (13%) relapsed (DFS, median FU: 8.7 years). Enrichment of hallmarks related to apoptosis, inflammatory response, hypoxia and oncogenic signaling (PI3K/Akt, Ras, c-Myc) was associated with worse survival. Conclusion: This represents, to the best of our knowledge, the largest set of gene expression data for patients with ILC, issued from a clinical trial where histology was reviewed centrally. These results could be used to personalize treatment for patients with ILC. This project is funded by the Breast Cancer Research Foundation.

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Identifying oncogenic enhancer elements in TNBC of the Basal-like subtype using single-cell ATAC-seq and RNA-seq

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Identification of the cis-regulatory elements controlling oncogenic transcriptional programs is critical to understanding tumor biology. To find cis-regulatory elements (i.e. gene enhancers) of oncogenic dependencies in Triple-Negative Breast Cancers (TNBC) of the Basal-like gene expression subtype, we generated matched single-cell transcriptome (scRNA-seq) and chromatin accessibility (scATAC-seq) profiles for two human Basal-like tumors and four normal mammary reduction samples. This unique dataset enabled us to correlate variations in chromatin structure with variations in gene expression revealing putative enhancers that are specifically active within cancer cells, but not within normal mammary ductal epithelial cells. We then leveraged the Cancer Dependency Map (DepMap) portal at the BROAD Institute to infer gene expression dependencies in breast cancer cell lines of the Basal-like molecular subtype. Putative cancer-specific enhancers were prioritized based on the transcriptional dependency of their target gene(s) in Basal-like cell lines as reported by the DepMap portal. Based on our

preliminary analyses, we report several cancer-specific enhancers that drive the expression of important transcription factors such as EN1 and SOX4. These transcription factors are known to have profound effects on tumor biology, especially considering that high expression of EN1 is associated with brain metastasis and SOX4 is known to regulate immune evasion and PI3K/Akt signaling. Moreover, both of these transcription factors portend a worse outcome in TNBC patients. Thus, our analysis suggests that high levels of expression of these transcription factors is sustained specifically within the malignant cell types of these tumors, by the activity of these cancer-specific enhancers that are not typically active in normal epithelial cells. We are now performing CRISPR dCas9-KRAB experiments to epigenetically silence these cancer-specific enhancers and measure the consequences on expression of their predicted target genes. Additionally, we are investigating the trans-acting transcription factors that may physically bind to these enhancers to further regulate oncogenic transcription. By defining the regulatory logic of cancer cells at single-cell resolution, our work highlights the importance of cancer-specific and clinically relevant oncogenic regulatory elements in TNBC of the Basal-like subtype.

Disclosure(s):

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Clonal hematopoiesis of indeterminate potential after (neo)adjuvant chemotherapy versus endocrine therapy for early breast cancer: the CIRCE-eBC prospective cohort study

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Title: Clonal hematopoiesis of indeterminate potential after (neo)adjuvant chemotherapy versus endocrine therapy for early breast cancer: the CIRCE-eBC prospective cohort study
Background: Clonal hematopoiesis of indeterminate potential (CHIP) is an age-related condition associated with higher risk of hematologic malignancies, cardiovascular disease, and all-cause mortality. Patients (pts) with early breast cancer (eBC) receiving chemotherapy (CT) have increased risk of treatment-related myeloid neoplasms (tMN); the benefit of CT in eBC pts is often limited. Little is known about the prevalence and dynamics of CHIP in eBC pts. Methods: We prospectively identified two cohorts of pts with eBC: cohort A – pts receiving (neo)adjuvant CT with or without adjuvant endocrine therapy (ET); cohort B – pts receiving ET only. Blood was collected prior to initiation of treatment (T1) and after either (neo)adjuvant CT or 6-18 months of adjuvant ET (T2). We performed targeted sequencing of cryopreserved peripheral blood mononuclear cell (PBMC)-derived genomic DNA and defined CHIP as the presence of ≥ 1 pathogenic somatic mutation at variant allele fraction (VAF) ≥ 0.02 . In additional analyses we used VAF ≥ 0.005 . Results: We enrolled 118 and 116 pts in cohorts A and B, respectively. Pts in cohort A were younger (median age 51 vs 57, $p < 0.001$), less frequently Caucasian (83.9 vs 96.6%; $p = 0.005$) and former/current smokers (28.0 vs 43.1%, $p = 0.038$). All pts in cohort B had hormone receptor-positive (HR+) eBC; in cohort A 50% of pts had HR+/HER2-, 16% had HR+/HER2+, 8.5% had HR-/HER2+ and 25.4% had HR-/HER2- eBC ($p < 0.001$). Pts in cohort A had higher stage (stage II-III 68.7 vs 27.6%; $p < 0.001$) and grade (grade 3 65.3 vs 15.5%; $p < 0.001$) tumors. Genetic testing was more frequently performed in pts receiving CT (88.1 vs 68.1%, $p < 0.001$), though the rate of germline pathogenic variants was similar (13.5 vs 17.7%, $p = 0.079$). In cohort A, 38% received anthracyclines, 7% platinum and 57%

anthracycline/platinum-sparing CT. Median time between T1 and T2 was 189.5 (150,406) and 280 (147, 425) days in cohort A and B ($p < 0.001$). The prevalence of CHIP, defined by mutations at $VAF \geq 0.02$, was similar at T1 in cohort A (14.4%) vs B (18.1%) ($p = 0.556$). Number of pts with new CHIP variants at T2 was also similar (A 3.4% vs B 6.0%) ($p = 0.373$). After adjusting for age and stage, odds ratio (OR) of developing new CHIP variants in cohort B vs A was 1.28 (95% CI 0.32 – 5.68, $p = 0.733$). Age correlated with baseline prevalence of CHIP ($p < 0.001$). Most frequent new CHIP variants at T2 in cohort A were DNMT3A (3), PPM1D (1), NF1 (1). To investigate whether pts receiving CT were more likely to have emergence of small hematopoietic clones, we assessed pathogenic variants present at $VAF \geq 0.005$. These were detected at T1 in 55 (46.6%) and 61 (52.6%) pts in cohort A and B, respectively. Few pts without pathogenic variants at T1 developed them at T2 (3 pts in cohort A and 4 in cohort B). 21 pts (27 variants) in cohort A and 11 pts (12 variants) in cohort B had new variants at T2. Pts with new variants vs not (32 vs 202 pts) had similar characteristics, excepting age (median 60.5 vs 54.0, $p = 0.011$). After correcting for age and stage, OR of developing new pathogenic variants given ET vs CT was 0.25 (95% CI 0.10-0.62, $p = 0.003$). Most frequent newly detected variants were in DNMT3A (14), PPM1D (5), TET2 (4) and TP53 (2) in cohort A; DNMT3A (3), TET2 (3) and ZNF318 (2) in cohort B. Conclusions: In the CIRCE-eBC study, CT administration did not lead to emergence of CHIP over a 6-9 month period vs ET alone. This finding is reassuring in the setting of long life-expectancy for eBC pts and the association of CHIP with significant morbidity and mortality. However, consistent with known risk of development of MN, CT was associated with emergence of low frequency pathogenic variants in PPM1D and TP53, which have been associated with elevated risk of tMN. The evolution and prognostic role of these small clones is unclear and warrants additional investigation.

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Genomic characterization of hormone receptor-positive advanced breast cancer with high tumor mutational burden: fresh-frozen tissue genomic analysis from MUTATION-1 study (KCSG BR17-04)

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Background The hormone receptor (HR)-positive metastatic breast cancer (MBC) patients show a diverse range of tumor mutational burden (TMB), but its biological and clinical implication has been largely unrevealed. Here we report genomic landscape of 117 HR+ MBC patients who were included in the pre-screening tissue genomic analysis of MUTATION-1 study (SABCS 2021; Abs P1-19-03) according to TMB of tumors. **Patients and method** The MUTATION-1 study (NCT03608865) enrolled HR-positive MBC patients who received prior ≥ 1 line of systemic therapy, and performed prescreening with whole exome sequencing (WES) and RNA-seq of fresh-frozen tissue of metastatic or recurred tumors. Patients who met upper 30% of TMB were eligible for treatment phase and received durvalumab plus tremelimumab. This study analyzed 117 prescreening tissues of MUTATION-1 study patients for mutation and transcriptomic landscape analysis. (WES, n=117; RNA-seq, n=107) **Results** The 117 patients showed diverse TMB (range 0~21.7 mut/Mb, median 2.0 mut/Mb) and genomic alterations. The most frequently mutated gene included PIK3CA (29.1%), TP53 (27.4%), ESR1 (23.9%), GATA3 (19.7%), and MAP3K1 (12.0%). There was no association between patient survival and TMB. We estimated single base substitution (SBS) mutational signature of patients with SigMA algorithm. The patients were classified according to their dominant mutational signatures: APOBEC (25.6%), HRD (41.0%), clockwise (28.2%), SBS8, and SBS17. The APOBEC patients showed higher TMB (median 3.47 mut/Mb) and higher mutation prevalence in PIK3CA (63.3% vs. 29.1%), ARID1A (16.7% vs. 6.0%), and NF1 (16.7% vs. 6.8%) compared with other patients. The high TMB positively correlated with time from MBC diagnosis to biopsy. Tumors with TMB ≥ 5 mut/Mb were exclusively found in patients diagnosed as MBC ≥ 36 months before the timing of biopsy. In the matched RNA-seq analysis, TMB was higher in luminal B and HER2-enriched intrinsic subtype patients than basal or luminal A subtype. The high TMB (≥ 3.16 mut/Mb, cutoff used for treatment phase patient selection) patients showed upregulation of G2/M checkpoint, MYC, E2F1, and MTORC1 signature compared to low TMB patients. In the tumor microenvironment analysis by CIBESORT, PIK3CA mutant patients showed lower score of cytotoxic T cell than others. **Conclusions** The high TMB in HR+ breast cancer was associated with longer time duration from MBC diagnosis to biopsy, high APOBEC signature, and cell cycle/MYC signature gene upregulation. Further therapeutic targeting of high TMB patients is warranted based on their genomic and immunologic characteristics.

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Tumor Genomic Landscape in Older Women with Metastatic Breast Cancer (MBC)

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Background. Patients (pts) who develop MBC at older ages are underrepresented in clinical trials, are less likely to be included in comprehensive biomarker characterization studies, and experience worse breast cancer-specific survival than their younger counterparts. Elucidating genomic underpinnings of MBC and possible therapeutic targets for older breast cancer patients are critical priorities. Methods. We identified pts age >70 years at MBC diagnosis and a younger cohort (ages 50-69; age < 50), who were treated for MBC at a single center and who had their metastatic (or if not available, the primary) tumor, assessed by a targeted, tumor-only next generation sequencing (NGS) platform (OncoPanel) between 2013-2020. The NGS panel included mutations, copy number variation, tumor mutational burden (TMB), and hypermutation (HM) status, with mutations classified as oncogenic using the OncoKB tool and additional annotation. Copy number events were selected as being "oncogenic" if a high amplification was called for an oncogene or a deep deletion for a tumor suppressor. We compared findings for older (age >70) vs. younger (age < 50 and ages 50-69) MBC pts using Chi-Square and Kruskal-Wallis tests. To determine genomic event enrichment, logistic regression (LR) models were used, controlling for age (continuous), background rate, and tumor subtype (those with unknown subtype [n=27] were excluded from models). False discovery rate (FDR) was used to correct for multiple hypothesis testing. Results. The final analytic cohort included 2,380 pts. The

median age at MBC diagnosis was 54.1 years overall (range 18.5- 91.9) and 73.6 years for those age >70. A total of 137 metastatic and 76 primary tumors were sequenced in pts age >70; in those age < 70, 1383 metastatic and 784 primary tumors were sequenced (for age < 50 [n=857] and 50-69 [n=1310]). Older pts were more likely to present with HR+/HER2- tumors (70.9% v. 62.4% v. 52.4%), and less likely to present with HER2+ (9.4% v. 14.4% v. 22.8%) or triple-negative breast cancer (TNBC) (18.8% v. 21.9% vs. 24.0%) at MBC diagnosis (listed >70, 50-69, < 50; P=1e-7). Older pts had higher average TMB vs. younger pts (9.57 in pts > 70, 8.56 in ages 50-69, 7.34 in ages < 50; P=3.5e-5). This was due to older pts having a higher incidence of hypermutation status as defined as TMB >10: 26.3% in age >70, 23.2% in ages 50-69, 16.8% in age < 50. Using q=0.1 as the threshold of significance, the presence of CDH1, PIK3CA, MAP3K1, TET2, and AKT oncogenic mutations were also enriched in older pts, while the presence of oncogenic GATA3, BRCA2, and TP53 mutations, as well as any mutation in BRCA1 were enriched in younger pts (too few oncogenic BRCA1 mutations were present for accurate modeling). The frequency of oncogenic PIK3CA mutations in HR+/HER2- tumors was highest in the oldest pts (44.4% in pts age >70 v. 31.6% in age 50-69 v. 26.7% in age < 50). Of pts who had oncogenic BRCA1/2 mutations identified on tumor-only NGS testing and underwent clinical germline testing (n=7 v. 60 v. 67, oldest to youngest), older pts had the lowest incidence of germline BRCA pathogenic variants (14.3% vs. 47.2% vs. 67.2%; p=0.01); most BRCA mutations identified on NGS testing in older patients were considered likely somatic. When assessing enrichment in copy number events, ERBB2, RAD21, and BRIP1 amplifications were all significantly less frequent in older pts (q< 0.1), even when accounting for tumor subtype. Conclusions. In a large cohort of pts with MBC, the mutational and copy number landscape for older pts differs from that in younger pts, even after controlling for tumor subtype. Key actionable findings include a higher proportion of high TMB and PIK3CA-mutated tumors, emphasizing the importance of genomic profile testing in this pt population and further exploration of efficacy and tolerability of relevant therapies in those age >70 years.

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12/8/2022

5:00 PM - 6:15 PM

P5-14-07

Somatic mutations of ER and HER2 subtypes exhibit divergent evolutionary trajectories determined by selective epistasis revealed in phylogenetic reconstruction and stage-specific analyses

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Estrogen-receptor positive (ER+) and human epidermal growth factor receptor positive (HER2+) subtypes of breast cancers feature distinct histopathologies and prognoses. Their molecular profiles inform subtype-specific treatment combinations and possible therapeutic targets. However, the evolutionary trajectory of somatic mutations within each subtype has not been characterized, despite its utility in prioritizing drug development and therapeutic approaches. Quantifying the selective effects of somatic mutations on cancer conveys the likely efficacy of extant targeted therapies between subtypes. Furthermore, knowledge of epistatic interactions involving targetable mutations enables precision therapy at any stage of tumorigenesis. The strength of these interactions differ between receptor subtypes, mediated by differences in the adaptive landscape of each subtype. To investigate differences in subtype etiologies, we quantified selection on single-nucleotide mutations within ER and HER2 receptor subtypes using an aggregated multi-institutional cohort of tumor samples. We observed differential selection acting on mutations: PIK3CA H1047R is a strongly selected variant for which selection varied significantly based on the receptor subtype, experiencing maximal selection in ER+ HER2- breast cancer. On a stage-specific basis, we show that adaptive landscapes change, altering optimal timings for treatment. We then infer epistasis by 1) stage-specific analysis that suggests likely orderings of mutations, 2) calculation of pairwise selective epistasis amongst mutations, which lends mechanistic explanations to these orderings, and 3) phylogenetic reconstruction of the evolution of ten breast cancers, revealing common orderings that further support inferred selective epistatic interactions. Our estimates of differential and stage-specific selection and epistasis between subtypes suggest distinct adaptive landscapes for breast cancer subtypes. These estimates should inform the development of targeted therapeutics and guide treatment schedules based on molecular profiling of the cancer.

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P5-14-08

Machine learning based histopathology images analysis reveals cancer stemness in TNBC patient with 17p loss

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Background: The area of computational pathology has made huge progresses due to advances in artificial intelligence (AI) and machine learning technologies. It has been applied to many research and translational tasks which provide great improvement on medical diagnosis and treatment. Cancer stem-like cells (CSC) have been consistently reported for its key role in Triple negative breast cancer (TNBC) . Given the large amount of existing H&E stained histological slides of TNBC, digital identification of CSC could benefit the evaluation of tumor status and prediction of patients' response to chemotherapy. Here we proposed an AI framework based on Convolutional Neural Network (CNN) to predict CSC from the histological images of TNBC patient. And our preliminary work suggested that chromosome 17p loss, a common genetic variations in breast cancer, is linked to cancer stemness. **Methods:** A modified GoogleNet model was adopted as our CNN classifier. Consecutive breast cancer tissue microarrays (TMA), which stained with H&E ,SOX2, OCT4 and NANOG antibodies respectively by IHC, were used as training dataset for the CNN model. Gene expression data from the TCGA and METABRIC datasets were used to identify gene signatures associated with CSC. The connectivity map (CMAP) and Cancer Cell Line Encyclopedia (CCLE) were used for screening compounds that target stemness in cancer cell lines with chromosomal 17p loss. HS578T and EO771 cells with or without heterozygous 17p loss (11b in EO771) were used for in vitro experiments. Female immunodeficient nude (Nu/J) mice were used for animal studies. **Results:** The well trained GoogleNet model was applied to TNBC patient diagnosis images in TCGA BRCA dataset. By analyzing patient genomic alteration on chromosomal level, we found that loss of chromosome 17p associate with high cancer stemness in TNBC. Flow cytometry assays also demonstrated higher ALDH1 activity and higher CD44+/CD24-/low cell population in HS578T cells with 17p loss. RNA-seq of HS578T cells revealed that most CSC marker genes were located in the unregulated differentially expressed genes (DEGs) of 17p loss cells. We next compared the cytotoxicity of chemotherapy drugs including doxorubicin, paclitaxel, docetaxel and cisplatin on 17p loss and 17p intact HS578T cells, 11b loss and 11b intact

EO771 cells, in terms of IC50 value. The IC50 value of indicated drug on 17p loss HS578T cells with were 3-6 fold higher than their IC50 on 17p intact HS578T cells. Similar result was observed in EO771 cells. Next, 17p loss and 17p intact HS578T cells were orthotopically implanted into the Nu/J mice. Under the doxorubicin treatment, mice bearing 17p loss HS578T derived tumors had larger and heavier tumors in compare to mice bearing 17p intact tumors. Next, we did a computational drug screening to identify compounds that can target the cancer stemness in 17p loss cells. Screened out compounds were tested for their cytotoxicity on 17p loss and 17p intact HS578T cells and FK866 showed the most pronounced efficacy on inhibiting the viability of 17p loss cells, compared to 17p intact cells. Followup experiments demonstrated that FK866 can decrease the CSC features induced by doxorubicin, both in vitro and in vivo. FK866 also potentiates the effect of doxorubicin on treating TNBC cells with 17p loss, which provide a drug combination potential for TNBC patient with 17p loss. Conclusions: A CNN based model was developed to identify CSC from TNBC histopathology images. The images analysis combined with patient genomic data revealed that chromosome 17p loss associated with cancer stemness in TNBC. This result was confirmed using assays on TNBC cells with or without 17p loss. A computational drug screening was performed to identify candidates that targeting stemness in 17p loss cells. FK866 was identified and it potentiates the anti-tumor effect of doxorubicin on treating TNBC cells with 17p loss. Our study provides a novel strategy on applying AI to precision treatment for cancers.

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Comparison of cell-free DNA genomics of breast cancer associated-chest wall disease vs. age & subtype matched controls with metastatic breast cancer not involving the chest wall

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Background: Breast cancer associated-chest wall disease (CWD) clinically behaves in an aggressive manner. However, little is known about the genomics of CWD. Cell-free DNA (cfDNA) can identify oncogenic mutations in metastatic breast cancer (MBC). We hypothesized

that the cfDNA genomics of CWD may vary from MBC cases without CWD. We compared the cfDNA genomics of patients with CWD to that of age and subtype matched MBC controls without CWD.

Methods: Patients with MBC at an academic institution who underwent cfDNA testing (Guardant360, next generation sequencing (NGS), 74 gene assay) from 2/2016-2/2021 were identified. Patients with documented CWD (chest wall recurrence with nodules, ulceration, and/or skin metastases on imaging and/or examination) at the time of cfDNA testing (coinciding with MBC diagnosis) were included in the CWD cohort. Age and subtype matched MBC controls without CWD (CON) during the same time period with cfDNA results at MBC diagnosis were identified. A retrospective review was conducted to determine clinical features and cfDNA genomics of CWD and CON. A two-sample test of proportions was used to compare CWD to CON, with $p < 0.05$ for statistical significance.

Results:

Thirty-one patients with CWD and 63 CON were identified. Both groups were well-matched in median age at MBC diagnosis (CWD 57 vs. CON 59 years, $p=0.93$) and subtype distribution (CWD: TNBC 35%, HR+/HER2- 58%, HER2+ 6%; CON: TNBC 29%, HR+/HER2- 65%, HER2+ 6%, $p=0.78$). Patients also had similar racial distribution in both cohorts ($p=0.57$).

Ninety percent (28/31) of CWD vs. 90% (57/63) of CON had ≥ 1 mutation detectable in cfDNA ($p=0.62$). Median number of cfDNA mutations for CWD was 4.5 (range 0-16) vs. 4 (range 0-21) in CON ($p=0.32$). The most common cfDNA mutations in CWD were TP53 (58%), NOTCH1 (19%), PIK3CA (16%), BRCA1 (13%), NF1 (13%), FGFR2 (13%), ESR1 (13%), STK11 (10%), NTRK1 (10%), APC (10%), and KIT (10%). In comparison, the most common cfDNA mutations in CON were TP53 (54%), PIK3CA (35%), ESR1 (14%), GATA3 (13%), and ATM (11%). Table 1 depicts mutations that varied between CWD and CON which were statistically significant in ≥ 1 cohort analyzed. In HR+/HER2- MBC, NOTCH1, STK11, NTRK1, DDR2, and NF1 were significantly more common in CWD than CON. For TNBC, NOTCH1 was numerically more common in CWD vs. CON ($p=0.06$).

Conclusions: The cfDNA genomic spectrum of CWD varies from MBC that does not infiltrate the chest wall. Mutations that are associated with metastasis (NOTCH1), inhibition of tumor suppression (STK11), tumor migration (DDR2), proliferation (NTRK1), and endocrine resistance (NF1) were significantly more common in HR+/HER2- CWD than matched controls. Further research is needed to validate these findings and determine the impact of matched targeted therapies for CWD.

Table 1

Mutation	Entire cohort CWD (n=31) vs CON (n=63)	TNBC: CWD (n=11) vs CON (n=18)	HR+/HER2- CWD (n=18) vs CON (n=41)	HER2+ CWD (n=2) vs CON (n=4)
<i>NOTCH1</i>	19% vs 3%, p=0.0056	18% vs 0%, p=0.06	22% vs. 4.8%, p=0.03	N/A
<i>STK11</i>	9.6% vs. 0%, p=0.009	N/A	17% vs. 0%, p=0.004	N/A
<i>CCNE1</i>	6.4% vs. 0%, p=0.035	9% vs. 0%, p=0.19	0.06% vs 0%, p=0.1	N/A
<i>NTRK1</i>	9.6% vs 1.5%, p=0.056	0% vs 0.06%, p=0.43	17% vs 0%, p=0.004	N/A
<i>DDR2</i>	6% vs. 1.6%, p=0.18	0% vs. 0.06%, p=0.43	11% vs. 0%, p=0.02	N/A
<i>NFI</i>	13% vs. 4.7%, p=0.13	0% vs 0.06%, p=0.43	22% vs. 2%, p=0.0068	0% vs. 25%, p=0.44

N/A: mutation not observed

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P5-14-10

**Targetable alterations and genomic signatures within breast cancer brain metastases:
Data from comprehensive genomic profiling of 761 breast cancer brain metastases**

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Background: Breast cancer brain metastasis (BCBM) represents an area of unmet clinical need. We previously demonstrated the genomic differences between primary BC and BCBM. In this study we examined the genomic differences between BCBM by BC subtypes and the potential actionable targets that might be taken forward for each subtype in clinical trials. Material and Methods: A total of 761 BCBMs were analyzed by comprehensive genomic profiling (CGP) for alterations in up to 395 genes (Foundation Medicine, USA). The samples were classified by immunohistochemistry (IHC) of the BCBM to ER+ (ER+/HER2-, ER+/HER2+), ER-/HER2+ and ER-/HER2-. Homologous recombination deficiency (HRD-gLOH; cutoff 16%), tumour mutational burden (TMB; cutoff 10 mutations/Mb), microsatellite instability (MSI) and PD-L1 prevalence and expression by IHC using the VENTANA SP142 assay (Immune Cell Score [IC] cutoff 1%) were also investigated. Results: For all BC subtypes the most enriched gene alterations in BCBM (>20% prevalence)

were: TP53, MYC and PIK3CA. ESR1 and ERBB2 were more prevalent in ER+ and HER2+ tumours respectively, with ESR1 alterations significantly enriched in ER+/HER2- BCBMs ($p < 0.0001$). Frequently altered genes by BCBM subtype were: ER+/HER2-: CDH1 (8%) and BRCA2 (7%); ER+/HER2+: PIK3C2B (11%), MDM4 (11%), TBX3 (9%) and AKT2 (8%); ER-/HER2+: LYN (9%). Significantly enriched genes ($p < 0.01$) by BCBM subtype were: HER2+: CDK12 (15%); ER-/HER2-: BRCA1 (14%), CCND3 (9%), VEGFA, JAK2 (8% each) and the immune checkpoint inhibition (ICPI) biomarkers PDCD1LG2 (PDL2), CD274 (PDL1) (7% each). HRD-gLOH was high in ER+/HER2-: (43%) and ER-/HER2-: (70%). TMB and MSI were present in 10%-21% and 1-3% of BCBM respectively, whereas PDL1 protein expression by subtypes was: ER+/HER2- 23%, ER+/HER2+ 27%, ER-/HER2+ 57% , ER-/HER2- 48%. Table 1 summarizes the proportion of BCBMs with actionable alterations and selected clinical trials in BCBM.

Conclusion:

Clinically-relevant genomic alterations were identified across all BCBM subtypes. High HRD-gLOH, TMB and MSI were observed across all the BCBMs subtypes whereas PDL1/PDL2 alterations were a distinctive feature of ER-/HER2- BCBM. These data highlight the need to assess the genomic landscape of BCBM to enable rational treatment decisions with targeted agents, as well as to enable enrichment of relevant populations within clinical trials.

Table 1. Selected studies with targeted therapy and/or immunotherapy in breast cancer brain metastases.

Altered Gene / Pathway	Targeted Therapy	Phase	ClinicalTrials.gov Identifier	ER+/HER2- BCBM	ER+/HER2+ BCBM	ER-/HER2+ BCBM	ER-/HER2- BCBM
ERBB2/HER2 alterations	Tucatinib, T-DM1	Phase 3	NCT03975647	2.83%	100%	100%	2.01%
	Pertuzumab, Trastuzumab	Phase 2	NCT02536339				
	Afatinib, T-DM1	Phase 2	NCT04158947				
	Cabozantinib, Trastuzumab	Phase 2	NCT02260531				
	GDC-0084, Trastuzumab	Phase 2	NCT03765983				
	Everolimus, Vinorelbine, Trastuzumab	Phase 2	NCT01305941				
	Pyrotinib, Vinorelbine	Phase 2	NCT03933982				
	G8R1005, Trastuzumab, 18F-FLT	Phase 2	NCT01480583				
	Neratinib, Capecitabine, T-DM1	Phase 2	NCT03494662				
	Afatinib, Vinorelbine	Phase 2	NCT03441596				
	Tucatinib, Capecitabine, Trastuzumab	Phase 2	NCT02614794				
	Trastuzumab deruxtecan	Phase 2	NCT04420598				
	68GaNOTA-Anti-HER2 VHR11	Phase 2	NCT03331601				
Afatinib, Targeted radiotherapy	Phase 1/2	NCT02768337					
PIK3CA mutations	GDC-0084	Phase 1	NCT04192981	38.21%	24.24%	36.47%	23.49%
	GDC-0084, Abemaciclib, Ertrectinib	Phase 2	NCT03994796				
	Buparlisib, Capecitabine, Trastuzumab	Phase 2	NCT02000882				
BRAC1/2 mutations	Veliparib, Cisplatin	Phase 2	NCT02595905	5.19%/7.55%	ND	2.35%/2.35%	14.43%/6.04%
	Olaparib,	Phase 3	NCT02032823				
	Olaparib, Durvalumab	Phase 1/2	NCT04711824				
PDL1	Pembrolizumab, Anti-HER2/3 Dendritic Cell Vaccine	Phase 0	NCT04348747	ND	1.52%	ND	7.72%
	Nivolumab, Stereotactic radiotherapy	Phase 1	NCT03807765				
PDL1/TMB	Atezolizumab, Trastuzumab, Vinorelbine	Phase 2	NCT04759248	11.40%	9.68%	21.33%	17.41%
TP53+multiple gene mutations	Fluorouracil, Docetaxel, Etoposide, Irinotecan, Mitomycin, Vinorelbine	Phase 1	NCT02576665	43.87%	54.55%	78.82%	90.60%
VEGFA	Bevacizumab, Etoposide, Cisplatin, Whole Brain Radiotherapy	Phase 2	NCT02185352	ND	1.52%	3.53%	8.05%

The percentage (%) of actionable alterations by ER and HER2 status is summarized. ND: Not Detectable.

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5:00 PM - 6:15 PM

P5-14-11

Rearrangements in CDH1, ESR1, and ERBB2 are commonly observed in breast cancer and may influence diagnosis and treatment

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Background The status of CDH1, ERBB2, and ESR1 is important for the diagnostic and treatment workup for patients with breast cancer. Most alterations in these genes occur in the form of short variants (eg missense and indel alterations) or copy number alterations (eg amplifications of ERBB2 or deletions in CDH1). The prevalence and characteristics of rearrangement events have been understudied. **Materials and Methods:** Comprehensive genomic profiling using a hybrid-capture based approach was performed on 44,842 breast carcinomas during the course of routine clinical care (FoundationOne® or FoundationOne®CDx) examining all classes of alterations in up to 395 genes, including CDH1, ESR1, and ERBB2. All rearrangements were included in the analysis (known/likely pathogenic and variants of uncertain significance). Estrogen receptor status was extracted from pathology reports for a subset of samples. **Results:** Rearrangements in CDH1, ESR1, and ERBB2 were observed in 0.26% (115/44842), 0.34% (153/44842), and 1.33% (598/44842) of breast cancer samples, respectively. As expected, CDH1 rearrangements were most common in invasive lobular carcinoma (ILC) (0.64%; 16/2516) though events were observed in samples originally submitted as invasive ductal carcinoma (IDC) (0.16%; 26/15,836), suggesting possible misdiagnosis. CDH1 rearrangements were predominantly loss of function consisting of large deletions, inversions, and truncation events. ESR1 rearrangements were observed at the highest frequency in ER+/HER2- tumors (0.58%) and were never seen in ER-/HER2- and ER-/HER2+ tumors. ESR1 rearrangements were observed with a variety of partners, with recurrent events with CCDC170, SYNE1, RMND1, PLEKHG1, ARMT1, MTHFD1L, and ZBTB2. Consistent with a possible role in therapy resistance, ESR1 rearrangements were enriched in metastatic samples relative to those biopsied from the breast (OR = 2.25; p = 8E-05). ERBB2 rearrangement events were commonly observed in HER2 amplified tumors (13.4%) and rarely in other subtypes (0.12% in ER+/HER2- and 0.28% in ER-/HER2-). Most of the events were intra-chromosomal and typically represented non-fusion duplication fragments that may have generated the ERBB2 amplification. Fusions were much rarer. Out of the 598 rearrangement events, only 18 were predicted to create in-frame and in-strand fusion products retaining the HER2 kinase domain following manual review of the events. Most fusion events were unique,

though a fusion with IKZF3 was seen recurrently (n=2). Conclusions Rearrangement events in diagnostically important breast cancer genes (CDH1, ESR1, and ERBB2) were commonly observed in breast cancer with subtype-specific enrichment. Since these alterations have implications in disease diagnosis and therapy response (eg endocrine therapy resistance), comprehensive genomic profiling can provide value in breast cancer care.

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5:00 PM - 6:15 PM

P5-14-12

ESR1-alterations in HR+HER2- breast cancer patients

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Introduction/Background

Endocrine therapy remains the fundamental treatment for advanced HR+ breast cancer (BC). For those patients who become refractory to endocrine therapy, resistance may be associated with mutations, amplifications, and fusions in the ESR1-encoded estrogen receptor. Here we examine the frequency of ESR1 alterations and the associated genomic landscape.

Methods

HR+/HER2- BC samples were sequenced with the Oncomap™ ExTra assay, which uses whole-exome DNA sequencing with germline subtraction to detect somatic single nucleotide substitutions, indels, and copy number alterations (CNAs), and uses RNA sequencing to detect gene fusions. Tumor mutational burden (TMB) and microsatellite instability (MSI) are also reported. For analysis, BC samples were grouped by site: local (primary breast or regional lymph node) versus metastatic. Prior treatment history was unknown. Testing for a possible association between ESR1 and other biomarkers (genes, MSI, and TMB) was done using Fisher's Exact Test ($p \leq 0.05$).

Results

A total of 988 HR+/HER2- breast cancer patient samples were included in the analysis. Of these, 821 (83.1%) were local samples and the remaining 167 were metastatic samples, with liver (63, 37.7%), bone (20, 12.0%), skin (16, 9.6%) and chest wall (15, 9.0%) being the most common locations. ESR1 alterations were present in 84 tumor samples, 37 local and 47 metastatic, representing 4.5% and 28.1% of samples, respectively. ESR1 alterations included missense mutations (54 samples), fusions (29 samples), and amplifications (8 samples). The most common missense mutations were Y537S (20 samples, 37.0%), D538Q (20 samples, 37.0%), and E380Q (6 samples, 11.1%), which were located in the ligand binding domain and included both clonal and subclonal events. There were 30 ESR1 fusions identified, 17 (2.1%) in local and 13 in metastatic (7.7%) samples. Most fusions (24 samples, 82.8%) involved the same partner, CCDC170, while the other 6 fusions had unique partners. Examination of the 143 other biomarkers altered among ESR1-altered samples revealed 15 genes and MSI-high status that appeared to be over-represented (Table 1). However, none of the associations were statistically significant after correcting for multiple comparisons. Further, there was no evidence that the prevalence of ERBB2, TP53, AKT1 and PIK3CA alterations differed by ESR1 status (Table 1).

Conclusions

ESR1 alterations were significantly more common in HR+/HER2- metastatic breast cancer samples compared to local samples. Comprehensive genomic profiling with RNA sequencing identified both common and rare ESR1 fusions, which were most frequent in the metastatic samples. No significant difference in the molecular profile of ESR1 altered vs ESR1 wildtype samples was found in this cohort. Clinical trials with novel selective ER degraders (SERDs) to target these ESR1 alterations are ongoing.

Table 1. Biomarkers that showed the highest association with ESR1 and other notable breast cancer biomarkers.

Co-mutated biomarker	ESR1 alteration (N=84)	No ESR1 mutation (N=904)
<i>FGF19</i>	18 (21.4%)	101 (11.2%)
<i>FGF3</i>	16 (19.0%)	82 (9.1%)
<i>FGF4</i>	16 (19.0%)	79 (8.7%)
<i>CTTN</i>	7 (8.3%)	24 (2.7%)
<i>FADD</i>	4 (4.8%)	13 (1.4%)
<i>CDKN2A</i>	4 (4.8%)	12 (1.3%)
<i>TUBB3</i>	4 (4.8%)	12 (1.3%)
<i>AR</i>	3 (3.6%)	7 (0.8%)
<i>SMAD4</i>	3 (3.6%)	5 (0.6%)
<i>PMS2</i>	3 (3.6%)	2 (0.2%)
<i>MLH1</i>	2 (2.4%)	2 (0.2%)
<i>AURKA</i>	2 (2.4%)	1 (0.1%)
<i>KDM5A</i>	2 (2.4%)	1 (0.1%)
<i>MSH6</i>	3 (3.6%)	0 (0.0%)
MSI-high	2 (2.4%)	1 (0.1%)
<i>AKAP9</i>	2 (2.4%)	0 (0.0%)
<i>TP53</i>	26 (31.0%)	217 (24.0%)
<i>PIK3CA</i>	35 (41.7%)	416 (46.0%)
<i>AKT1</i>	4 (4.8%)	48 (5.3%)
<i>ERBB2</i>	1 (1.2%)	32 (3.5%)

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5:00 PM - 6:15 PM

P5-14-13

Benefits of Oncotype DX genomic screening in a geriatric vs. non-geriatric cohort. Analyzing key factors in therapy decision making process

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Introduction

In early luminal HER2 negative breast cancer Oncotype DX® Recurrence-Score (RS) has been broadly validated in pre- and postmenopausal patients and can predict prognosis and benefit of chemotherapy. Its value in elderly breast cancer populations has not been deeply addressed. This study analyses clinical and pathologic factors, RS distribution and outcomes in an elderly vs. non-elderly breast cancer population with the purpose of establishing RS added value to the therapy decision-making process in a geriatric cohort.

Methods

This is a retrospective analysis of available data from patients with early luminal HER2 negative breast cancer treated at the University Hospital Basel and the Cantonal Hospital Baselland between 2010 and 2022. Cohort A (A) consists of patients < 70 years old and cohort B (B) of patients aged ≥70 years. At moment of decision for adjuvant treatment all patients had known RS result.

Results

A and B included 266 (81%) and 60 (19%) patients, respectively. The median age in A was 55.2 and in B, 74 years. The following clinical and pathologic factors were different in B vs. A: co-morbidities (55 % vs. 35%, p=0.005), BMI (BMI≥25 (overweight vs. normal, p=0.023), tumor size (31.3 mm vs 23.6 mm p=0.021). Geriatric patients also tended to have a clinically higher risk status (83% vs. 70%; p=0.05). There was a trend for a higher mastectomy rate in B vs. A (41.7% vs. 29%, p=0.065), significantly less radiotherapy use (65% vs. 81%, p=0.009) and more osteo-oncologic treatment (61% vs 43%, p=0.013). RS distribution was not significantly

different between cohorts (A vs. B was: RS 1-15: 44.3% vs 41.7%, RS 16-25 41.2% vs 35% and RS \geq 26 14.5% vs 23.3%; p=0.234). Adjuvant chemotherapy was performed in 11.5% of B and 22.9% of A (p=0.116) and adjuvant endocrine therapy in 98.3% of B vs. 93.5% of A (p=p=0.214). Tumor board suggested systemic treatment was not implemented in 22% vs 15 %, (B vs. A; p =0.087). With a median follow-up of 36.6 months, recurrence rate was higher, but not statistically significant in B vs. A (10% vs 6%, p=0.259). Relapse rate was higher with RS \geq 26 vs. RS 0-25 (13.5% in B vs. 5.7% in A; p=0.043).

Conclusions

Older breast cancer patients tend to have higher clinical risk status, more co-morbidities and higher BMI. RS distribution was not significantly different between the two cohorts, however higher RS did pose a higher relapse rate for older patients in our cohort. Although RS based guidelines, still apply in therapy decision making in the case of geriatric breast cancer patients, clinical practice points to a rather individualized treatment in which all clinical and pathological factors are weighted.

Demographics			
Characteristics	All	<70 years	\geq 70 years
Age			
Mean (SD)	58.6 (11.8)	54.9 (9.4)	74.7 (3.2)
Range (Min, max)	29.1, 85.4	(29.1, 69.4)	(70.2, 85.4)
Sex			
Female	315 (97.8)	257 (98.1)	58 (96.7)
Male	7 (2.2)	5 (1.9)	2 (3.3)
Comorbidities			
No	197 (61.2)	170 (64.9)	27 (45)
Yes	125 (38.8)	92 (35.1)	33 (55)
ASA			
1	7 (2.3)	6 (2.4)	1 (1.7)
2	151 (49.5)	121 (49)	30 (51.7)
3	147 (48.2)	120 (48.6)	27 (46.6)
BMI			
<18.5	9 (2.9)	9 (3.6)	0 (0)
18.5-24.9	154 (49.5)	131 (51.8)	23 (39.7)
25-29.9	96 (30.9)	69 (27.3)	27 (46.6)
\geq 30	52 (16.7)	44 (17.4)	8 (13.8)

Tumor Characteristics			
Characteristics	All	<70 years	\geq 70 years
Histology			
IDC	251 (79.7)	203 (79)	48 (82.4)
DC	55 (17.5)	48 (17.9)	7 (15.5)
Other	1 (0.3)	1 (1.1)	1 (1.7)
IC-47			
Low	145 (45)	123 (46.9)	22 (36.7)
High	177 (55)	139 (53.1)	38 (63.3)
Grade			
I	30 (9.5)	27 (10.5)	3 (5)
II	177 (55.6)	142 (55.3)	35 (58.3)
III	110 (34.7)	88 (34.2)	22 (36.7)
Tumor size (mm)			
Mean (min, max)	25.1 (4-130)	23.6 (4-130)	31.3 (6-122)
pT stage			
pT1	168 (52.2)	150 (57.3)	18 (30)
pT2	122 (37.9)	90 (34.4)	32 (53.3)
pT3	30 (9.3)	21 (8)	9 (15)
pT4	2 (0.6)	1 (0.4)	1 (1.7)
pN stage			
pN0	186 (57.9)	147 (56.1)	39 (66.1)
pN1	126 (39.3)	108 (41.2)	18 (30.5)
pN2	3 (0.9)	3 (1.1)	0 (0)
pN3	6 (1.9)	4 (1.5)	2 (3.4)
Clinical risk			
Low	88 (27.8)	78 (30.4)	10 (16.9)
High	228 (72.2)	179 (69.6)	49 (83.1)

Therapy				
Characteristics	All	<70 years	\geq 70 years	p
Breast surgery				
BCS	221 (68.6)	186 (71)	35 (58.3)	0.005
Mastectomy	101 (31.4)	76 (29)	25 (41.7)	
Auxiliary surgery				
Distal DS	238 (80.1)	213 (81.3)	45 (75)	0.284
ALND	64 (19.9)	49 (18.7)	15 (25)	
Adjuvant ChT				
No	254 (79.9)	202 (77.1)	52 (86.7)	0.116
Yes	68 (21.1)	60 (22.9)	8 (13.8)	
Compliance to ChT				
No	15 (22.1)	14 (23.3)	1 (6.7)	0.674
Yes	53 (77.9)	46 (76.7)	7 (87.5)	
AdJ. ChT				
<4 cycles	60 (88.2)	53 (88.3)	7 (87.5)	1.00
\geq 4 cycles	8 (11.8)	7 (11.7)	1 (12.5)	
Endocrine therapy				
No	18 (5.6)	17 (6.5)	1 (1.7)	0.214
Yes	304 (94.4)	245 (93.5)	59 (88.3)	
Oral endocrine therapy (tamoxifen/aromatase?)				
No	365 (53.6)	343 (57)	22 (38.6)	0.013
Yes	313 (96.4)	308 (43)	5 (8.4)	
AdJ. Radiotherapy				
No	70 (22)	49 (19)	21 (35)	
Yes	248 (78)	209 (81)	39 (65)	0.009

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5:00 PM - 6:15 PM

P5-14-14

The genomic landscape of radiotherapy-induced breast angiosarcoma: an ACC initiative for an unmet need in cancer

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Introduction Radiotherapy-induced breast angiosarcoma (RIBAS) is a late, uncommon complication of radiotherapy (RT) in breast cancer. The incidence of RIBAS (0.3 – 1% of post-RT cases) is expected to increase in the next few years, following the widespread adoption of breast-sparing surgery in combination with RT[1–4]. RIBAS is poorly responsive to chemotherapy, and life expectancy is as low as 25% at five years. No actionable gene mutations are described for this disease.

Aims The aims of the present study are: 1) to understand the genomic aberrations of RIBAS and identify actionable mutations for novel targeted therapies; 2) to compare the genomics of RIBAS with those sporadic breast angiosarcoma (sBAS); 3) to understand the association of genomic aberrations with clinical features of RIBAS and its outcomes in clinical practice.

Patients and methods We have retrospectively collected FFPE tumor and germline samples, obtained by surgery or biopsy, from 2 European centers (INT - Milan and IRCCS San Martino - Genoa). Specimens from a third center, Katholieke Universiteit of Leuven, are being selected for analysis. Samples were subjected to whole exome sequencing (WES, NovaSeq 6000 Illumina). Raw data were analyzed using the opensource nf-Sarek pipeline[5].

Results We identified samples with matched normal tissue from 43 cases (30 RIBAS, 8 sBAS, 5 with no clinical info). All the patients were female, the overall median age at diagnosis was 68.8 years (IQR: 52.1 – 75.1), 69.8 (IQR: 61.4 – 76) for RIBAS and 41.2 (IQR: 28.6 – 53.7) for sBAS patients. WES was performed on 20 cases (14 RIBAS, 6 sBAS). The main mutations in RIBAS involve coding regions related to transcription factors and cytoskeletal, microtubule, and musculoskeletal-associated proteins. Among actionable mutated genes, MTOR and MAP3K21 were identified. The most significant CNAs were MYC amplifications[6] and collagen α 1 chain gene family deletions and were shared between RIBAS and sBAS. FLT4 for a recurrent, potentially actionable amplification[7]. To our knowledge, our study is the first to address the genomic landscape of RIBAS in the effort of linking its physiopathology with clinical management. Our results may shed light on novel prognostic and predictive biomarkers in this neglected but increasingly frequent tumor. Associations with treatment, RNAseq and methylation arrays results, as well as data from the extended data cohort, will be presented at the meeting.

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References 1. Monroe, A. T. et al. *Cancer*, 2003. 2. Sheth, G. R. et al. *Oncologist*, 2012. 3. Torres, K. E. et al. *Ann. Surg. Oncol.*, 2013. 4. West, J. G. et al. *Breast J.*, 2005. 5. Garcia, M. et al. *F1000Res*, 2020. 6. Fraga-Guedes, C. et al. *Breast Cancer Res. Treat.*, 2015. 7. Gordon, K. et al. *Hum. Mutat.*, 2013.

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5:00 PM - 6:15 PM

P5-15-01

Rediscovering IRF5: A prognostic indicator with novel roles in mammary gland development, ribosome biogenesis, tumor initiation, and metastasis

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Breast cancer is the second leading cause of death for women in the United States. However, only 10% of breast cancers have been linked to inherited genomic mutations. Thus, identifying biomarkers to predict cancer progression and metastasis remains a clear need in the research and medical world. Here, we report a novel role for Interferon Regulatory Factor 5 (IRF5) in mammary gland development, tumorigenesis, and metastasis. Historically, IRF5 has been studied as a transcription factor in the context of genetic risk for autoimmune diseases. However, mining of The Cancer Genome Atlas revealed that loss of IRF5 expression in human breast cancer is significantly linked with progression to high grade carcinoma, increased metastasis, and decreased overall and recurrence-free survival. Supporting these analyses, we demonstrated that female *Irf5*^{-/-} BALB/c mice have higher incidence of spontaneous atypical ductal hyperplasia (ADH), increased progression to DCIS, and ultimately, increased incidence of IDC. Using qPCR, FISH and IHC, we confirmed that IRF5 is expressed in both luminal and basal myoepithelial cells, but expression is higher in basal cells. Histologic analysis of whole mount preparations of *Irf5*^{-/-} mammary glands revealed aberrant ductal morphogenesis, characterized by expansion of luminal and basal myoepithelial cells with a loss of organized glandular structure. RNAseq of primary mammary epithelial cells from wild type and *Irf5*^{-/-} littermate mice showed *Irf5*^{-/-} mammary epithelial cells to be enriched in ribosome biogenesis pathways, the physiologic consequences of which were demonstrated through increased rates of protein synthesis. Transferring our studies in vivo, we demonstrated that loss of tumor IRF5 expression resulted in decreased tumor-infiltrating lymphocytes and increased pulmonary metastasis in the murine orthotopic 4T1 implantation model. Mechanistically, we found that—as in our studies utilizing primary mammary epithelial cells—IRF5 expression in tumors regulated protein translation and ribosome biogenesis. In light of these findings, we propose IRF5 as a novel prognostic biomarker, loss of which alters mammary gland development, drives tumor initiation and metastasis, and dysregulates mammary epithelial cell protein synthesis.

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Discussion 1 + Q&A: PD13-01, PD13-02, PD13-03 & PD13-04

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Discussion 2 + Q&A: PD13-05, PD13-06, PD13-07 & PD13-08

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5:00 PM - 6:15 PM

Discussion 3 + Q&A: PD13-09, PD13-10, PD13-11 & PD13-12

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5:00 PM - 6:15 PM

Poster Spotlight Discussion 13: Therapeutic Approaches for HR+/Her2- Breast Cancer

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5:00 PM - 6:15 PM

PD13-01

PD13-01 Elacestrant in postmenopausal women with estrogen receptor positive and HER2-negative early breast cancer: primary efficacy and safety analysis of the preoperative, window of opportunity SOLTI-1905-ELIPSE trial

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Introduction Elacestrant is the first oral, non-steroidal, selective estrogen receptor degrader (SERD) to demonstrate improved efficacy compared to standard of care endocrine treatment, with greater relative benefit in ESR1-mutated tumors, and manageable safety profile in pretreated patients with metastatic breast cancer (BC) (Bidard F.C., JCO 2022). SOLTI ELIPSE trial (NCT04797728) is a prospective, multicenter, window of opportunity trial designed to assess whether a short-course of preoperative elacestrant may suppress tumor proliferation in postmenopausal women with estrogen receptor positive (ER+)/HER2-negative early BC (Vidal M., SABCS 2021). Here, we present the results of the primary efficacy and safety study

analysis. Methods Eligible patients with operable, untreated ER+/HER2-negative BC that were T1c (≥ 1.5 cm)-T3 by ultrasound, clinically or radiologically N0 and had a locally assessed Ki67 $\geq 10\%$, received elacestrant 400 mg once a day continuously for a total of 4 weeks. At the study treatment completion, patients were treated according to local practice. Centralized assessment of post-treatment (D28) Ki67 from surgical specimen or tumor biopsy was required for the primary endpoint evaluation. Primary efficacy endpoint was complete cell cycle arrest (CCCA), defined as Ki67 $\leq 2.7\%$, at D28. Ki67 geometric relative change, variation in tumor infiltrating lymphocytes (TILs), switch in PAM50 subtypes and differential expression of 192 genes from baseline (D1) to D28 was also explored. Adverse events (AEs) were graded according to CTCAE v5.0. Results Between April 2021 and February 2022, 24 patients were enrolled and 22 were evaluable for the primary endpoint. Baseline characteristics were: mean age 69 years (range 50-81); ductal histology 74%; T1c 61%; T2 39%; grade 1-2 83%; median local Ki67 20% (10-70). Baseline PAM50 subtypes distribution was: Luminal A (n=12), Luminal B (n=8), Basal-like (n=1), Normal-like (n=1). At D28, CCCA was achieved in the 27% (n=6) of the patients. Fourteen patients (64%) had D28 Ki67 $\leq 10\%$. Paired centralized Ki67 was available in 19 patients. A statistically significant 41% (95% CI, -24 to -58) Ki67 relative reduction (rr) from D1 was observed (p=0.007). CCCA rate was 31% and 17% in patients with D1 Ki67 < 20% (n=13) and D1 Ki67 $\geq 20\%$ (n=6), respectively. Ki67 varied consistently in both Ki67 < 20% (rr=-38%; 95% CI, -16 to -60) and Ki67 $\geq 20\%$ (rr=-46%; 95% CI, -20 to -72) groups. Overall, elacestrant was associated with a shift towards a more endocrine sensitive and less proliferative phenotype based on PAM50 gene signatures. CCCA occurred in 45% of Luminal A tumors, whereas no CCCA was observed among Luminal B tumors. Levels of TILs were significantly higher at D28 (mean difference, +3.73; p=0.004). Elacestrant induced high expression of immune-response genes including IGJ, GZMB, CD4, CD8a and suppressed proliferation (e.g., UBE2T, MYBL2, BIRC5, MK67) and estrogen-signaling (e.g., ESR1, PGR, CCND1, BRCA2) genes (false discovery rate 5%). These changes in gene expression were observed both in tumors with D28 Ki67 $\leq 2.7\%$ and in those with D28 Ki67 > 10%. Overall, 87% of the patients reported any grade AEs. Treatment-related AE occurred in 1 patient (grade 3 cutaneous rash) and led to treatment discontinuation. Most frequently reported AEs (all grade 1) were hot flush (n=6), dyspepsia (n=2), anemia (n=2) and constipation (n=2). No serious AEs were reported. Conclusions In untreated ER+/HER2-negative early BC a short-course preoperative treatment with elacestrant was associated with relevant biological and molecular response and with manageable safety profile. Globally, these findings support further exploration of this highly potent, novel oral SERD in early BC.

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5:00 PM - 6:15 PM

PD13-02

PD13-02 Exploratory gene expression analysis of coopERA Breast Cancer (BC): a study evaluating neoadjuvant giredestrant versus anastrozole alone and in combination with palbociclib in ER-positive, HER2-negative untreated early BC

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Background: Endocrine therapy remains the mainstay treatment for ER+ BC. CDK4/6 inhibitors induce cell cycle arrest and decrease tumor cell proliferation, as measured by the biomarker Ki67, when used in combination with aromatase inhibitors (AI) such as anastrozole (A). Giredestrant is an oral, well-tolerated, and highly potent selective ER degrader (SERD) that achieves robust ER suppression and has demonstrated antitumor activity in the metastatic setting either as monotherapy or in combination with the CDK4/6 inhibitor palbociclib. The randomized, phase 2 coopERA Breast Cancer study (NCT04436744) evaluated giredestrant in postmenopausal women with untreated ER+/HER2- early BC and met its primary endpoint, demonstrating superior Ki67 suppression with giredestrant vs A after two weeks of single agent treatment. This suppression was maintained at surgery where giredestrant vs A was evaluated in combination with palbociclib. Here, we present gene expression analysis and associations with Ki67 response. Methods: 221 eligible patients with measurable ER+/HER2- untreated early BC and baseline Ki67 \geq 5% were randomized 1:1 to receive 30 mg oral daily (PO QD) giredestrant or 1 mg PO QD A on Days 1–14 of a neoadjuvant window-of-opportunity phase, followed by four 28-day cycles of PO QD giredestrant or A with 125 mg PO QD palbociclib on Days 1–21 before surgery. FFPE specimens were collected at baseline, week 2 and surgery; and RNA-sequencing (seq) was performed. Gene expression analysis included ER pathway activity, PAM50 intrinsic subtypes, and other pathway analyses, assessed by Ki67 response. Results: 112 and 92 patients had paired tumor samples at baseline/week 2 and baseline/surgery, respectively, that were evaluable for RNA-seq and Ki67. The trend for greater Ki67 protein suppression by giredestrant vs A from baseline to week 2 was maintained in the RNA-seq evaluable subset. Interestingly, the same subset revealed similar suppression of both proliferation gene signatures and ER pathway activity between A and giredestrant. PAM50 subtyping showed that 69% of tumors were luminal (Lum) A and 29% were LumB at baseline. Less than 1% were classified as basal or HER2. Interestingly, giredestrant (G) showed greater suppression of both Ki67 and ER pathway activity vs A in LumB tumors (Ki67: -82% [G] vs -62% [A]; ER activity: -0.83 [G] vs -0.66 [A]) compared to LumA at week 2 (Ki67: -74% [G] vs -71% [A]; ER activity: -0.60 [G] vs -0.70 [A]). Moreover, at week 2, 83% (13/18) of LumB tumors at baseline transitioned into a LumA subtype after giredestrant treatment compared to 46% (5/11) of A-treated tumors. Giredestrant-treated tumors also achieved lower mean ER pathway activity compared to those treated with A at surgery ($p=0.023$). Gene set enrichment analysis showed downregulation of cell-cycle and ER-related pathways at week 2 and surgery in both treatment arms. A subset of cytokine signaling and immune response pathways were increased at week 2 compared to baseline after treatment with A but not with giredestrant. These pathways were also associated with Ki67 resistance (Ki67 \geq 7.4%) in A-treated tumors. This was consistent with differential expression analysis of samples collected at week 2, in which cytokine signaling pathways were enriched in A compared to giredestrant. Notably, IL12 signaling was enriched in tumors resistant to A but not giredestrant. Conclusions: Giredestrant has a greater effect on Ki67 protein suppression in ER+/HER2- early BC compared to A, which is more pronounced in LumB tumors. This benefit may involve differential regulation of cytokine and immune responses. These exploratory findings reveal novel mechanisms that may differentiate the activity of SERDs vs AIs, which warrant further validation.

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PD13-04

PD13-04 Exploratory subgroup and biomarker analyses of acellERA Breast Cancer: Phase II study of giredestrant (GDC-9545) vs physician's choice of endocrine therapy for previously treated, estrogen receptor+, HER2– advanced breast cancer

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BACKGROUND

Endocrine therapy (ET) is the mainstay for management of estrogen receptor (ER)+ advanced breast cancer (aBC). Giredestrant is a highly potent, nonsteroidal, oral selective ER antagonist and degrader (SERD) that achieves robust ER occupancy. The Phase II randomized, open-label acellERA BC study (NCT04576455) evaluated giredestrant vs physician's choice of ET (PCET) in the second- or third-line ER+, HER2– aBC setting. While the study did not reach statistical significance for its primary endpoint of investigator-assessed progression-free survival (INV-PFS), the giredestrant arm demonstrated a numerical improvement vs the PCET arm, with a hazard ratio of 0.81 (95% confidence interval: 0.60, 1.10), and encouraging results

for key secondary efficacy endpoints (clinical benefit rate [CBR]: 32% vs 21%, respectively; objective response rate [ORR]: 13% vs 7%, respectively). We report exploratory subgroup analyses of these efficacy endpoints by prior treatments and by baseline circulating tumor (ct)DNA biomarkers.

METHODS

Patients were post- and pre- or peri-menopausal women, or men, with ER+, HER2– aBC who had progressed after 1–2 lines of systemic therapy in the advanced setting (≤ 1 targeted agent; ≤ 1 chemotherapy regimen; prior fulvestrant allowed). Randomization was 1:1 to giredestrant (30 mg oral daily) or PCET between fulvestrant or an aromatase inhibitor (AI), stratified by disease site (visceral vs non-visceral), prior CDK4/6 inhibitor, and prior fulvestrant. Biomarkers were assessed in baseline ctDNA isolated from plasma using the FoundationOne Liquid CDx or PredicineCARE assays. ESR1 mutations were defined as short variants with known or likely impact on ER protein function.

RESULTS

Among the 303 patients enrolled, prior aBC therapies included CDK4/6 inhibitors (42%), fulvestrant (19%), and chemotherapy (32%). Overall, most baseline characteristics were balanced across arms in subgroups. Efficacy in key subgroups by prior treatment and in ESR1-mutated tumors is shown in the table. Efficacy by PCET (75% received fulvestrant; 25%, an AI) and by type of ESR1 mutation will be presented. Clinical benefit (INV-PFS, CBR, ORR) was most prominently observed with giredestrant in patients with ESR1-mutated tumors. In the baseline ctDNA-evaluable population (232/303 patients; 77%), ESR1 and PIK3CA were the most prevalent mutations overall (39% and 36%, respectively). The most common ESR1 mutations were D538G, Y537S, Y537N, and E380Q; 54% of baseline ctDNA samples classified as ESR1-mutated had multiple ESR1 mutations detected (range of 2–7 mutations), demonstrating clonal heterogeneity. Clinical benefit was also observed with giredestrant in patients expressing different ESR1 mutations. Updated data will be presented.

CONCLUSIONS

Exploratory subgroup analyses showed favorable outcomes with giredestrant in terms of INV-PFS, CBR, and ORR across most key subgroups. The benefit was more pronounced in a) patients with ESR1-mutated tumors and b) patients who received prior fulvestrant (the majority of AI-treated patients in the PCET arm). Overall, these data support continued investigation of giredestrant to advance and improve treatment outcomes in hormone receptor+ BC.

Exploratory subgroup analyses

Exploratory subgroup analyses	INV-PFS HR _{us} (95% CI)	Median INV-PFS, months	CBR, %	ORR, %
Prior CDK4/6i				
giredestrant (n = 63)	0.80	3.7	27.0	14.3
PCET (n = 62)	(0.52, 1.23)	3.5	11.3	1.6
No prior CDK4/6i				
giredestrant (n = 88)	0.92	7.2	35.2	11.4
PCET (n = 90)	(0.61, 1.38)	5.6	27.8	11.1
Prior chemotherapy for aBC				
giredestrant (n = 47)	0.92	5.6	36.2	14.9
PCET (n = 49)	(0.53, 1.58)	5.5	24.5	10.2
No prior chemotherapy for aBC				
giredestrant (n = 104)	0.87	5.5	29.8	11.5
PCET (n = 103)	(0.61, 1.24)	5.4	19.4	5.8
Prior fulvestrant				
giredestrant (n = 29)	0.65	5.5	17.2	6.9
PCET (n = 29)*	(0.35, 1.23)	3.6	6.9	0
<i>ESR1</i> mutation				
giredestrant (n = 51)	0.55	5.3	25.5	13.7
PCET (n = 39)	(0.33, 0.93)	3.5	2.6	0

* Almost all received an AI.
aBC, advanced breast cancer; AI, aromatase inhibitor; CBR, clinical benefit rate (complete or partial response, or stable disease for ≥6 months, calculated in the full analysis set); CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CI, confidence interval; HR_{us}, unstratified hazard ratio; INV-PFS, investigator-assessed progression-free survival; ORR, objective response rate (confirmed complete or partial response, calculated in the full analysis set); PCET, physician's choice of endocrine therapy.

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12/8/2022

5:00 PM - 6:15 PM

PD13-05

PD13-05 Updated results of a Phase 1b study of gedatolisib plus palbociclib and endocrine therapy in women with hormone receptor positive advanced breast cancer: Subgroup analysis by PIK3CA mutation status

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Background: Addition of PI3K/mTOR inhibitor after progression on CDK4/6 inhibitor (CDK4/6i) and endocrine therapy (ET) can potentially restore sensitivity to CDK4/6i and prevent adaptive activation of the PI3K/mTOR pathway. To evaluate this hypothesis, we conducted a Phase Ib study of gedatolisib (G), a dual inhibitor of PI3K/mTOR, palbociclib (P) a CDK4/6i, and ET (with letrozole [LET] or fulvestrant [FUL]) in women with hormone receptor positive (HR+)/HER2-advanced breast cancer (ABC). Manageable toxicity and preliminary antitumor activity were observed in 35 patients(pts) enrolled in the dose escalation portion of the study (Forero-Torres, ASCO 2018) and 103 pts enrolled in the expansion portion of the study (Layman, SABCS 2021). Here, we report updated efficacy and safety data and sub-group analysis by PIK3CA mutation status in the four expansion study arms with a March 3, 2022, data cut-off.

Methods: Pts with HR+/HER2- ABC were treated in four expansion arms: A) G+P+LET as first-line treatment, B) G+P+FUL as 2nd line treatment in pts without prior CDK4/6i; C & D) G+P+FUL as 2nd or 3rd line therapy in pts with prior CDK4/6i. P, LET, and FUL were administered at standard doses. G 180 mg was intravenously administered weekly in Arms A, B, and C and three weeks on/one week off in Arm D. The primary endpoint was investigator assessed objective response rate (ORR). Secondary endpoints included safety, duration of response and progression free survival (PFS).

Results: Of the 103 pts treated with G+P+ ET in the expansion arms (A-D), 100% had measurable disease at baseline, 71% (73/103) lacked PIK3CA mutations (wild type; WT), 27% (28/103) had PIK3CA-mutations (MT), 70% (72/103) had evidence of bone metastases, and 59% (61/103) had liver metastases. The most frequent grade 3 and 4 treatment related AEs (TRAE) with G+P+ET included neutropenia (63%), stomatitis (27%), rash (20%), fatigue (11%) and hyperglycemia (7%). Treatment discontinuation due to TRAEs was 6.5% in Arm A, 15.4% in Arm B, 9.4% in Arm C and 3.7% in Arm D. Efficacy data for each arm is presented in Table 1. Promising ORR and PFS were seen in all arms regardless of PIK3CA mutation status. In Arm D, ORR was 63% overall, 73% in PIK3CA-MT pts, and 60% in PIK3CA-WT pts. Median PFS in Arm D was 12.9 months with a median follow up of 29 months. 60% and 48% of pts in the PIK3CA-MT and PIK3CA-WT Arm D sub-groups, respectively, were progression free at 12 months.

Conclusions: These preliminary data demonstrate promising activity of G+P+ET combination in pts who were CDK4/6i-naïve and in those whose disease progressed on or after CDK4/6i therapy regardless of PIK3CA mutation status. Encouraging results in CDK4/6i treatment naïve patients warrant further evaluation of gedatolisib in combination with CDK4/6i treatment in the front-line setting. Arm D results provide a strong basis for the initiated Phase 3 study (VIKTORIA-1) in pts whose disease progressed on or after CDK4/6i therapy.

Table 1. Efficacy Data by Expansion Arms

Arm	A		B		C		D	
N (full, resp. evaluable)	31, 27		13, 13		32, 28		27, 27	
Patients	1L: CDK4/6i-Naïve		2L+: CDK4/6i-naïve		2L/3L: CDK4/6i-pretreated		2L/3L: CDK4/6i-pretreated	
PIK3CA Status	WT / MT ^c (78% / 19%) ^a (81% / 16%) ^b		WT / MT (69% / 31%) ^{a,b}		WT / MT (71% / 29%) ^a (75% / 25%) ^b		WT / MT ^c (56% / 41%) ^{a,b}	
ORR ^a (evaluable)	85%		77%		36%		63%	
	WT 81%	MT 100%	WT 78%	MT 75%	WT 25%	MT 62.5%	WT 60%	MT 72.7%
mPFS (mos) ^b	Not Reached		12.9		5.1		12.9	
Median follow-up (mos) ^b	33.1		Not Reached		27.6		29.0	
PFS % at 12 mos ^b	72.1%		54.5%		24.9%		53.2%	
	WT 74.1%	MT 60.0%	WT 50.0%	MT 66.7%	WT 23.5%	MT 29.2%	WT 48.5%	MT 60.0%

^a Response evaluable analysis set per RECIST v1.1 including uPR; ^b full analysis set; ^c Baseline PIK3CA mutation status missing for one pt; 1L= first line; 2L= second line; 3L= third line; mos= months; WT= wild type; MT = PIK3CA Mutation

Disclosure(s):

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5:00 PM - 6:15 PM

PD13-06

PD13-06 Long-Term and Very-Long-Term Disease Control in Patients From BYLieve Study Cohort A With PIK3CA-Mutant, Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative, Advanced Breast Cancer

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Introduction: PIK3CA mutations, seen in ~40% of patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (ABC), are associated with treatment (Tx) resistance and shorter survival. Alpelisib (ALP) is an α -selective PI3K inhibitor and degrader indicated for treating this population in combination with fulvestrant (FUL) after endocrine therapy (ET). Previous results from the SOLAR-1 study showed that progression-free survival (PFS) ≥ 18 mo is achievable for pts treated with ALP on/after prior Tx with aromatase inhibitor (AI). Here, we analyze pts from BYLieve study Cohort A who achieved long-term (LT) and very-long-term (VLT) disease control with ALP + FUL after prior Tx with cyclin-dependent kinase 4/6 inhibitor (CDK4/6i) and AI.

Methods: BYLieve was a Phase II, nonrandomized, open-label, 3-cohort study of ALP + ET in pts with PIK3CA-mutated, HR+, HER2- ABC whose disease progressed on/after prior CDK4/6i. In Cohort A, median (m) PFS was 7.26 mo. LT disease control was defined as ≥ 12 mo PFS and VLT disease control as ≥ 18 mo PFS. Pts with < 12 mo PFS were defined as non-LT. Baseline characteristics are summarized by duration of disease control. Incidence rate (IR) per 100 patient-treatment years (PTY) was calculated to assess exposure-adjusted adverse events (AE). To assess tumor complexity in LT/VLT pts, median circulating tumor DNA (ctDNA) fraction, chromosome (chr) 8/11 amplification, and ESR1 mutations were determined by next-generation sequencing.

Results: In BYLieve Cohort A, 31 of 121 pts (25.6%) achieved LT disease control with an mPFS of 24.8 mo (95% CI 18.2 mo to not estimable [NE]) and 20 of 121 pts (16.5%) achieved VLT disease control (mPFS NE; 95% CI 22.1 mo to NE). Pts with LT/VLT disease control had lower BMI and ECOG score, longer time from initial diagnosis to first recurrence/relapse, more frequent bone-only lesions, and fewer liver metastases than non-LT pts (Table). Median ALP relative dose intensity was 86.7%, 91.7%, 85.0%, and 85.1% for all Cohort A pts (n=127), non-LT (n=96), LT (n=31), and VLT disease control (n=20), respectively, whereas median ALP exposure was 5.13 mo, 3.61 mo, 21.29 mo, and 25.25 mo respectively. The IRs per 100 PTY of diarrhea, hyperglycemia, and rash were lower in LT (IR 128.4, n=24; IR 78.0, n=20; IR 21.6, n=10 respectively) and VLT (IR 93.5, n=15; IR 51.2, n=11; IR 24.9, n=8 respectively) pts than non-LT pts (IR 250.5, n=57; IR 251.5, n=56; IR 85.4, n=30 respectively). In LT and VLT pts ctDNA fraction was 2% and 5% respectively, whereas ctDNA fraction in non-LT pts was 14%. Incidence of chr 8/11 amplification was 10% in both LT and VLT pts and 20% in non-LT pts; incidence of ESR1 mutations was 26%, 25%, and 27% in LT, VLT, and non-LT pts respectively.

Conclusions: In pts with PIK3CA-mutated, HR+, HER2- ABC treated with ALP + FUL after CDK4/6i, LT and VLT disease control was observed in 25.6% and 16.5% of patients, respectively. Visceral disease, development of AEs, and ESR1 mutations did not preclude LT/VLT disease control. These data confirm that targeting the PIK3CA driver mutation with ALP + FUL post-CDK4/6i Tx may lead to LT disease control.

Table – Baseline characteristics in BYLieve Cohort A overall and by duration of disease control				
	Overall population (n=127)	Non-LT disease control (<12 mo PFS) (n=96)	LT disease control (≥12 mo PFS) (n=31)	VLT disease control (≥18 mo PFS) (n=20)
Age, median (range), y	56.7 (48.0-65.0)	58.0 (47.5-64.5)	57.0 (48.0-67.0)	60.0 (50.0-68.0)
Body mass index, median (range), kg/m ²	25.3 (16.1-46.6)	26.1 (16.1-46.6)	24.7 (16.5-35.3)	24.3 (16.5-33.5)
Eastern Cooperative Oncology Group performance status, n (%)				
0	81 (63.8)	59 (61.5)	22 (71.0)	16 (80.0)
1	41 (32.3)	33 (34.4)	8 (25.8)	4 (20.0)
2	2 (1.6)	2 (2.1)	0	0
Missing	3 (2.4)	2 (2.1)	1 (3.2)	0
Time from initial diagnosis to first recurrence/relapse, median (range), mo	33.1 (0.4-239.7)	29.2 (0.7-239.7)	70.4 (0.4-201.4)	83.6 (0.5-201.4)
Extent of metastatic disease, n (%)				
Central nervous system	2 (1.6)	2 (2.1)	0	0
Bone	108 (85.0)	79 (82.3)	29 (93.5)	18 (90.0)
Bone only	24 (18.9)	12 (12.5)	12 (38.7)	6 (30.0)
Breast	6 (4.7)	4 (4.2)	2 (6.5)	1 (5.0)
Visceral	85 (66.9)	69 (71.9)	16 (51.6)	12 (60.0)
Lung	43 (33.9)	33 (34.4)	10 (32.3)	8 (40.0)
Liver	59 (46.5)	53 (55.2)	6 (19.4)	4 (20.0)
Other visceral	8 (6.3)	6 (6.3)	2 (6.5)	1 (5.0)
Skin	4 (3.1)	2 (2.1)	2 (6.5)	1 (5.0)
Lymph nodes	36 (28.3)	32 (33.3)	4 (12.9)	3 (15.0)
Other	12 (9.4)	9 (9.4)	3 (9.7)	2 (10.0)
Soft tissue	1 (0.8)	1 (1.0)	0	0
Number of prior lines of medical therapy in metastatic setting, n (%)				
0	2 (1.6)	2 (2.1)	0	0
1	101 (79.5)	74 (77.1)	27 (87.1)	17 (85.0)
2	23 (18.1)	19 (19.8)	4 (12.9)	3 (15.0)
3	1 (0.8)	1 (1.0)	0	0

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5:00 PM - 6:15 PM

PD13-07

PD13-07 Combination therapy with the AKT inhibitor, ipatasertib, endocrine therapy, and a CDK4/6 inhibitor for hormone receptor positive (HR+)/HER2 negative metastatic breast cancer (MBC): results from the phase I TAKTIC trial.

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Background: Cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) in combination with endocrine therapy (ET) provide significant clinical benefit in patients with HR+/HER2- metastatic breast cancer (MBC) and have become a standard of care treatment. Prior insights from tumor profiling and preclinical analyses suggest that AKT1 activation can induce CDK4/6i resistance. We hypothesized that targeting AKT1 following CDK4/6i progression may be an effective therapeutic strategy and conducted a clinical trial to evaluate both doublet (ET+AKTi) and triplet (ET+AKTi+CDK 4/6i) therapy in the ≥ 2 nd line MBC setting. Methods: TAKTIC is an open-label phase Ib clinical trial (clinicaltrials.gov NCT03959891) evaluating the combination of the AKT inhibitor ipatasertib (ipat) with fulvestrant (Arm A), an aromatase inhibitor (Arm B), or the triplet combination (Arm C) with fulvestrant + palbociclib (palbo). The primary objective is to evaluate the safety (NCI CTCAE 5.0) and tolerability of ipat in combination with endocrine therapy +/- CDK4/6i. Secondary objectives include clinical efficacy, as determined by objective response rate (RECIST v1.1), clinical benefit rate (CBR), progression-free survival (PFS), and overall survival (OS). Key inclusion criteria include unresectable HR+/HER2- MBC; at least 1 prior therapy for MBC including any CDK4/6i; up to 2 prior lines of chemotherapy for MBC (no limit on prior endocrine therapy). Here, we present an updated interim analysis from all study arms. Results: The trial completed accrual with 77 pts enrolled from June 2019 – February 2022, including 19 on Arm A, 16 on Arm B, and 42 on Arm C. Median age was 62 (range 32-88) and 65/77 pts (84%) received prior CDK4/6i (median no. of prior lines = 3, range 1-13). 56/77 pts (73%) had measurable disease at baseline and 50/77 pts (65%) had visceral metastases in the liver/lung (68% Arm A, 44% Arm B, 71% Arm C). Pts enrolled on Arms A and B received ipat at 400mg in combination with fulvestrant or an aromatase inhibitor, respectively. In Arm C, 27/42 pts enrolled into the dose escalation phase and received ipat + palbo at varying doses in combination with fulvestrant. Two DLTs were observed in the 300mg ipat + 125mg palbo cohort (grade 4 neutropenia ≥ 7 days). ET+400mg ipat + 100mg palbo was determined to be the recommended phase 2 dose (R2PD), and the remaining 15/42 pts on Arm C were treated at this dose level in the expansion phase. Treatment was well tolerated in all arms. Grade 3 and 4 toxicities included neutropenia (39/77, 50.6%), leukopenia (15/77, 19.5%), diarrhea (11/77, 14/3%), transaminitis (7/77, 9.1%), lymphopenia (6/77, 7.8%), rash (6/77, 7.8%), and thrombocytopenia (3/77, 3.9%). As of 6/28/2022, 16/77 pts remain on treatment. The median treatment duration for all pts is estimated at 6 months (range 0.5-39). Among the 56 pts with measurable disease, 11 had partial response (PR) and 32 had stable disease (SD) as the best response. CBR, defined as percentage of pts who achieved PR or SD > 6 months, was 48% across the study (53% Arm A, 31% Arm B, 57% Arm C). The median PFS was 5.5 months (95% confidence interval [CI]: 3.8 – 7.4) and the median OS was 24.5 months (95% CI: 17.1 – 33.9). Conclusions: The combination of ipat with endocrine therapy +/- palbo is well tolerated in heavily pre-treated pts, with preliminary evidence of clinical activity. This trial demonstrates how molecular insights related to CDK4/6i resistance inform potential therapy combinations. Further studies are needed to evaluate AKTi-based combinations in pts with HR+ MBC.

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12/8/2022

5:00 PM - 6:15 PM

PD13-08

PD13-08 Phase 1 TROPION-PanTumor01 Study Evaluating Datopotamab Deruxtecan (Dato-DXd) in Unresectable or Metastatic Hormone Receptor–Positive/HER2–Negative Breast Cancer (BC)

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Background: Datopotamab deruxtecan (Dato-DXd) is an antibody-drug conjugate (ADC) consisting of a humanized anti-TROP2 IgG1 monoclonal antibody covalently linked to a highly potent topoisomerase I (Topo I) inhibitor payload via a stable, tumor-selective, tetrapeptide-based cleavable linker. Dato-DXd demonstrated compelling single-agent antitumor activity in heavily pretreated patients (pts) with metastatic triple-negative BC (Krop, SABCS 2021). This is the first report of results from the TROPION-PanTumor01 study in pts with unresectable or metastatic hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-; including HER2-low and HER2-zero) BC.

Methods: TROPION-PanTumor01 (NCT03401385) is a phase 1, multicenter, open-label, 2-part dose-escalation/expansion study evaluating Dato-DXd in previously treated pts with solid tumors. Based on previous clinical findings and exposure-response results from pts with NSCLC, Dato-DXd 6 mg/kg IV Q3W is being evaluated in pts with unresectable or metastatic HR+/HER2- BC that progressed on standard therapies. The primary objectives were safety and tolerability. Tumor responses, including ORR (complete response [CR] + partial response [PR]) and DCR (CR + PR + stable disease [SD]), were assessed per RECIST version 1.1 by blinded independent central review.

Results: As of the April 29, 2022, data cutoff, 41 pts had received Dato-DXd (median follow-up, 10.9 mo [range, 7-13]); 9 pts were ongoing. The primary cause of treatment discontinuation was disease progression (63%; progressive disease [PD] or clinical progression). Median age was 57 y (range, 33-75); 54% had de novo metastatic disease. Pts were heavily pretreated (Table) with a median of 5 (range, 3-10) prior regimens in the advanced setting; 95% had prior CDK4/6i (adjuvant/metastatic). Median time from initial treatment for metastatic disease to the first dose of Dato-DXd was 42.7 mo (range, 10.2-131.1). Treatment-emergent adverse events (TEAEs; all cause) were observed in 98% (any grade) and 41% (grade ≥ 3) of pts. Most common TEAEs (any grade, grade ≥ 3) were stomatitis (80%, 10%), nausea (56%, 0%), fatigue (46%, 2%), and alopecia (37%, 0%). Serious TEAEs were observed in 6 pts (15%); 1 pt died due to dyspnea, which was not considered to be treatment related. Dose reductions occurred in 5 pts due to stomatitis (n=3), fatigue (n=2), keratitis (n=1), and decreased appetite (n=1) (>1 AE per pt); 14 pts had treatment delayed due to stomatitis (n=8), retinopathy (n=1), dysphagia (n=1), fatigue (n=1), malaise (n=1), COVID-19 (n=1), cellulitis (n=1), urinary tract infection (n=1), decreased lymphocyte count (n=1), and nasal congestion (n=1; >1 AE per pt). Three pts discontinued treatment due to keratitis (n=1) and pneumonitis (n=2); 1 case of pneumonitis was adjudicated as grade 2 drug-related interstitial lung disease. The ORR was 29% (11 confirmed PRs; 1 pending confirmation), the DCR was 85% (35/41), and the clinical benefit rate (CR + PR + SD ≥ 6 mo) was 41% (17/41).

Conclusions: Dato-DXd demonstrated a manageable safety profile and encouraging antitumor activity, with high disease control in heavily pretreated pts, the majority having received prior CDK4/6i. Based on these findings, the TROPION-Breast01 (NCT05104866) randomized phase 3 study comparing 2L+ Dato-DXd vs investigator's choice chemotherapy is currently enrolling pts with HR+/HER2- BC.

Prior Therapies in the Adjuvant or Metastatic Setting

Prior treatment, %	(N=41)
Endocrine and chemotherapy	98
CDK4/6i	95
≤12 months	44
>12 months	51
Capecitabine	83
Taxanes	59
Anthracyclines	54
(Neo)adjuvant chemotherapy	37
PI3KCAi	20
PARPi	15
Immunotherapy	7
Topo I inhibitor-based ADC therapy	0

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12/8/2022

5:00 PM - 6:15 PM

PD13-09

PD13-09 Clinical outcomes of patients with HR+ HER2- advanced breast cancer with early progression on CDK4/6 inhibitors

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Background: CDK4/6 inhibitors (CDK4/6i) paired with endocrine therapy (ET) are considered first-line (1L) therapy for patients (pts) with HR+ HER2- advanced breast cancer (aBC). A minority of pts will demonstrate primary resistance to CDK4/6i, as characterized by early progression. Thymidine kinase 1 (TK1) is a cell-cycle regulated enzyme downstream of CDK4/6 and involved in nucleotide metabolism during DNA synthesis. Prior studies have shown TK1 may serve as a biomarker of response to CDK4/6i, with early TK1 activity (TK1a) suppression after initiation of CDK 4/6i therapy associated with improved PFS. Lack of TK1a suppression may be associated with primary resistance to CDK4/6i. In this study, we aim to analyze response to subsequent lines of therapy and overall survival (OS) of pts with early progression on 1L CDK4/6i. Methods: Pts with HR+ HER2- aBC from a phase II trial of an alternative schedule of palbociclib (palbo alt dosing trial NCT 3007979) and from a retrospective palbociclib study were included in this analysis. Pts in the palbo alt dosing trial underwent baseline and C1D15 TK1a analysis after initiation on CDK4/6i. C1D15 TK1a suppression was defined at TK1a < 30 Du/L. Pts in the retrospective palbociclib study included pts receiving palbo as part of their standard of care 1L therapy for HR+ HER2- aBC at Washington University in Saint Louis from 2016 to 2021. Clinical information, including treatment start and stop dates on each of the next-line therapies, were collected from the electronic medical record. PFS was estimated by the treatment duration on a specified treatment regimen. Early progression on CDK4/6i was defined as PFS < 6 mo. Best response was defined as next line of therapy with the numerically longest PFS. OS was defined as time to death from the initiation of CDK4/6i. Results: Of the 54 pts enrolled on the palbo alt dosing trial, 51 pts were evaluable for clinical

benefit and 46 pts were evaluable for TK1a suppression rate at C1D15. 7 pts (15.2%) were found without TK1a suppression at C1D15. This lack of TK1a suppression on palbo was associated with a significantly shorter PFS (median PFS=3.1 mo) compared to not reached in pts with TK1a suppression at C1D15. We conducted clinical analysis on N=26 pts who exhibited early progression on CDK4/6i which included 10 pts from the palbo alt dosing trial and 16 from the retrospective study. The average subsequent line of therapies in this cohort was 3, with the most common second line (2L) therapy being chemotherapy (N=17, 65.4%) and ET (N=8, 30.8%). The median PFS for pts receiving 2L chemotherapy and ET was 4.09 mo and 3.64 mo, respectively. 10 pts received both chemotherapy and ET with 7 (70.0%) achieving best response with chemotherapy compared to 3 pts (30.0%) who achieved best response with ET. The median OS for the cohort was 14.6 mo. Conclusions: Early progression on CDK4/6i is associated with a particularly poor prognosis. In our cohort, the median OS was far below the expected median OS for pts receiving 1L palbo as reported in the PALOMA-2 trial (14.6 mo vs 53.9 mo). Early progression on CDK4/6i is associated with more aggressive disease which may respond more favorably to chemotherapy, as demonstrated by best response to therapy. Further prospective studies are warranted to explore this treatment approach.

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5:00 PM - 6:15 PM

PD13-10

PD13-10 Impact of Proton Pump Inhibitors (PPI) on Palbociclib (PAL) Outcomes in Hormone Receptor-Positive, HER2-Negative Advanced Breast Cancer (HR+/HER2- ABC): Exploratory Analysis of the PARSIFAL Trial

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Background The use of PPI among cancer patients (pts) is quite frequent. PAL is an oral, cyclin-dependent kinase 4 and 6 inhibitor recommended to be taken under fed conditions. PAL showed a reduced solubility when gastric pH is >4.5, a level commonly achieved by PPI. Observational, retrospective studies on concomitant PPI with PAL or ribociclib showed a shorter progression-free survival (PFS) among PPI users than nonusers. In the randomized, phase 2 PARSIFAL trial, PAL plus fulvestrant demonstrated no improvement in PFS and overall survival (OS) versus PAL plus letrozole as frontline treatment in HR+/HER2- ABC pts (Llombart-Cussac et al, JAMA Oncol 2021). Here we assessed the impact of PPI on PAL efficacy and safety in pts included in the PARSIFAL study. **Methods** Pts with endocrine-sensitive HR+/HER2- ABC and no prior therapy in advanced setting were randomly assigned to receive PAL (hard capsule formulation) plus either fulvestrant or letrozole. Pts with ≥ 1 PPI received over the entire PAL-based regimen were defined as PPI users, or PPI naïve (N-PPI) if no PPI was administered over the whole study treatment. We carried out two analyses considering early PPI users (E-PPI) –composed by pts who were receiving PPI since the PAL-based regimen initiation– and long-term PPI users (LT-PPI) –composed by pts who received

PPI over the entire or $\geq 2/3$ of the PAL-based regimen. PPI users defined as neither E-PPI nor LT-PPI were excluded from the analysis to avoid biases due to the PPI limited exposition. PFS, OS, and safety were compared among groups. Landmark analysis at 3, 6, 12, 18, 24, and 30 months (mo) was used for survival estimates conditional on surviving to certain time points and adjust for immortality bias in comparison between N-PPI and PPI users. Analyses were adjusted by stratification factors and patient characteristics. Results Of 486 pts included in the study, 325 (66.9%) were N-PPI. Among 161 (33.1%) PPI users, 64 (13.2%) were E-PPI and 91 (18.7%) were LT-PPI. Omeprazole was the most prescribed PPI in 80.7% (130 of 161) of PPI users. Median exposition to PPI for PPI users, E-PPI, and LT-PPI was 13.6, 15.9, and 19.4 mo, respectively. Compared with N-PPI, E-PPI and LT-PPI were older (median age, 60.5 vs 66.5 vs 67.0 years, respectively; $P < 0.001$) and had a worse functional status (ECOG PS of 0, 60.0% vs 34.0% vs 43.0%, respectively; $P = 0.002$). Median follow-up for the whole population was 32 mo. Median PFS was 28.7 mo in N-PPI compared with 23.0 mo in E-PPI (HR 1.5; 95%CI 1.1–2.2; $P = 0.024$) and 23.0 mo in LT-PPI (HR 1.4; 95%CI 1.0–1.9; $P = 0.035$). Both PPI groups had poorer median PFS than N-PPI by landmark analysis at 3 and 12 mo. Subgroup analysis showed a consistent trend regardless of endocrine partner. Three-year OS rate was 81.1% in N-PPI compared with 63.5% in E-PPI (HR 2.2; 95%CI 1.3–3.7; $P = 0.003$) and 62.0% in LT-PPI (HR 2.1; 95%CI 1.4–3.4; $P = 0.001$). Both PPI groups had poorer 3-year OS rate than N-PPI by landmark analysis at 3, 6, 12, and 18 mo. Grade ≥ 3 hematological adverse events (AEs) occurred in 71.7% (233 of 325 pts) of N-PPI compared with 57.8% (37 of 64 pts; $P = 0.021$) of E-PPI and 54.9% (50 of 91 pts; $P = 0.003$) of LT-PPI. Dose reductions and delays due to hematological AEs were reported in 70.8% (230 of 325 pts) of N-PPI compared with 56.3% (36 of 64 pts; $P = 0.018$) of E-PPI and 52.7% (48 of 91 pts; $P = 0.002$) of LT-PPI. At 3 mo, 45.8% (149 of 325 pts) of N-PPI required a dose reduction or delay due to hematological AEs compared with 39.1% (25 of 64 pts; $P = 0.42$) of E-PPI. Conclusions Early and sustained coadministration of PPI with PAL and endocrine therapy were associated with lower efficacy, hematological toxicities, and dose modifications. Despite the post-hoc nature of the study, these findings suggest pharmacokinetic interactions between PPI and PAL capsules. Further confirmatory studies including the tablet formulation of PAL, which is expected to assure its optimal absorption, are needed.

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PD13-11

PD13-11 Final Overall Survival Analysis of Monarch 2 : A Phase 3 trial of Abemaciclib Plus Fulvestrant in Patients with Hormone Receptor-Positive, HER2-Negative Advanced Breast Cancer

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Background Abemaciclib is approved for patients (pts) with hormone receptor-positive (HR+), HER2-negative (HER2-) advanced breast cancer (ABC) with progression on prior endocrine therapy (ET). The MONARCH 2 trial showed a statistically significant benefit in progression-free survival (PFS) (hazard ratio [HR]: 0.553; 95% CI: 0.449-0.681; $p < 0.001$), overall survival (OS) (HR: 0.757; 95% CI: 0.606-0.945; $p = 0.01$) and a manageable safety profile for abemaciclib plus fulvestrant compared with fulvestrant alone. Here we report the pre-specified final overall survival (OS) analysis from the MONARCH 2 trial (NCT02107703). Methods MONARCH 2 was a global, randomized, placebo-controlled, double-blind phase 3 trial of abemaciclib or placebo, plus fulvestrant for treatment of pre-, peri- or postmenopausal women with CDK 4 & 6 inhibitor naïve HR+, HER2- ABC that progressed during ET. Pts were randomized 2:1 to receive abemaciclib or placebo, 150 mg twice daily, plus fulvestrant. Randomization was stratified based on site of metastasis (visceral, bone only, or other) and resistance to prior ET (primary versus secondary). OS and safety were key secondary endpoints, and chemotherapy-free survival was an exploratory endpoint defined as the time from randomization to initiation of chemotherapy or death, whichever occurs the earliest. Kaplan-Meier (KM) method was used to analyze time-to-event variables. A stratified Cox proportional hazards model was used to estimate treatment effect hazard ratio (HR). The prespecified final analysis was planned to occur based on approximately 441 OS events. Data cutoff was March 18, 2022. Results 669 women were randomized 2:1 to receive abemaciclib ($n = 446$) or placebo ($n = 223$), plus fulvestrant. Baseline characteristics have been previously reported (Sledge et. al., *Jama Oncol* 2020). The median follow-up time was approximately 80 months and at the time of the data cutoff, 11% of pts were still receiving study drug in the abemaciclib arm versus 2% in the placebo arm. 440 OS events were observed in the ITT population (abemaciclib arm: 283 events; placebo arm: 157 events). The median OS was 45.8 months in the abemaciclib arm and 37.2 months in the placebo arm (HR: 0.784; 95% CI: 0.644-0.955). The maintained separation of the KM curves beyond the medians is illustrated by the differences in the estimated 5- and 6-year OS rates between arms (5-year: 41.2% versus 29.2%; 6-year: 34.7% versus 23.7%; abemaciclib versus placebo respectively). While OS benefit was generally consistent across subgroups, a more pronounced benefit is noted in subgroups associated with a poorer prognosis such as visceral disease (HR: 0.643; 95% CI: 0.499-0.829), primary resistance to ET (HR: 0.634; 95% CI: 0.436-0.922) or negative progesterone receptor status (HR: 0.623; 95% CI: 0.405-0.959). Moreover, the addition of abemaciclib to fulvestrant deferred the initiation of chemotherapy (HR: 0.674; 95% CI: 0.562-0.809), with substantial difference in yearly chemotherapy-free survival rates (3 year: 42% vs 29.3%; 4 year: 37% vs 18.6%; 5 year: 32.4% vs 14.7%). Notably with longer exposure to

abemaciclib, no new additional safety risks or cumulative toxicities were identified. Conclusions At the prespecified final OS analysis of the MONARCH 2 trial, with a median follow-up of 6.5 years, the statistically significant benefit previously demonstrated was confirmed and maintained. OS benefit was generally consistent across subgroups, with numerically greater effect size observed among patients with poorer prognosis. Importantly, the survival benefit came with a substantial extension of the chemotherapy-free survival time, which is an important consideration for pts with ABC. The results also provide assurance of the safety of abemaciclib with longer-term use.

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12/8/2022

5:00 PM - 6:15 PM

PD13-12

PD13-12 Imlunestrant, an oral selective estrogen receptor degrader, in combination with abemaciclib with or without an aromatase inhibitor, in estrogen receptor-positive advanced breast cancer: Results from the phase 1a/b EMBER study

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Background: Imlunestrant is a novel, orally bioavailable selective estrogen receptor degrader (SERD) with pure antagonistic properties that result in sustained inhibition of estrogen receptor (ER)-dependent gene transcription and cell growth. Preclinically, imlunestrant has favorable efficacy and pharmacokinetic (PK) properties, including antitumor activity in ESR1-mutant models, along with enhanced efficacy when combined with abemaciclib. In dose escalation (Phase 1a) and dose expansion (Phase 1b) in the EMBER study, imlunestrant monotherapy was well tolerated with favorable safety, PK and encouraging antitumor activity in heavily pre-treated ER+, HER2- advanced breast cancer (aBC) patients (Jhaveri, ASCO 2022); imlunestrant recommended phase 2 dose (RP2D) was determined as 400mg QD. Here, we present the phase 1b dose expansion of imlunestrant with abemaciclib ± aromatase inhibitor (AI) in EMBER (NCT04188548).

Methods: Phase 1b enrolled patients with ER-positive (ER+), HER2-negative (HER2-) aBC [shown prior endocrine therapy (ET) sensitivity or untreated de novo aBC; ≤1 prior therapies for aBC but must not have received a prior CDK4/6 inhibitor]. Patients were randomized, based on menopausal status and presence of visceral metastases, to receive imlunestrant + abemaciclib OR imlunestrant + abemaciclib + AI. Men and premenopausal women received a concomitant GnRH agonist. Serial plasma samples were obtained for PK and ctDNA analysis. Key endpoints included safety and tolerability, PK, objective response rate (ORR) per RECIST v1.1 (ORR: complete response [CR] or partial response [PR]) in patients with measurable disease), and clinical benefit rate (CBR: CR or PR, or stable disease ≥24 weeks) in patients enrolled ≥24 weeks prior to data cut.

Results: As of 26 May 2022, 85 patients have received imlunestrant [n=80 at 400 mg (RP2D); n=5 at 800 mg] in combination with abemaciclib (150mg twice daily) ± AI. Forty-eight (56%) patients had visceral disease and 9% had at least 1 ESR1 mutation detected in ctDNA at baseline. Patients were predominantly (75%) ET pre-treated, 51% with an AI; and 8% and 5%, respectively, had received prior chemotherapy or fulvestrant, for aBC. The most common treatment-emergent adverse events were diarrhea (87%), nausea (58%), fatigue (45%), neutropenia (39%) and abdominal pain (34%). The majority of treatment-related AEs (TRAEs)

were Grade 1 or 2, with Grade ≥ 3 TRAEs occurring in 36% of patients. Most common TRAEs at RP2D (400mg) were diarrhea (81%), nausea (45%), fatigue (33%) and neutropenia (35%). No patient discontinued treatment due to an AE. Dose reductions were required of both imlunestrant and abemaciclib in 6 (7%) patients and of either imlunestrant in 3 (4%) or abemaciclib in 22 (26%) patients. Preliminary efficacy is presented in Table 1.

Conclusion: Imlunestrant in combination with abemaciclib \pm AI showed acceptable safety and tolerability, comparable to the MONARCH 2 trial of fulvestrant + abemaciclib, along with evidence of clinical activity in ER+, HER2- aBC patients. These data suggest no additive toxicity of imlunestrant when administered in combination with abemaciclib, along with comparable clinical benefit to that observed in MONARCH 2. Further data will be presented at the meeting. The phase 3, EMBER-3 study is ongoing; evaluating imlunestrant, investigator's choice ET, and imlunestrant + abemaciclib in ET pre-treated ER+, HER2- aBC patients (NCT04975308).

Table 1. Preliminary efficacy in combination therapies in EMBER

Endpoint	Imlunestrant + abemaciclib N=42	Imlunestrant + abemaciclib + AI ^{a,b} N=43
ORR, n/N (%)	10/28 (36)	15/34 (44)
CBR, n/N (%)	26/37 (70)	28/38 (74)

N = number of subjects in population; n = number of subjects in the specified category

^a21 (49%) patients had received a prior AI. ^bORR includes 4 patients and CBR includes 1 patient with unconfirmed PR at the time of data cut, all of which have since been confirmed as PRs.

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12/8/2022

5:00 PM - 6:15 PM

Discussion 1 + Q&A: PD14-01, PD14-03, PD14-05, PD14-08, PD14-09

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Discussion 2 + Q&A: PD14-02, PD14-04, PD14-06, PD14-07

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5:00 PM - 6:15 PM

Poster Spotlight Discussion 14: Breast Cancer Risk Modeling

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5:00 PM - 6:15 PM

PD14-01

PD14-01 A model to assess the utility of risk-based screening algorithms

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Background:

Breast cancer screening recommendations vary around the world, but most are based on age or inherited genetic risk factors. For instance, the American Cancer Society recommends annual mammography plus breast MRI starting at age 30yr for women at high risk of breast cancer based mainly on family history or high-risk genes. Women at average risk (no strong family history or high-risk genes) are recommended to have the option of annual mammography starting at age 40yr. Risk-based screening, which aims to personalise screening to an individual woman's risk of breast cancer based on a more comprehensive risk assessment than just age, family history, or high-risk genes, might improve current screening strategies.

Methods:

We developed a deterministic model to estimate the incidence of advanced (node-positive) breast cancer (plus number of screens) for different risk-based screening strategies in a UK setting. The proportion of screen-detected and interval cancers was estimated for various

screening intervals using a model developed by Launoy et al. and parameters for sensitivity (0.92) and annual transition rate from asymptomatic to symptomatic disease (0.25) from The Swedish Two-County Trial. The proportion of node-positive cancers was estimated for screen-detected (22%) and interval (53%) cancers, using data from the NHS Breast Screening Programme (England, 2015-18, women aged 47yr+).

Choice of mammography screening regimen was based on Tyrer-Cuzick 10yr risk (v8 including age, family history, reproductive factors, benign breast disease, SNPs and breast density). The proportion of women in each risk group was estimated from a UK cohort study investigating breast cancer risk at screening (PROCAS). In a hypothetical cohort of 3.45M women, 1M women would be identified as either high-risk (>8% 10yr risk; n=241,379) or low-risk (< 1.4% 10yr risk; n=758,621). In these 1M high/low-risk women, we evaluated two risk-based screening scenarios, comparing their effects with usual triennial screening starting at age 50yr (which was proposed for the 2.45M women at intermediate-risk (1.4-8% 10yr risk)).

Scenario (1): Changing screening interval based on risk (high-risk every 1yr; low-risk every 5yr) for screening between 50-70yr.

Scenario (2): Changing the starting age of screening based on risk (high-risk start annual screening at 45yr followed by triennial screening from 50yr; low-risk start triennial screening at 55yr); follow-up 45-55yr.

We assessed the trade-off between the decreased/increased number of node-positive breast cancers and increased/decreased number of screens with the high/low-risk regimens, respectively. A sensitivity analysis considered risk stratification without breast density.

Results:

Scenario (1): Changing screening interval based on risk reduced the number of node-positive cancers in high-risk women by 2,194 (with 3.14M additional mammograms) and increased the number of node-positive cancers in low-risk women by 910 (with 2.28M fewer mammograms) when compared with usual screening; a difference of 1,284 fewer node-positive cancers and 862,069 additional screens.

Scenario (2): Additional annual mammograms for high-risk women at 45-49yr reduced the number of node-positive cancers by 1,392 (with 1.21M additional mammograms); starting triennial screening at 55yr rather than 50yr for low-risk women increased the number of node-positive cancers by 841 (with 1.52M fewer mammograms); a difference of 551 fewer node-positive cancers and 310,345 fewer screens.

Excluding breast density from risk assessment reduced the number identified as high or low-risk, and thus the number of advanced cancers prevented and screens required, but the overall findings were unchanged.

Conclusion:

Changing the starting age of screening based on risk of breast cancer is likely to be more effective per screen required at reducing the rate of advanced breast cancer than changing the screening interval based on risk.

Table 1: Results for Scenario (1)

Population	N (%)	Usual screening		Risk-based screening		Risk-based versus Usual screening	
		Number of node+ (%)	Number of screens (%)	Number of node+ (%)	Number of screens (%)	Δ Number of node+ (%Δ)	Δ Number of screens (%Δ)
Tyrer-Cuzick 10yr risk group							
High (>8%)	241,379 (7%)	11,640 (15%)	1,689,655 (7%)	9,446 (12%)	4,827,586 (19%)	-2,194 (-19%)	+3,137,931 (+186%)
Intermediate (1.4-8%)	2,448,276 (71%)	58,975 (76%)	17,137,931 (71%)	58,975 (77%)	17,137,931 (69%)	N/A	N/A
Low (<1.4%)	758,621 (22%)	6,984 (9%)	5,310,345 (22%)	7,894 (10%)	3,034,483 (12%)	+910 (+13%)	-2,275,862 (-43%)
Entire 'cohort'	3,448,276 (100%)	77,599 (100%)	24,137,931 (100%)	76,315 (100%)	25,000,000 (100%)	-1,284 (-2%)	+862,069 (+4%)

Risk-based screening (changing screening interval based on risk: high-risk every 1 year; low-risk every 5 years) versus usual screening (every 3 years) between age 50-70 years (plus an additional 3 years of follow-up to adjust for the effect of screening on risk of breast cancer). N: Number; %: percentage; node+: Node-positive breast cancer; Δ: Difference; yr: Year; N/A: not applicable.

Table 2: Results for Scenario (2)

Setting	Results	
High-risk (>8% Tyrer-Cuzick 10yr risk; n=241,379; 24% of 1M high/low-risk)	Number of node+	Number of screens
Usual screening	2,741	0
Risk-based screening	1,349	1,206,897
	Δ Number of node+	Δ Number of screens
Risk-based versus Usual screening	-1,392	+1,206,897
Low-risk (<1.4% Tyrer-Cuzick 10yr risk; n=758,621; 76% of 1M high/low-risk)		
Usual screening	1,297	1,517,241
Risk-based screening	2,138	0
	Δ Number of node+	Δ Number of screens
Risk-based versus Usual screening	+841	-1,517,241
Trade-off (High-risk versus Low-risk)		
Risk-based versus Usual screening	-551	-310,345

Risk-based screening (changing the starting age of screening based on risk: high-risk start annual screening at age 45-49 years followed by triennial screening from age 50 years; low-risk start triennial screening at age 55 years) versus usual screening (triennial screening starting at age 50 years), with follow-up from age 45-55 years. n: Number; 1M: 1 million; node+: Node-positive breast cancer; Δ: Difference; yr: Year.

Table 3: Results for sensitivity analysis - Scenarios (1) and (2) with risk assessment including/excluding breast density

	Risk-based versus Usual screening			
	Tyrer-Cuzick model with breast density (high-risk n=241,379; low-risk n=758,621)		Tyrer-Cuzick model without breast density (high-risk n=172,414; low-risk n=620,690)	
	Δ Number of node+	Δ Number of screens	Δ Number of node+	Δ Number of screens
Scenario (1)				
High-risk (>8% Tyrer-Cuzick 10yr risk)	-2,194	+3,137,931	-1,609	+2,241,379
Low-risk (<1.4% Tyrer-Cuzick 10yr risk)	+910	-2,275,862	+607	-1,862,069
Trade-off (High-risk versus Low-risk)	-1,284	+862,069	-1,002	+379,310
Scenario (2)				
High-risk (>8% Tyrer-Cuzick 10yr risk)	-1,392	+1,206,897	-1,021	+862,069
Low-risk (<1.4% Tyrer-Cuzick 10yr risk)	+841	-1,517,241	+561	-1,241,379
Trade-off (High-risk versus Low-risk)	-551	-310,345	-460	-379,310

Scenario (1): Risk-based screening (changing screening interval based on risk: high-risk every 1 year; low-risk every 5 years) versus usual screening (every 3 years) between age 50-70 years (plus an additional 3 years of follow-up to adjust for the effect of screening on risk of breast cancer). Scenario (2): Risk-based screening (changing the starting age of screening based on risk: high-risk start annual screening at age 45-49 years followed by triennial screening from age 50 years; low-risk start triennial screening at age 55 years) versus usual

screening (triennial screening starting at age 50 years), with follow-up from age 45-55 years. n: Number; node+: Node-positive breast cancer; Δ : Difference; yr: Year.

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12/8/2022

5:00 PM - 6:15 PM

PD14-02

PD14-02 Ten-year follow-up of an image-based AI risk model for breast cancer

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Background: Artificial intelligence based, image-derived short-term risk models for breast cancer have shown high discriminatory performance compared to traditional lifestyle familial-based risk models. However, the long-term performance has not yet been investigated. Methods: In this study, we investigated the long-term performance for predicting breast cancer throughout 10 years using an image-based risk model and compared the results to a traditional lifestyle familial-based risk model. We performed a nested case-control study based on a mammography screening cohort conducted since 2010 in Sweden for women aged 40-74. Mammograms, age, lifestyle and familial risk factors were collected at study entry. In the breast cancer register update in 2022; 2,028 incident breast cancers were included together with 8,398 controls that were matched to the cases on year of prior baseline mammogram. The image-based model extracted mammographic features (density, microcalcifications, masses, left-right breast asymmetries of these features) and age from the baseline mammograms. Tyrer-Cuzick risk model used self-reported lifestyle and familial risk factors to estimate risk at study-entry. Absolute risks were estimated using the risk models. We estimated model performances using Area Under the receiver operating characteristic Curves (AUC) statistics of the absolute risks and, risk ratios of women classified as high-risk and low risk using NICE and USPSTF guidelines. Results: The AUCs of the image-derived risk model ranged from 0.76 (95%CI 0.72-0.81) to 0.66 (95%CI 0.65-0.67) for breast cancers developed 1-10 years after study-entry. The corresponding Tyrer-Cuzick AUCs were 0.68 (95%CI 0.63-0.73) to 0.62 (95%CI 0.60-0.63). For estrogen negative and symptomatic cancers, the AUCs for the image-derived model were ≥ 0.75 during the first 2 years. Women with high and low mammographic density showed similar AUCs. Throughout the 10-years of follow-up, 20% of all women with cancers were deemed high risk at study-entry by the image-derived risk model compared to 6% of all women with cancers identified as high risk by the lifestyle familial-based model ($p < 0.01$). Conclusion: The image-derived model outperformed the lifestyle familial-based model both for short-term and long-term risk assessment and, could be used for identifying women who possibly could benefit from additional examinations and primary prevention.

Disclosure(s):

Mikael Eriksson, n/a: iCAD: Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Royalty (Ongoing)

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5:00 PM - 6:15 PM

PD14-03

PD14-03 Reappraising the Fanconi Anemia DNA repair pathway in breast cancer risk and precision intervention: Insights and opportunities from the City of Hope INSPIRE study

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Background: Fanconi Anemia (FA) proteins facilitate homologous recombination (HR)-mediated repair of DNA interstrand cross-links. Germline monoallelic, pathogenic/likely pathogenic (P/LP) variants in the highly-penetrant (HP) breast cancer (BC) FA genes, BRCA1 (FANCS), BRCA2 (FANCD1) and PALB2 (FANCN)), compromise HR and predispose to hereditary BC. The effects of monoallelic, pathogenic variants in other non-HP BC FA genes upon HR and BC predisposition remain less understood. In this investigation we report the germline mutational landscape of FA gene P/LP variants and somatic molecular consequences of patients with BC diagnoses from City of Hope's (COH) INSPIRE (Implementing Next-generation Sequencing for Precision Intervention and Risk Evaluation) study.

Methods: COH-INSPIRE is a universal access study open to all patients at COH with a personal and/or family history of cancer. Patients undergo custom panel-based germline genetic testing to detect P/LP single nucleotide variants (SNVs), short insertions/deletions (indels) and exon-level deletions/duplications in 155 cancer-predisposition genes including the HP BC FA genes and 15 non-HP BC FA genes [FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCI, FANCI, FANCI, FANCI, FANCI (BRIP1), FANCL, FANCM, FANCO (RAD51C), FANCP (SLX4), FANCO (ERCC4) and FANCU (XRCC2)]. Patients' tumor specimens undergo somatic tumor (>400X)-normal (>180X) whole exome and transcriptome sequencing (>50 million reads). Somatic sequencing identifies P/LP SNVs, indels, copy number events, and fusions. Secondary analyses assessed somatic homologous recombination deficiency (HRD) by examining tumor mutational signatures, as well as an ensemble HRD score derived by combining individual genomic loss of heterozygosity, telomeric allelic imbalance and large-scale molecular transition scores. Reference comparison of germline and somatic features to current FDA therapeutic guidelines and NIH clinical trials registrations determined eligibility for precision therapeutic intervention and clinical trial enrollment.

Results: Of 7,584 patients enrolled in COH-INSPIRE, 1,651 (21.8%) patients had a BC diagnosis. Germline panel testing of BC patients identified 204 (12.4%) with germline P/LP variant in a FA gene. Greater than one third of FA gene-altered BC patients (37.7%) carried a P/LP variant in a non-HP BC FA gene. We observed that BC patients with a non-HP BC FA gene variant may demonstrate HR compromise as evidenced by presence of a Signature 3 mutational profile or an elevated combined HRD score (> 33 and/or > 42). (Table 1) Further, we identified ostensible segregation of triple negative BC in a family harboring a germline pathogenic variant in FANCG. With regard to precision clinical actionability (i.e. qualification for targeted therapeutic intervention [PARP inhibitor (PARPi)] and/or clinical trial) for patients with advanced stage BC: All patients with germline P/LP HP BC FA gene variant and 20.7% (N=16) of patients with a P/LP FA non-HPBC FA gene variant met criteria for treatment with on/off-label PARPi. 100% of patients with advanced BC with germline P/LP HP BC or non-HPBC FA gene variant qualified for a clinical trial.

Conclusions: Patients with BC often carry a germline monoallelic, P/LP FA gene variant; in more than one third, the FA gene alteration occurs in a non-HP BC FA gene. BC patients harboring a monoallelic germline non-HP BC P/LP FA gene may exhibit somatic mutational signatures and HRD scoring consistent with compromise of HR. Somatic tumor evaluation of BC patients with germline P/LP non-HP BC FA gene variants expands opportunities for precision therapeutic intervention and clinical trial enrollment. Continued appraisal will clarify emerging questions of germline non-HP P/LP FA gene-associated autosomal dominant BC risk and management as well as facilitate optimization of precision BC care.

Table 1 Summary Molecular Features of BC patients with P/LP Variants in FA gene from COH-INSPIRE

Gene	Number of BC Patients with P/LP Germline Variant	% Patients with P/LP FA Variant	Mean % Mutational Signature 3 (HR Deficiency)	% BC tumor specimens with HRD score ≥ 33	% BC tumor specimens with HRD score ≥ 42
Highly Penetrant BC Predisposition FA Gene					
BRCA2 (FANCD2)	53	62.3	27.8	93.1	79.3
BRCA1 (FANCS)	47		32.7	96.3	85.2
PALB2 (FANCN)	27		30.7	93.8	81.2
Other FA Genes					
FANCM	20	37.7	6.5	75.0	58.3
FANCA	18		14.4	57.1	35.7
FANCI (BRIP1)	12		17.8	85.7	57.1
FANCC	7		24.2	100	75.0
FANCD2	4		0.45	50.0	50.0
FANCG (ERCC4)	4		0.0	50.0	50.0
FANGL	3		0.0	100	100
FANCP (SLX4)	2		0.0	50.0	0.0
FANCG	2		30.1	100	100
FANCI	2		N/A	N/A	N/A
FANCO (RADS1C)	1		18.5	0.0	0.0
FANCE	1		0.0	0.0	0/0
FANCF	1		6.5	100	100

Disclosure(s):

Laura Kruper, MD: No financial relationships to disclose

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other intellectual property or other ownership interest excluding diversified mutual funds)

(Ongoing); GI OnDemand: Consulting Fees (e.g., advisory boards) (Ongoing), Ownership

Interest (stocks, stock options, patent or other intellectual property or other ownership interest

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5:00 PM - 6:15 PM

PD14-04

PD14-04 Whole mammogram image-based Cox regression improves 5-year breast cancer prediction

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To efficiently capture data from mammographic breast images and classify long-term risk of breast cancer, we developed FLIP, a novel Cox regression-based framework that fully utilizes data in the mammograms beyond current density measures. FLIP use the extensive existing data that are currently ignored in the context of breast cancer risk stratification. More than 20 studies support texture features add value to risk prediction beyond breast density. However, the entire mammogram imaging data has a high dimension of pixels (~13 million per image), greatly exceeding the number of women in a cohort. FLIP was fitted and cross-validated within the Joanne Knight Breast Health Cohort excluding cases diagnosed in the first 6 months of entry.

The Joanne Knight Breast Health Cohort is comprised of over 10,000 women undergoing repeated mammography screening at Siteman Cancer Center and followed since 2010. All women had baseline mammogram at entry, provided a blood sample and completed a risk factor questionnaire. Mammograms are all using the same technology (Hologic).

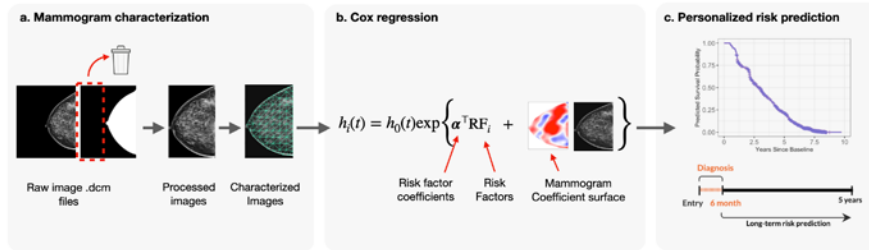
During follow-up through October 2020, we identified 246 incident breast cancer cases (pathology confirmed) and matched them to controls from the perspective cohort based on month of mammogram and age at entry.

We obtained an AUC of 0.68 (SE 0.03) including the whole mammogram image, age and BI-RADS (4th edition) density category; and AUC of 0.72 (SE 0.04) by adding in BMI and menopausal status to this model. These 5-year prediction performances exceed that of well-developed models based on epidemiologic risk factors ($P < 0.001$). FLIP offers standard statistical solutions and removes barriers to wider clinical use without prohibitive training data and extensive computational requirements, providing a transparent workflow ensuring high reproducibility. It should be accessible anywhere mammograms are used.

We conclude that using full mammogram images for breast cancer risk prediction captures additional information on breast tissue characteristics that relate to cancer risk, and improves prediction classification. This prediction algorithm can run efficiently in real time (in seconds) with processing of digital mammograms. Thus, this model can be easily implemented in mammography screening services and other clinical settings to guide real-time risk stratification to improve precision prevention of the leading cancer in women world-wide. Further analysis will quantify the value of adding other breast cancer risk factors, including polygenic risk scores. Addition of repeated mammogram images over time should further increase classification

performance. This approach has the potential to improve risk classification by using data already available for the vast majority of women already having repeated screening mammograms.

Schema overview of FLIP



The raw images are in the form of .dcm files before entering into FLIP. After automated processing and image alignment, the two CC-views (left and right) are average between the two breasts for characterization. The inputted 2D mammograms are first characterized with bivariate splines over triangulation to preserve spatial distribution of pixels and accommodate the irregular semi-circular breast boundary. The characterization is further optimized (see Supplemental Material) which provides a unique and closed-form solution. b. A simple Cox proportional hazards model is adopted using well-established risk factors (RF), including age, breast density (BI-RADS), BMI, menopausal status, parity, family history, and history of benign breast disease. The mammogram image acts as an additional risk factor in the Cox regression accompanied with a 2D coefficient surface. All inferential procedures with Cox regression are applicable to FLIP which provides a transparent workflow ensuring high reproducibility. $h_i(t)$ denotes the hazard function at time t for individual i , and $h_0(t)$ denotes the nonparametric baseline hazard function. c. Women who are diagnosed with breast cancer within the first 6 month of their mammogram date have been removed from this analysis and we focus on the 5-year risk. Discriminatory performance is assessed with AUC and validated via a 10-fold cross-validation.

Disclosure(s):

Shu Jiang, n/a: No financial relationships to disclose

Graham A. Colditz, n/a: No financial relationships to disclose

12/8/2022

5:00 PM - 6:15 PM

PD14-05

PD14-05 Prospective longitudinal validation of a breast cancer risk prediction model in a cohort of 130,058 women

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Background: Personalized breast cancer (BC) risk assessment depends on known traditional risk factors, specific germline mutations, and genome-wide polygenic risk scores (PRS). PRS explains a substantial proportion of genetic BC susceptibility. Accuracy of BC risk prediction may be improved by combining a PRS with traditional risk factors. We recently developed and validated a 149-SNP PRS for women of diverse ancestries using ancestry-informative genetic markers and combined this with version 7 of the Tyrer-Cuzick (TC) model to generate a Combined Risk Score (CRS). Here, we describe a pre-specified prospective longitudinal clinical validation of CRS as a predictor of BC risk.

Methods: Women in the U.S. who were referred for clinical genetic testing between January 2017 and February 2019 were matched to medical and hospital claims in an anonymized dataset. Women with a pathogenic mutation in a BC-related gene were excluded from analysis. Follow-up began 4 months after testing and extended to the earliest date of BC diagnosis, censoring at the time of BC preventive treatment, or November 1, 2019. Incident BC events were determined by an ICD10 code of C50.* and confirmed by relevant treatment codes. CRS calibration was evaluated by the ratio of observed (O) to expected (E) incident BCs for the full cohort, and for women split into event-based 5-year CRS risk deciles. Cox proportional hazards models were used to evaluate discriminatory accuracy in terms of hazard ratios (HR) with 95% confidence intervals (CI) and p-values from likelihood ratio chi-squared statistics.

Kaplan-Meier analysis was used to examine risk for women split into high- or low-risk groups according to a 3% 5-year CRS risk threshold.

Results: 130,058 women with 148,349 total patient years met study eligibility criteria and were matched to claims data. Over a median (range) follow-up of 12.1 (4.0-29.5) months, 340 incident BC events were observed. The CRS was well calibrated in the overall cohort with an O/E ratio of 1.11 (95% CI=0.99-1.23) and within deciles of predicted risk (Table). Importantly, in the highest risk decile, the O/E was 0.91 (95% CI=0.63-1.27) with CRS, but 0.67 (95% CI=0.46-0.94) with TC alone, illustrating the superior calibration of CRS. In a Cox model adjusted for age at testing, PRS had an HR per standard deviation (SD) of 1.48 (95% CI=1.33-1.64, $p=2.55 \times 10^{-13}$); the HR/SD was 1.43 (95% CI=1.29-1.59, $p=1.61 \times 10^{-11}$) after adjusting for family history. In a bivariate analysis using both CRS and TC to predict time to BC, CRS added significantly to the model after accounting for TC (HR/SD=2.89, 95% CI=2.12-3.94, $p=1.20 \times 10^{-11}$), whereas TC did not add significant information after accounting for CRS. 15,986 (12.3%) women were above the CRS high-risk threshold, including 123 with events. A total of 10,248 (7.9%) women were reclassified by the CRS model compared to the TC model. Among women who were classified as high-risk by TC, 32.6% were reclassified as low-risk by CRS; among those classified as low-risk by TC, 4.3% were reclassified as high-risk by CRS. The CRS high-risk group experienced events at over three times the rate of the low-risk group (HR=3.75, 95% CI=3.00-4.68, $p=6.39 \times 10^{-27}$).

Conclusion: The CRS was well-calibrated in predicting BC and significantly improved upon a traditional risk factor model. Clinical use of the CRS may lead to improved BC prevention and screening strategies.

Table: Absolute risk calibration by 5-year risk decile

Risk decile	Expected incidence	Observed incidence (95% CI)	O/E (95% CI)
<0.68%	0.55	1.00 (0.69-1.40)	1.83 (1.27-2.56)
0.68-1.04%	1.52	2.24 (1.55-3.13)	1.48 (1.02-2.06)
1.04-1.37%	2.21	2.93 (2.03-4.10)	1.33 (0.92-1.86)
1.37-1.70%	2.86	3.50 (2.42-4.89)	1.22 (0.85-1.71)
1.70-2.29%	3.74	2.76 (1.91-3.86)	0.74 (0.51-1.03)
2.29-2.80%	4.84	4.92 (3.41-6.87)	1.02 (0.70-1.42)
2.80-3.34%	5.91	6.61 (4.58-9.23)	1.12 (0.77-1.56)
3.34-4.04%	7.13	7.83 (5.43-10.95)	1.10 (0.76-1.53)
4.04-5.26%	9.00	9.00 (6.23-12.58)	1.00 (0.69-1.40)
>5.26%	13.59	12.38 (8.57-17.30)	0.91 (0.63-1.27)

Incidence is reported per 1,000 women-years. 34 breast cancers were observed per decile.

Disclosure(s):

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Prelude: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing);
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12/8/2022

5:00 PM - 6:15 PM

PD14-06

PD14-06 Polygenic risk score added to risk calculator improves prediction of breast cancer in U.S. Black women

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We recently derived an absolute breast cancer risk prediction model, the Black Women's Health Study (BWHS) model, for breast cancer in U.S. Black women using data from three large case-control studies and validated it in independent prospective data from the Black Women's Health Study (Palmer 2021). The BWHS model includes epidemiologic risk factors as well as family history of breast cancer and family history of prostate cancer. It does not include genetic variants because at the time of model development breast cancer polygenic risk scores performed poorly in women of predominantly African ancestry, primarily due to differences in allele frequency and linkage disequilibrium. More recently, Gao et al. (2022) developed and tested a polygenic risk score (PRS) using 56,943 SNPs for breast cancer in women of African ancestry (AA) based on 9,235 breast cancer cases and 10,184 controls from a large pooled analysis of studies from African American and African women; the c-statistic from cross-validation was 0.581, considerably better than in previous efforts. We evaluated whether adding this AA-PRS to the BWHS risk prediction model would improve risk stratification. We conducted a nested case-control study of 901 breast cancer cases and 1,576 controls matched on age and most recent questionnaire completed from among BWHS participants for whom genome-wide association data were available and who had not been included in the collaboration from which the PRS was derived and tested. We examined discriminatory accuracy, estimated by the area under the receiver operating characteristic curve (AUC), for the risk prediction model alone, the PRS alone, and the combination of risk prediction model and PRS, controlling for the matching factor "questionnaire cycle". We conducted the analyses within strata of 5-year age and then combined results using inverse-variance weighting. In preliminary analyses, the AUC was 0.579 for the risk prediction model alone and 0.600 for the AA-PRS alone. When the AA-PRS and the BWHS risk prediction model were both used as predictors in a logistic regression model, the AUC increased from 0.579 to 0.622. This improvement in risk stratification is similar to what Kachuri et al. (2020) obtained in an analysis of U.K. Biobank data, where adding a PRS to epidemiologic and personal risk factors showed an improvement from 0.572 to 0.635 in women of European ancestry. The present study provides external validation of a recently derived AA PRS and demonstrates the potential for improving risk stratification for U.S. Black women by adding a PRS to a breast cancer risk prediction model that already includes family history of breast cancer.

Disclosure(s):

Gary R. Zirpoli, PhD: No financial relationships to disclose

Kathryn L. Lunetta, PhD: No financial relationships to disclose
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PD14-07

PD14-07 Associations of Breast Cancer Risk Level and Prediction of Tumor Aggressiveness in the Athena Breast Health Network

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Background: The Athena Breast Health Network (Athena) is a University of California (UC) initiative integrating clinical care and research to drive improvements in breast cancer screening. Through standardized, self-reported clinical intake forms, a patient's breast health status and information regarding their breast cancer risk is captured before each mammography appointment. Breast cancer risk models provide a level of risk to develop breast cancer but do not take into account aggressiveness of breast cancer. Here, we evaluated outcome data of a large screening cohort for association between risk level and aggressiveness at diagnosis. Methods: We calculated Breast Cancer Surveillance Consortium (BCSC) risk scores for a cohort of 8,923 consented UCSF Athena participants from the years 2012-2018 with a median follow-up of 5-years. To identify those who developed invasive breast cancer on or after completing an Athena intake form, we performed a cancer linkage with the San Francisco Mammography Registry (SFMR), a local registry that regularly collects cancer data from the California Cancer Registry. We classified tumors as aggressive if they met one or more of the following criteria: hormone receptor (HR)-negative, HER2-positive, grade 3. All other tumors were classified as non-aggressive. We used student's t-tests to examine associations between BCSC 5-year risk score, the development of invasive breast cancer, and tumor aggressiveness among cases. To account for the association between older age and higher BCSC risk score (as well as HR-positive subtypes), we stratified by percentiles of BCSC risk by age (top 2.5% vs. bottom 97.5%). The top 2.5% by age threshold consistently identifies women with lifetime risk of 23–28% and was chosen as high-risk threshold to trigger annual screening in the WISDOM study (Dreher: PMID34843026). Results: Of 8,923 participants, 170 (2%) developed breast cancer during the follow-up period. The average 5-year BCSC risk score for women with breast cancer was 1.81% and 1.47% for those without ($p < 0.001$). Among women with breast cancer, 123 (72%) developed non-aggressive cancers and 47 (28%) developed aggressive cancers. The average 5-year BCSC risk score for women with non-aggressive and aggressive cancers was 1.89% and 1.60%, respectively ($p = 0.13$). In analyses stratified by percentile of BCSC risk by age, 521 (6%) participants had a BCSC 5-year risk score in the top 2.5% by age and 8,402 (94%) participants had a BCSC 5-year risk score in the bottom 97.5%. A higher percentage of women with non-aggressive cancers vs healthy women (controls) were in the top 2.5% by age ($p = 0.001$), but the percentage of aggressive cancers vs healthy women in the top 2.5% by age was similar ($p = 0.61$). Conclusion: Through this study we confirmed that higher 5-year BCSC risk scores are associated with higher overall breast cancer development. Interestingly, participants with the highest 5-year BCSC risk scores (top 2.5% by age), are more likely to develop cancers with non-aggressive features (low grade, hormone positive). This suggests that the BCSC model may preferentially predict less aggressive tumors, and those with the highest 5-year BCSC risk may be more likely to benefit from endocrine risk reduction therapy. There remains a gap in our ability to identify those at risk for aggressive cancers. Our findings highlight the need for screening programs to better understand who is at risk for what type of breast cancer. Current work is focused on developing models tailored to risk prediction of aggressive cancers.

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Katherine Leggat-Barr, BS: No financial relationships to disclose

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Rosalyn Sayaman, PhD: No financial relationships to disclose

Paige Warner, BS: No financial relationships to disclose

Kathy Malvin, B.A.: No financial relationships to disclose

Leah Sabacan, MBA: No financial relationships to disclose

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5:00 PM - 6:15 PM

PD14-09

PD14-09 The effect of timing of TP53 genetic testing on treatment and outcomes among women with Li-Fraumeni syndrome and breast cancer

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Background: Li-Fraumeni syndrome (LFS) is a pan-cancer predisposition syndrome caused by pathogenic germline TP53 variants. Breast cancer (BC) is the most prevalent tumor in women with LFS. The risk of secondary malignancies, including multiple primary BCs, other LFS-related cancers, radiation-induced sarcomas, and local recurrences are important clinical concerns in the LFS setting. The diagnosis of LFS may influence treatment decisions and outcomes. Methods: In this international multicenter study, we analyzed women with pathogenic or likely pathogenic germline TP53 variants and BC (DCIS or invasive breast carcinoma) diagnosed 2002-2022 from three retrospective LFS cohorts (Dana Farber Cancer

Institute, USA; Institut Gustave Roussy, France; Hospital Sírio-Libanês, Brazil). We excluded carriers of TP53 unconfirmed possibly mosaic variants, carriers of a 2nd pathogenic variant in another BC susceptibility gene, and those with missing data related to timing of genetic testing (TGT) or date of 1st BC diagnosis (dx). The overall cohort was divided in two groups: genetic testing before or at 1st BC dx (group A) and those with testing ≥ 1 year after 1st BC dx (group B). In cases with synchronous bilateral BC, we included the tumor of higher risk of recurrence (invasive, higher stage, more aggressive tumor biology) and excluded the other. The chi-square test was used to measure the association between TGT and other categorical variables. Results: 209 patients (pts) met criteria for this analysis. The median age of 1st BC dx was 35 years (IQR, 31-42). BC was the 1st cancer dx in 87.5% of the pts. Among 1st breast tumors, 38 were DCIS, 147 were early-stage BC (61 I, 49 II, 37 III) and 7 stage IV (17 missing). There were no differences between groups A and B regarding staging at dx. Missense TP53 variants were the most common type of germline mutation (n=154, 73.6%), with 60.4% (n=93) in the DNA-binding domain and 38.9% (n=60) in the tetramerization domain. Median follow-up from 1st BC dx was 6 years (IQR, 3-10). 53.1% of pts (n=111) underwent TP53 germline testing only after 1st BC dx. Family history of BC < 50 and non-BC malignancy prior to or synchronous with 1st BC dx were not associated with TGT (p=0.3 and p=0.2, respectively). 35.4% of pts developed a second primary BC (25 ipsilateral; 49 contralateral). Among pts without synchronous bilateral BC or metastatic BC at dx, 97 pts underwent contralateral risk reducing mastectomy (CRRM), 56.7% (55/97) as part of treatment surgery for the 1st BC. CRRM uptake was associated with TGT (A 70.3% vs B 41.6%, p=0.001). Of 194 pts with detailed data on surgical treatment (1st BC), 146 underwent mastectomies and 48 breast conserving surgery (BCS). Group A had more mastectomies (79.5% vs 61.2%, p=0.001) and less radiation therapy (10.2% vs 45.9%, p< 0.001). Among the irradiated pts, 9.8% (n=5) developed sarcomas in the irradiated field. Thirty-eight pts had BC recurrence: 21 loco-regional (A 6 vs B 15, p< 0.05), mostly in-breast, and 17 distant relapses. There was a significant statistical association between TGT and type of BC surgery (p=0.001), radiation-therapy (p< 0.001), CRRM uptake (p=0.001) and local relapses (p< 0.05). Conclusion: This analysis of BC in our sizable cohort of LFS patients with treatment data confirms that, timing of genetic testing affects some treatment options and outcomes, including surgical procedures and use or avoidance of radiation. These decisions appear to influence the risk of local recurrence or additional primary BC and radiation-induced sarcoma. Recognition of germline TP53 variants in breast cancer patients as part of genetic testing at diagnosis appears to have implications for treatment options and outcomes.

Disclosure(s):

Renata Sandoval, MD, PhD: No financial relationships to disclose

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Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory

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5:00 PM - 6:15 PM

Discussion 1 + Q&A: PD15-01, PD15-02, PD15-03 & PD15-11

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Discussion 2 + Q&A: PD15-04, PD15-05, PD15-06 & PD15-07

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Discussion 3 + Q&A: PD15-08, PD15-09, PD15-10 & PD15-12

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Poster Spotlight Discussion 15: Local Regional/Management of the Axilla

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5:00 PM - 6:15 PM

PD15-01

PD15-01 AXILLARY NODAL RECURRENCE IS RARE IN PATIENTS WITH NODE-POSITIVE BREAST CANCER UNDERGOING SLNB FOLLOWING NEOADJUVANT CHEMOTHERAPY : EARLY RESULTS OF THE NEOSENTITURK-TRIAL/MF-18-03

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Background:

Whether axillary lymph node dissection (ALND) following sentinel lymph node biopsy (SLNB) could be spared in patients with initially clinically positive axilla after neoadjuvant chemotherapy (NAC) is still controversial even though recent studies indicate that axillary recurrence seems to be a rare event. Our aim is to find out whether omitting ALND could be oncologically safe in patients undergoing SLNB after NAC.

Material and Methods

Of patients presented with c T1-4N1-3M0 disease, those undergoing SLNB after NAC were included in the prospective multicentre registry trial " MF18-03/BHWG" (ClinicalTrials.gov/NCT04250129). Cases with inflammatory breast cancer, distant metastases, pregnancy, bilateral breast cancer, or other cancers and those without adjuvant nodal radiotherapy were excluded from the study. The end points of the present report are the axillary nodal recurrence (AR) and locoregional recurrence (LRR) rates at a median follow-up more than 2 years, and determine factors associated with AR and LRR . The locoregional recurrences included ipsilateral, and contralateral axillary recurrences, infra-and supraclavicular recurrences, and recurrences in the mammaria interna region.

Results

Between January 2018 to January 2021, 2358 patients with cN(+) disease, who became cN0 after NAC, and underwent SLNB, were analyzed. Median age was 47 (range, 21-86). Of those, the majority of patients had cT1-2 (80.5%) and N1 (80.3%) disease. Following NAC, half of the patients (50%) had breast conserving surgery, whereas the remaining half had mastectomy (50%). Of 2358 patients, 908 (38.5%) had ALND following SLN (ypN+, 85%) and 1450 (61.5%) underwent SLNB alone (ypN0, 72%). SLNB was performed by using the blue dye technique-alone in 66.6% of patients and by targeted axillary dissection in 659 patients (27.9%). Of those, 819 (34.8%) were HER2(+) and 373 (15.8%) were triple negative. The pCR rates for the axilla, breast and both for the axilla and breast were 50%, 35% and 28%, respectively. At a median follow-up time of 28 months (range, 12-62), the LRR, AR and isolated AR rates were 0.6% (n=14), 0.25% (n=6) and 0.13% (n=3), respectively. Furthermore, no significant difference could be found in LRR- and AR- rates between SLNB-alone and ALND groups regardless of the definitive nodal pathology (Table 1). Nodal recurrences were seen at a median of 12 months after the surgery. Of 6 cases with AR, 3 had synchronous local recurrences in breast, and 2 of them also had lung metastases in addition to local recurrence. All patients with AR were interestingly found to have HER2(+) or triple negative breast cancer at the initial diagnosis, and had residual invasive cancer in the breast surgical specimen. Logistic regression analyses revealed that patients with AR were significantly more likely to be younger than 45 (RR=7.81 ; 95% CI, 0.91-66.91) and have a cN2-3 (RR=4.1; 95% CI, 0.83-20.38), and non-luminal breast cancer (RR=12.47; 95% CI, 1.45-106.9) at the initial diagnosis (Table 2). Similarly, patients with LRR were more likely to present with cN2-3 disease (RR=3.09; 95% CI, 1.07-8.94) and non-

luminal pathology (RR=6.27; 95%CI, 1.96-20.06) .

Conclusion: This large prospective registry data also suggest that nodal recurrences can be detected at very low rates within 3 years after surgery in patients with clinically node-positive disease following NAC regardless of the extent of axillary surgery or nodal pathology as long as regional nodal radiation is provided. Since patients with early nodal recurrences have an aggressive tumor biology with a potential of systemic recurrences, effective adjuvant systemic therapies should be considered in those with HER2(+) or triple negative residual breast cancer after surgery following adjuvant nodal radiation.

Table 1. Local, locoregional and systemic recurrences in cT1-4N1-3 patients with ypN0/ypN(+) disease (n=2358)

Variables	All (n=2358) n(%)	SLNB (n=1450) n(%)	ALND (n=908) n(%)	<i>p</i>	SLNB(-) (n=1042) n(%)	SLNB(+) (n=408) n(%)	<i>p</i>	AD(-) (n=137) n(%)	AD(+) (n=771) n(%)	<i>p</i>
Local recurrence after BCT*										
Yes	13(1.1)	9(1.1)	4(1.1)	0.999 ^a	8(1.3)	1(0.5)	0.459 ^a	0(0)	4(1.3)	0.999 ^a
No	1173(98.9)	805(98.9)	368(98.9)		593(98.7)	212(99.5)		57(100)	311(98.7)	
Chest wall recurrence after mastectomy										
Yes	13(1.1)	5(0.8)	8(1.5)	0.384 ^b	4(0.9)	1(0.5)	0.999 ^a	0(0)	8(1.8)	0.612 ^c
No	1159(98.9)	631(99.2)	528(98.5)		437(99.1)	194(99.5)		80(100)	448(98.2)	
Locoregional recurrence**										
Yes	14(0.6)	6(0.4)	8(0.9)	0.245 ^b	5(0.5)	1(0.2)	0.999 ^a	2(1.5)	6(0.8)	0.346 ^a
No	2344(99.4)	1444(99.6)	900(99.1)		1037(99.5)	407(99.8)		135(98.5)	765(99.2)	
Ipsilateral Axillary recurrence										
Yes	6(0.25)	3(0.2)	3(0.3)	0.682 ^a	3(0.3)	0(0)	0.564 ^a	0(0)	3(0.4)	0.999 ^a
No	2352(99.75)	1447(99.8)	905(99.7)		1039(99.7)	408(100)		137(100)	768(99.6)	

*BCT=Breast Conserving Therapy

**=Axilla, infraclavicular, supraclavicular, mammaria interna and contralateral axillary metastases

p<0.05. **a**=Fisher's Exact Test, **b**=Pearson Chi-Square Test, **c**= Pearson Chi-Square Test.

Table 2. Factors associated with axillary and locoregional recurrences (AR=axillary recurrences, LRR=locoregional recurrences, pCR= pathologic complete response)

	AR (n=6) (%)	Patients without AR (%)	p	LRR (N=14) (%)	Patients without LRR (%)	p
<45	5 (0.5)	919 (99.5)	0.037*	7 (0.76)	917 (99.24)	0.421
>45	1 (0.07)	1433 (99.9)		7 (0.5)	1427 (99.5)	
Tumor pathology						
luminal	1(0.1)	1678(99.9)	0.009*	4(0.2)	1675(99.8)	0.001*
Non-luminal	5(0.7)	674(99.3)		10(1.5)	669(98.5)	
cN1	3(0.2)	1891(99.8)	0.095	8(0.4)	1886(99.6)	0.040*
cN2-3	3(0.6)	461(99.4)		6(1.3)	458(98.7)	
pCR (Breast)						
(+)	0(0)	820(100)	0.098	0(0)	820(100)	0.003*
(-)	6(0.4)	1532(99.6)		14(0.9)	1524(99.1)	

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PD15-02

PD15-02 Long Term Outcome in Patients with Nodal-Positive Breast Cancer Treated with Sentinel Lymph Node Biopsy Alone After Neoadjuvant Chemotherapy

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Importance:

The use of neoadjuvant chemotherapy (NAC) in the clinical care of breast cancer patients has increased considerably over recent years especially in node positive cases. For patients who have axillary nodal metastases prior to NAC, the prevailing standard of care is to undergo an axillary lymph node dissection (ALND), regardless of response to therapy. Sentinel lymph node biopsy (SLNB) has yet to be accepted as the standard staging procedure in patients who had clinical complete response in the axilla following NAC. This is due to the presumed high false negative rate associated with SLNB in such scenario. But there are limited data on the long term outcome of these patients who are only treated with SLNB alone.

Aim:

A retrospective cohort study comparing the long term outcome of breast cancer patients with clinically node positive disease (N1) but turned clinically node negative (N0) following NAC, receiving SLNB alone versus ALND.

Methods:

Patients who had pathologic proven N1 breast cancer (before NAC) treated with NAC and turned clinically N0 from January 2009 to December 2014 were identified from Asan Medical Center breast cancer database in South Korea. Primary endpoint was axillary recurrence rate (ARR) and secondary endpoints were disease-free survival (DFS) and overall survival (OS). These outcomes were reported for patients who had SLNB alone versus ALND.

Results:

561 patients with clinically stage N1 (cN1) cancer treated with NAC and turned clinically stage N0 (cN0) were identified. 253 (45.1%) patients received SLNB only while 308 (54.9%) patients had ALND. The clinicopathological features of these patients were illustrated in Table 1. Majority of these patients received adjuvant radiotherapy, 81.2% in the SLNB group and 76.5% in the ALND group. In the pathologically stage N0 (ypN0) group, at a median follow up of 69 months, ARR was 3.0% in the SLNB only group and 1.7% in the ALND group (p=0.704). DFS and OS were not significantly different between patients with SLNB alone versus ALND (p=0.561 and 0.810 respectively). Median number of SLN harvested in the SLNB only group is 5 (range 1 -17).

In the pathologically stage N1 (ypN1) group with only 1-2 lymph node positive for metastasis, at a median follow up of 66 months, ARR was 5.8% in the SLNB group and 4.7% in the ALND group (p=0.768). There was no significant difference in DFS and OS between the SLNB and ALND group (p=0.537 and 0.645). In the SLNB only group, the median number of positive lymph node was 1 (range 1-2), the median number of sentinel lymph node was 6 (range 2-18).

Conclusion:

In cN1 breast cancer patients who were converted to cN0 following NAC, axillary recurrences were rare. No statistically significant differences were noted in DFS and OS between patients with SLNB or ALND. Our findings suggest that these patients may be safely treated with SLNB only, even when there are up to 2 positive SLNs.

Table 1 Clinicopathological features of breast cancer patients with nodal disease and NAC

	ypN0 (N=477)				P	ypN0 or ypN1mi (N=133)				P
	SLNB (N=314)		ALND (N=163)			SLNB (N=58)		ALND (N=75)		
Median follow-up (months)	66		61			65		66		
	N	%	N	%		N	%	N	%	
Menopausal status					0.166					0.399
Premenopausal	194	61.8	90	55.2		38	65.5	46	61.3	
Postmenopausal	120	38.2	73	44.8		20	34.5	29	38.7	
T stage					0.010					0.567
T1 and 2	259	82.5	118	72.4		44	75.9	60	80.0	
T3 and 4	55	17.5	45	27.6		14	24.1	15	20.0	
Grade					0.688					0.808
1	2	0.6	0	0.0		0	0	0	0	
2	202	64.4	109	66.9		47	81.0	62	82.7	
3	110	35.0	54	33.1		11	19.0	13	17.3	
Receptor status *					0.719					0.570
ER+ Her 2-	78	24.8	35	21.5		28	48.3	34	45.3	
ER+ Her 2+	91	29.0	48	29.4		16	27.6	19	25.3	
ER- Her 2+	61	19.4	38	23.3		4	6.9	11	14.7	
ER- Her 2-	84	26.8	42	25.8		10	17.2	11	14.7	
Complete Pathological Response					0.877					NA
Yes	168	53.5	86	52.8		NA	NA	NA	NA	
No	146	46.5	77	47.2		NA	NA	NA	NA	
Axillary recurrence	10	3.2	3	1.8	0.398	7	12.1	3	4.0	0.095
Local recurrence	5	1.6	9	5.5	0.022	4	6.9	4	5.3	0.728
Distant metastasis	19	6.1	19	11.7	0.032	7	12.1	7	9.3	0.610

*ER estrogen receptor

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PD15-03

PD15-03 Incorporation of Repeated Core Needle Biopsy and Targeted Fine Needle Aspiration to Optimize Axillary Surgery After Neoadjuvant Chemotherapy in Node-positive Breast Cancer: A Prospective Feasibility Study

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Background

It is of substantial importance to tailor axillary surgery after neoadjuvant chemotherapy (NAC) based on tumor biology and response to treatment. This study aimed to determine the accuracy of repeated core needle biopsy (RCNB) in breast to predict nodal response after NAC.

Methods

Eligible patients with clip insertment into pathologically-proven positive node underwent RCNB during NAC. Targeted fine needle aspiration (TFNA) of clipped lymph node (CLN) was performed in a subset of patients after NAC. All patients ultimately underwent axillary surgery. RCNB and TFNA results were compared with surgical pathology.

Results

Data from 189 eligible patients were analyzed. The overall axillary pCR was 57.1%. The false-negative rate (FNR) of RCNB across the whole cohort was 12.1% (95% CI, 5.3%–18.9%), and exploratory subgroup analysis revealed an excellent ability to predict the presence of residual nodal disease in estrogen receptor-positive breast cancer with a low FNR of 1.6% (95% CI, 0.0%–4.9%) (Table 1). Adopting a strategy where only patients with negative RCNB undergo targeted axillary dissection (TAD) would potentially reduce the FNR of TAD from 9.3% to 2.3%. Furthermore, combination of RCNB and TFNA demonstrated a FNR of 2.2% (95% CI, 0.0%–6.6%), and negative predictive value of 94.1% (95% CI, 81.6%–100.0%) (N = 87) (Table 2). The proposed algorithm based on RCNB and TFNA is helpful in optimizing axillary surgery by avoiding 25 unnecessary attempts as well as 2 false-negative cases in TAD and conferring 10 patients omission of axillary surgery.

Conclusions

Combination of RCNB and TFNA allows for an accurate assessment of nodal response after NAC. These results may facilitate reliable identification of suitable candidates for de-escalation or elimination in axillary surgery.

Table 1. Overall Cohort Diagnostic Accuracy of Repeated Core Needle Biopsy to Predict Nodal Response (N = 189)

	% (95%CI)
All subtypes (n = 189)	
Accuracy	70.4% (63.8-76.9)
Sensitivity	87.9% (81.1-94.7)
Specificity	54.1% (44.0-64.1)
NPV	82.8% (73.3-92.3)
PPV	64.0% (55.5-72.5)
ER+HER2- (n = 53)	
Accuracy	84.9% (74.9-94.9)
Sensitivity	100.0% (100.0-100.0)
Specificity	38.5% (7.9-69.1)
NPV	100.0% (100.0-100.0)
PPV	83.3% (72.4-94.3)
ER+HER2+ (n = 50)	
Accuracy	70.0% (56.8-83.2)
Sensitivity	95.2% (85.3-100.0)
Specificity	51.7% (32.4-71.1)
NPV	93.8% (80.4-100.0)
PPV	58.8% (41.4-76.3)
ER-HER2+ (n = 52)	
Accuracy	61.5% (47.9-75.2)
Sensitivity	56.3% (28.9-83.6)
Specificity	63.9% (47.4-80.4)
NPV	76.7% (60.6-92.7)
PPV	40.9% (18.6-63.2)
ER-HER2- (n = 34)	
Accuracy	61.8% (44.6-79.0)
Sensitivity	84.6% (61.9-100.0)
Specificity	50.0% (26.0-74.0)
NPV	47.6% (24.3-70.9)
PPV	52.4% (29.1-75.7)

Abbreviations: ER, estrogen receptor; HER2, human epidermal factor receptor 2; NPV, negative predictive value; PPV, positive predictive value.

Table 2. Diagnostic Accuracy of Repeated Core Needle Biopsy in Breast, Targeted Fine Needle Aspiration and the Combination in Cohort 2 (N = 87)

	RCNB alone, % (95%CI)	TFNA alone, % (95%CI)	Combination, % (95%CI)
% (95%CI)			
Accuracy	64.4% (54.1-74.6)	74.7% (65.4-84.0)	70.1% (60.3-79.9)
Sensitivity	87.0% (76.8-97.1)	54.3% (39.4-69.3)	97.8% (93.4-100.0)
Specificity	39.0% (23.4-54.6)	97.6% (92.6-100.0)	39.0% (23.4-54.6)
NPV	72.7% (52.5-92.9)	65.6% (53.3-77.8)	94.1% (81.6-100.0)
PPV	61.5% (49.4-73.7)	96.2% (88.2-100.0)	64.3% (52.8-75.8)

Abbreviations: NPV, negative predictive value; PPV, positive predictive value; RCNB, repeated core needle biopsy; TFNA, targeted fine needle aspiration.

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5:00 PM - 6:15 PM

PD15-04

PD15-04 Overall survival following breast conserving surgery and adjuvant radiotherapy compared with mastectomy for early stage breast cancer: a systematic review and meta-analysis

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Background Breast conserving surgery with adjuvant radiotherapy (BCS+RT) and mastectomy are currently offered as oncologically equivalent options for the surgical management of early breast cancer based on findings from randomised controlled trials (RCTs) conducted over four decades ago. Since then, locoregional and systemic breast cancer treatments have improved significantly and several recent observational studies suggest a survival advantage in patients receiving BCS+RT compared to those having mastectomy. If BCS+RT is oncologically superior to mastectomy, this may dramatically impact surgical treatment recommendations. The aim of this systematic review was to identify, critically appraise and summarise the contemporary literature comparing survival following BCS+RT and mastectomy to inform surgical decision-making for patients with early breast cancer. Methods A systemic search of MEDLINE, Cochrane Central Register of Controlled Trials and Embase identified studies published between 1st January 2000 to 22nd September 2021. Included were primary research studies published in English comparing overall survival in women undergoing primary surgery with either BCS+RT or mastectomy for unilateral stage I to III breast cancer. Excluded were studies evaluating neoadjuvant chemotherapy; rare breast cancer subtypes (e.g. mucinous) or in specific patient populations (e.g. pregnancy associated breast cancer) and those that completed recruitment before 1st January 1990. We used the ROBINS-I tool to assess the risk of bias in study results and GRADE to assess the overall certainty of evidence. All papers without critical risk of bias were included in a quantitative meta-analysis. Where more than one study reported outcomes in overlapping population-based registry cohorts, the study with the most recent data on the largest cohort was selected for analysis. The primary analysis was a random effects meta-analysis with a fixed effect model undertaken as sensitivity analysis. A

secondary meta-analysis was performed for studies only including triple negative breast cancers. All analyses were conducted using STATA17. Results 10,876 abstracts were screened and 157 full-text papers assessed for eligibility, of which 93 (17 multi-centre observational studies, 30 were single-centre observational studies and 46 registry-based studies) met the inclusion criteria for the review. 25 papers were excluded from meta-analysis due to an overall critical risk of confounder bias and 27 were excluded due overlapping study populations. 36 studies (34 with serious risk of bias and 2 with moderate risk of bias) reporting survival outcomes on 1,321,291 patients (729,789 undergoing BCS+RT and 591,502 undergoing mastectomy) were included in the meta-analysis. The pooled hazard ratio was 0.72 (95% CI 0.64– 0.81, $p < 0.001$, I² 97.6%) demonstrating improved overall survival for patients undergoing BCS+RT compared with those receiving mastectomy. The sensitivity analysis, using a fixed effect model, showed a hazard ratio of 0.88 (95% CI 0.87 – 0.89, $p < 0.001$, I² 97.6%) for survival in women undergoing BCS+RT compared with mastectomy. Meta-analysis of 8 studies reporting survival in 17,181 patients with triple negative breast cancer showed a hazard ratio of 0.73 (95% CI 0.68 – 0.79), $p < 0.001$, I² 34.7%) for those receiving BCS+RT versus mastectomy. Discussion This meta-analysis provides further, albeit very low certainty evidence, that overall survival is improved following BCS+RT compared with mastectomy in a contemporary cohort of patients treated for early-stage breast cancer. These results should be interpreted with caution due to the heterogeneity of included studies and the high risk of bias associated with observational data. As future RCTs will not be feasible, well-designed large-scale prospective observational studies are needed to provide better evidence to support surgical decision-making in early-stage breast cancer.

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5:00 PM - 6:15 PM

PD15-05

PD15-05 Breast Conserving Therapy Has Improved Survival Without An Increased Risk Of Locoregional Recurrence Compared To Mastectomy In Both Clinically Node Positive And Node Negative Patients.

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Background:

Randomized trials demonstrated equivalent survival between breast conserving surgery (BCS) combined with radiotherapy (Breast conserving therapy, BCT) and mastectomy (MT).

Subsequent meta-analysis confirmed no difference in survival, despite higher rates of local recurrence with BCT. Advances in early detection, systemic therapy, and expanded indications for radiotherapy have led to improved survival from breast cancer, and in turn, contemporary studies show improved survival with BCT. These studies use pathological stage of the primary tumor and the nodal status for the analysis, yet this information is unknown to the surgeon at

the time of deciding between MT and BCS. To mimic real-world surgical decision-making and its influence on outcomes, this study assesses overall survival (OS), breast cancer specific survival (BCSS), and locoregional recurrence (LRR) in a modern population-based cohort in patients with clinically node-positive and node-negative breast cancer.

Methods:

Female patients aged 18-69 treated with BCT or MT with or without adjuvant radiation in 2006-2016 for T1-3N0-3M0 breast cancer were identified from our prospective provincial database. Patients treated with neoadjuvant chemotherapy were excluded. The cohort was stratified based on clinical nodal status and multivariable logistic regression was used to assess the effect of local treatment type on OS, BCSS, and LRR for both strata. Comprehensive sensitivity analyses were performed using imputation to assess cases with missing variables. In the node-negative cohort, where pathological nodal stage was upgraded, receipt of nodal irradiation was accounted for in the final model.

Results:

A total of 13,914 patients met inclusion criteria: 8,228 had BCT and 5,686 had MT. Baseline characteristics were not balanced, with higher risk clinical and pathological factors seen in the MT group. Median follow up for both groups was between 7.8-8.5 years.

In the clinically node-positive group, 485 patients had BCT with a median tumor size of 2.5 cm (IQR: 1.8-3.0) and 892 had MT with a median tumor size of 3.0 cm (IQR: 2.2-4.5). BCT patients had radiation only to the chest in 8.9% patients and 91.1% had both chest and regional nodal irradiation. 84% of MT patients had radiation, with 1.1% only to the chest, and 83% to both chest and regional nodes. On multivariable analysis, BCT was associated with improved OS (HR 1.46, $p=0.002$) and BCSS (HR 1.44, $p=0.008$), while locoregional recurrence was 6.6% after BCT and 6.7% after mastectomy, HR 0.89 ($p=0.7$).

For patients that were clinically node-negative, 7,743 had BCT with a median tumor size of 1.5 cm (IQR: 1.0-2.1) and 4,794 had MT with a median tumor size of 2.0 cm (IQR: 1.2-3.0). After surgery, 79% of BCT patients and 62% of MT patients remained node-negative. All BCT patients had radiation, with 80% only to the chest, and 20% to both chest and regional nodes. 38% of MT patients had radiation, with 5.4% radiation to only the chest and 33% to both chest and regional nodes. On multivariable analysis, BCT was associated with improved OS (HR 1.37, $p<0.001$) and BCSS (HR 1.32, $p<0.001$), while locoregional recurrence was 3.8% after BCT and 4.3% after MT, HR 0.84 ($p=0.1$).

Conclusion:

For women with both clinically node-positive and clinically node-negative breast cancer, BCT offers better survival than mastectomy without an increased risk of loco-regional recurrence. When feasible, BCT should be recommended to patients with breast cancer.

Table 1. Breast Cancer Specific Survival Multivariable Analysis.

	Node-negative			Node-positive		
	HR	95% CI	p-value	HR	95% CI	p-value
Procedure						
BCS	—	—		—	—	
Mastectomy	1.3	1.1, 1.6	<0.001	1.4	1.1, 1.9	0.008
Age at Diagnosis	1.0	1.0, 1.0	0.1	1.0	1.0	0.9
Tumour Size	1.3	1.2, 1.3	<0.001	1.1	1.1, 1.2	<0.001
Grade						
1	—	—		—	—	
2	3.2	2.2, 4.5	<0.001	1.7	0.9, 3.1	0.1
3	6.6	4.6, 9.4	<0.001	2.5	1.3, 4.7	0.004
LVI						
no	—	—		—	—	
yes	1.6	1.3, 1.9	<0.001	1.5	1.2, 1.9	<0.001
ER Status						
negative	—	—		—	—	
positive	1.1	0.9, 1.4	0.5	0.8	0.6, 1.2	0.2
PR Status						
negative	—	—		—	—	
positive	0.7	0.6, 0.8	<0.001	0.8	0.6, 1.1	0.2
HER2 Status						
negative	—	—		—	—	
positive	0.6	0.5, 0.7	<0.001	0.6	0.5, 0.8	<0.001
Systemic Therapy						
no	—	—		—	—	
yes	0.5	0.4, 0.7	<0.001	0.4	0.23, 0.7	<0.001
Nodal Radiation						
no	—	—		—	—	
yes	1.1	0.7, 1.6	0.8			

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5:00 PM - 6:15 PM

PD15-06

PD15-06 Pathologic complete response and breast-conserving surgery are associated with improved prognosis in patients with early-stage triple-negative breast cancer treated with neoadjuvant chemotherapy

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Background: Neoadjuvant chemotherapy (NACT) is standard of care for patients with triple-negative breast cancer (TNBC). Treatment response, especially pathologic complete response (pCR), is a strong predictive factor for treatment outcome. In the setting of up-front surgery, retrospective data have suggested improved outcome in patients with early TNBC that received breast-conserving surgery with adjuvant radiotherapy (BCT) as compared to mastectomy. Methods: We identified 2632 patients with early TNBC from the German Breast Group meta-database. Patients with cT1-2 cN0 and ypN0, available surgery and follow-up data were eligible for this project. A total of 1074 patients from 8 prospective NACT trials were analyzed. Endpoints of interest were locoregional recurrence as first site of relapse (LRR, other sites of recurrence were considered competing events), disease-free survival (DFS) and overall survival (OS); analyses were performed using univariate and multivariate Fine-Gray (for LRR) and Cox models including study, age, cT, surgery type and pCR. For the analyses including pCR as covariable, only patients at risk at the landmark time were evaluated. Results: Median age was 48 years, 69.6% of patients had cT2 tumors and 85.3% underwent BCS. Of the 1074 analyzed patients, 48.8% achieved pCR. After a median follow-up of 64 months, there were 94 (8.8%) locoregional events as first site of relapse. Upon univariate analysis, absence of pCR (hazard ratio [HR]=2.28; 95%CI 1.44-3.61; $p < 0.001$) and ypT-stage (ypT0/is vs. ypT1-3, HR=0.61; 95%CI 0.40-0.95; $p=0.028$) were significantly associated with LRR, while type of surgery, age and cT-stage were not. Upon multivariate analysis, absence of pCR was the only factor associated with increased risk of LRR (HR=2.22; 95%CI 1.38-3.58; $p=0.001$). Patients that underwent mastectomy (N=158) were significantly younger (age ≤ 50 years 72.8% vs. 59.9% for BCT [N=916]; $p=0.002$) DFS and OS was significantly better in patients who underwent BCT compared to mastectomy (DFS: HR=0.47; 95%CI 0.34-0.66; $p < 0.001$ and OS: HR=0.40; 95%CI 0.26-0.63; $p < 0.001$). In multivariate analysis, BCT was associated with a significantly better DFS and OS as compared to mastectomy (DFS: HR=0.51; 95%CI 0.36-0.72; $p < 0.001$; and OS HR=0.43; 95%CI 0.27-0.68; $p < 0.001$), whereas absence of pCR was associated with significantly worse DFS and OS (DFS: HR=2.43; 95%CI 1.78-3.31; $p < 0.001$; and OS: HR=3.15; 95%CI 1.94-5.10; $p < 0.001$). Conclusions: In this retrospective analysis from the GBG meta-database, treatment response, e.g. pCR, was the main determinant of locoregional recurrence in patients with early stage TNBC treated with NACT. BCT was associated with improved DFS and OS compared to mastectomy, which may at least in part reflect favorable patient selection.

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5:00 PM - 6:15 PM

PD15-07

PD15-07 7-gene predictive biosignature improves risk stratification for breast ductal carcinoma in situ patients compared to clinicopathologic criteria, identifying a low risk group not clinically benefiting from adjuvant radiotherapy

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Background: Prognostic and predictive tools are needed to optimize treatment for women diagnosed with ductal carcinoma in situ (DCIS). While radiotherapy (RT) is standard of care for DCIS after breast conserving surgery (BCS), those at low-risk for ipsilateral breast recurrence (IBR) risk may be treated without RT. Low-risk has been defined as the absence of high risk clinicopathologic (CP) factors, including larger (>2 cm), palpable, or high nuclear grade (NG) tumors, and younger age (< 50 yrs). However, prospective trials have failed to identify low risk patients (pts) who do not clinically benefit from RT after BCS (RTOG 9804). DCISionRT® (PreludeDx™, CA) is a 7-gene predictive biosignature providing a validated score (DS) to assess the 10-yr IBR risk and RT benefit, using individual tumor biology and CP factors. This study assessed total 10-yr IBR rates, RT benefit, and number needed to treat (NNT) for risk groups defined by biosignature and CP criteria.

Methods: DCIS patients (n=926) from four international cohorts (median follow up 8.5 yrs, 1-3rd quartile 5.8 – 10.2 yrs) treated with BCS (negative margins), with (n=641) and without RT (n=335), had formalin-fixed paraffin-embedded tissues analyzed at a CLIA lab (PreludeDx, Laguna Hills, CA) for DCISionRT with a Residual Risk subtype (RRt). A biosignature Low Risk group (DS≤2.8 without RRt) was contrasted to a High Risk group comprising Elevated Risk (DS>2.8 without RRt) and Residual Risk (DS>2.8 with RRt) groups. Low-risk CP groups were RTOG 9804-like (NG1-2, non-palpable, negative margins, screening detected) or (age >50 and NG 1-2). Total 10-yr IBR rates were evaluated using Cox Proportional Hazards and Kaplan Meier analysis by treatment, biosignature and CP risk groups. NNT was determined with 10-yr IBR rate differences with RT.

Results: The biosignature classified 37% (n=338) of women as Low Risk and 63% (n=588) as High Risk. Among women who did not receive RT, biosignature Low Risk pts had lower IBR than biosignature High Risk pts (5.6% vs. 25.7%, p<.001). About half of pts defined as CP low-risk by 9804-like (51%) or favorable Age/NG (58%) criteria were reclassified by the biosignature to High Risk. These pts had significant RT benefit: 9804-like group - HR 0.3, p=.007, absolute 10-yr IBR reduction of 12.7%, and for favorable Age/NG group - HR .34, p=0.012, absolute 10-yr IBR reduction of 11.2%. The corresponding NNTs were ~8-9. Overall, RT significantly reduced IBR for biosignature High Risk patients (p<.001, n=588), with an absolute 17.7% reduction and a NNT of ~6. For patients in CP high risk groups, 23% of not-9804-like and 31% of (age< 50 or NG 3) pts were reclassified as biosignature Low Risk. RT did not significantly reduce IBR in any Low Risk Biosignature group, including those in CP high-risk groups. IBR for not-9804-like group was 5.9% vs 3.0% without and with RT, p=.52, and for (age< 50 or NG 3) pts was 4.4% vs 3% without and with RT, p=.70. For CP low-risk and biosignature Low Risk

groups, RT reduced IBR by 0%. Overall, RT did not significantly reduce IBR rate for biosignature Low Risk patients (p=.71, n=338), with a 0.8% absolute 10-yr IBR rate difference and a NNT of ~100.

Conclusion: In a large multicenter population, DCISionRT was a better predictor of 10-yr prognosis and RT benefit than CP criteria alone. Pts with biosignature Low Risk disease, comprising about 1/3 of CP high-risk pts, had no significant RT benefit. Whereas pts with biosignature High Risk disease, comprising about 1/2 of CP low-risk pts, significantly benefited from RT, highlighting the lack of accuracy of these CP factors in assessing RT benefit.

Table 1. Ten-Year Risk of Ipsilateral Breast Recurrence (IBR)

Clinical-Pathologic Groups	Biosignature Low Risk group (DS≤2.8 without RRT)					Biosignature High Risk group (Combined Elevated/Residual Risk, DS>2.8 without or with RRT)				
	10-year IBR risk					10-year IBR risk				
	n (%)	No RT (95%CI)	RT (95%CI)	HR (95%CI)	P	n (%)	No RT (95%CI)	RT (95%CI)	HR (95%CI)	P
Overall	338 (37%)	5.6% (3, 12%)	4.8% (3, 9%)	0.8 (0.3, 2.3)	.71	588 (63%)	25.7% (14, 30%)	8.0% (3, 9%)	0.2 (0.1, 0.5)	<.001
RTOG 9804-like* 'good-risk' (low-risk)	232 (49%)	5.5% (2, 14%)	5.5% (3, 11%)	0.96 (0.3, 3.3)	.96	240 (51%)	19.5% (11, 34%)	6.8% (4, 13%)	0.3 (0.1, 0.7)	.007
Not RTOG 9804-like* (high-risk)	106 (23%)	5.9% (2, 22%)	3.0% (1, 12%)	0.5 (0.1, 3.8)	.52	348 (77%)	30.5% (21, 43%)	8.7% (6, 14%)	0.23 (0.1, 0.4)	<.001
Age ≥50 and Grade 1 or 2 (low-risk)	190 (42%)	6.3% (2, 16%)	6.3% (3, 14%)	0.9 (0.3, 3.0)	.88	263 (58%)	18.4% (11, 30%)	7.2% (4, 13%)	0.34 (0.2, 0.8)	.012
Age <50 or Grade 3 (high-risk)	148 (31%)	4.4% (1, 17%)	3.0% (1, 9%)	0.7 (0.1, 4.0)	.70	325 (69%)	34.3% (26, 48%)	8.5% (5, 14%)	0.2 (0.1, 0.4)	<.001

*RTOG 9804-like criteria (Nuclear Grade 1 or 2, non-Palpable, Screening Detected, Negative Margins)

Disclosure(s):

Rachel Rabinovitch, MD: PreludeDx: Contracted Research (Ongoing)

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12/8/2022

5:00 PM - 6:15 PM

PD15-08

PD15-08 Brazilian Randomized Study - BREAST-MRI Trial - Impact of Preoperative Magnetic Resonance in the Evaluation for Breast Cancer Conservative Surgery: Local recurrence and surgical outcomes

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Introduction: Breast magnetic resonance imaging (MRI) has high sensitivity in detecting invasive neoplasms. However, controversy remains as to whether preoperative staging with breast MRI impacts surgical outcomes and local recurrence. Materials and Methods: BREAST-MRI is a randomized, open-label trial including female breast cancer patients older than 18 years old, with stage 0-III disease, eligible for BCS. We performed a 1:1 stratified randomization by breast density according to ACR-BIRADS to divide patients into two groups; one in which preoperative MRI was used and the control group where the MRI was not used. The primary outcome was local relapse-free survival (LR). Secondary outcomes were overall survival (OS), repeat operation, and the proportion of patients whose surgical management was modified to mastectomy. Results: 524 were randomized, 257 included in the MRI group, and 267 in the control group. The baseline characteristics were similar between groups, except for chemotherapy use (table 1). The survival analysis showed a 6-year local recurrence-free survival was 99.2% in MRI group versus 98.9% in the control group, $p=0.702$, overall survival of 95.3% in the MRI group versus 96.3% in the control group, $p=0.481$. No difference was found in reoperation rates, 22 (8.7%) in the MRI group versus 23 (8.7%) in the control group ($p=0.85$)(table2). Surgical management changed in 21 ipsilateral breasts in the MRI group; 21 (8.3%) had mastectomies versus 1 in the control group ($p<0.01$). Conclusion: Preoperative MRI evaluation increased the mastectomy rates by 8%. The use of preoperative MRI did not influence local relapse-free survival, overall survival, or reoperation rates Keywords: breast magnetic resonance imaging; breast cancer; conservative surgery; MRI accuracy, surgical outcomes, randomized clinical trial

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5:00 PM - 6:15 PM

PD15-09

PD15-09 Impact of procedure type on the long-term patient-reported outcomes of immediate breast reconstruction: The UK Brighter Study

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Introduction: Women considering immediate breast reconstruction (IBR) after mastectomy for breast cancer require high-quality information about the short and long-term outcomes of different procedure types to allow them to make informed decisions about their surgical options. Long-term multicentre patient-reported outcomes (PROs) comparing the patients' perspectives of different techniques is currently lacking. The UK Brighter study aimed to compare the long-term patient-reported outcomes of different types of IBR to support informed decision-making. Methods: Women who underwent unilateral mastectomy and/or breast reconstruction for invasive breast cancer or ductal carcinoma in situ (DCIS) in England between 1 April 2008 and 31 March 2009 were identified from National Health Service (NHS) Hospital Episode Statistics

(HES), and current contact information for the surviving cohort were provided by the NHS Personal Demographic Service. Women were sent a letter inviting them to complete three validated patient report questionnaires, the BREAST Q, EQ-5D5L and ICECAP-A, electronically or by post at a minimum of 12 years following their index surgery. Questionnaires were scored according to developers' instructions and results compared by type of IBR procedure performed. Results: 11,977 women were invited to participate of whom 4,207 (35.1%) completed the questionnaires. Of these, 1,236 (29.4%) received IBR with 343 (27.8%) expander/implant (EI) reconstructions, 629 (50.9%) latissimus dorsi (LD) procedures with or without an implant, and 264 (21.4%) abdominal flap (AF) reconstructions. The mean age at index surgery was 52.1 years, standard deviation (SD) 9.5. The majority of respondents were white (n=1,179, 97.4%) and predominantly from areas of the lowest socioeconomic deprivation. The mean body mass index (BMI) was 24.6 (SD 3.9). 141 (11.6%) women actively smoked at the time of surgery and 227 (19.0%) had a complication requiring further surgery. Women undergoing AFs reported significantly higher 'Satisfaction with Breasts' (mean 67.7, SD 20.4) than those undergoing LD (mean 58.9, SD 21.1), or EI reconstructions (mean 54.7, SD 19.2), ($p < 0.001$). 'Satisfaction with Breasts' was also greater in women undergoing index surgery over 50 years of age ($p = 0.02$) and in those who did not smoke ($p = 0.03$) whereas experiencing post-operative complications was strongly associated with poorer 'Satisfaction with Breasts' in the multivariable analysis ($p = 0.001$). Women receiving AF also reported better 'Physical Well-being' (mean 87.8, SD 16.04) than women undergoing LD flap (mean 79.5, SD 20.5) or EI procedures (mean 82.1, SD 18.2), ($p < 0.001$). Overall, women undergoing AFs were more likely to rate the outcome of their surgery as 'excellent' or 'very good' (189/256, 73.8%) compared with those receiving other reconstruction types (LD - 386/610, 63.3%; EI - 175/331, 52.9%, $p < 0.001$). Conclusion: Women undergoing abdominal flap reconstruction report significantly better outcomes 12 years following IBR than women receiving other reconstruction types. These findings should be shared with women considering breast reconstruction to help them make informed decisions about their surgical options.

Disclosure(s):

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5:00 PM - 6:15 PM

PD15-10

PD15-10 Impact of procedure type on long-term revisional surgery and secondary reconstruction following immediate breast reconstruction: The UK Brighter national population-based cohort study

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Introduction: Women considering immediate breast reconstruction (IBR) after mastectomy for breast cancer require high-quality information about the short and long-term clinical outcomes of different procedure types, including the need for further surgery, to allow them to make fully informed decisions about their breast reconstruction options. Long-term outcome data is currently lacking. The UK Brighter population-based cohort study aimed to compare the need for revisional surgery and secondary reconstruction by type of IBR at a minimum of 12 years following the index procedure to support informed decision-making. Methods: Women who underwent unilateral mastectomy and IBR for invasive breast cancer or ductal carcinoma in situ

(DCIS) in England between 1 April 2008 and 31 March 2009 were identified using National Health Service (NHS) Hospital Episode Statistics (HES). Lists of procedure codes indicating revisional surgery, defined as operations performed to the same site as the index reconstruction and/or the donor site (if appropriate), excluding a single planned implant exchange in the expander group, or secondary reconstruction, defined as the replacement of one reconstruction with another, with or without a period of being flat, were iteratively developed and refined. Numbers of revision procedures and secondary reconstructions were compared by type of index reconstruction. Multivariable regression was used to control for potential confounders. Results: 2,260 women underwent IBR during the study period including 742 (32.8%) expander/implant (EI), 1,146 (50.7%) latissimus dorsi (LD) flap reconstructions with (n=649) and without (n=497) an implant and 372 (16.5%) abdominal free-flap (AFF) procedures. Women receiving reconstructions involving implants were significantly more likely to require more revisions over time, with 201/742 (27.1%) patients undergoing EI reconstruction and 154/649 (23.7%) those receiving an implant-assisted LD reconstruction requiring two or more post-reconstruction revision procedures compared with 77/497 (15.5%) patients undergoing autologous LD and 59/372 (15.9%) patients receiving AFF procedures ($p < 0.001$). Undergoing primary reconstructive surgery before the age of 50, and region of residence at the time of the mastectomy were factors influencing revisional surgery in the multivariable regression analysis. By 12 years, 128/742 (17.3%) of women who initially underwent an expander/implant reconstruction had received a secondary reconstruction compared with 34/1146 (3.0%) patients who had initially received an LD +/- implant procedure and 11/372 (3.0%) patients initially undergoing an AFF reconstruction ($p < 0.001$). Conclusions: The need for revisional surgery in women electing to undergo IBR involving implants is significantly greater than that for women electing to receive autologous reconstructions and almost 1 in 5 women undergoing primary EI reconstruction required a secondary reconstruction by 12 years. These findings should be shared with women considering IBR to support informed decision making and with healthcare providers and commissioners to support the provision of high-quality, evidence-based reconstructive care.

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5:00 PM - 6:15 PM

PD15-11

PD15-11 Axillary dissection to determine nodal burden to inform systemic therapy recommendations in patients with clinically node-positive breast cancer: Pre-planned substudy of TAXIS (OPBC-03, SAKK 23/16, IBCSG 57-18, ABCSG-53, GBG 101)

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Introduction: Chemotherapy is recommended for patients with luminal breast cancer and more than three positive nodes. In addition, recent landmark trials raised the question if the exact number of positive nodes is required to indicate genomic testing. In the neoadjuvant setting, response-driven therapy is increasingly used and may be influenced by surgical staging of the axilla. The present study addressed the role of axillary lymph node dissection (ALND) as decision aid for systemic therapy in a contemporary cohort of patients with clinically node-positive breast cancer in the adjuvant and neoadjuvant setting. **Methods:** The study was preplanned in the international multicenter phase-III OPBC-03/TAXIS trial (ClinicalTrials.gov Identifier: NCT03513614). The first 500 patients with clinically node-positive breast cancer who were randomized after tailored axillary surgery (TAS) to undergo ALND or axillary radiotherapy (ART) without ALND in the context of extended regional irradiation were included from August 2018 to June 2022. Clinically node-positive breast cancer was defined by confirmed nodal disease at the time of initial diagnosis; in case of neoadjuvant therapy, the finding of residual nodal disease was mandatory for randomization. TAS consisted of removal of palpably suspicious findings and the sentinel nodes with the option of image guidance. In the ART arm, the total number of positive nodes was not known. We analyzed the impact of ALND on rate and type of systemic therapy. **Results:** A total of 500 patients with a median age of 57 years (IQR: 48-69 years) were included at 44 breast centers from six European countries. Subtype was hormone receptor (HR) positive (+) and human epidermal growth factor receptor 2 (HER2) negative (-) in 393 (80.0%), HR+/HER2+ in 52 (10.6%), HR-/HER2+ in 5 (1.0%) and HR-/HER2- in 34 (6.9%) patients. Of 343 patients (68.6%) who were treated in the adjuvant setting, 297 had HR+/HER2- disease. Of these 297 patients, 145 (48.8%) underwent ART without ALND and 152 (51.2%) underwent ALND after TAS. In the ART arm, the median number of lymph nodes removed was five (IQR 4-8), three (IQR 1-4) of which were positive and in the ALND arm, the number was 19 (IQR 14-26), four (IQR 2-9) of which were positive ($p < 0.001$). The use of ALND had no significant impact on the rate of patients with HR+/HER2- disease undergoing adjuvant chemotherapy (51.0% in the ART and 57.9% in the ALND arm, $p=0.2$), and there were no significant differences in type of systemic therapy with the exception of tamoxifen, which was 18.4% with ALND versus 9.0% without ($p=0.018$). A total of 143 patients (28.6%) underwent neoadjuvant chemotherapy, 13 had neoadjuvant antihormonal treatment and one had neoadjuvant double HER2-blockade without chemotherapy. Of the 143 patients who received neoadjuvant chemotherapy, 71 (49.7%) underwent ART without ALND and 72 (50.3%) underwent ALND. In the ART arm, the median number of lymph nodes removed was four (IQR 3-6), one (IQR 1-3) of which was positive and in the ALND arm, the number was 16 (IQR 12-19), two (IQR 1-5) of which were positive ($p < 0.001$). The use of ALND in patients after neoadjuvant treatment had no significant impact on the rate of adjuvant systemic therapy (71.8% in the ART and 65.3% in the ALND arm, $p=0.4$), with no significant differences in type of chemotherapy (e.g., capecitabine: 11.3% vs 12.5%, $p=0.8$; T-DM1: 11.3% vs. 11.1%, $p>0.9$) or antihormonal therapy (e.g., aromatase inhibitors: 49.3% vs. 41.7%, $p=0.4$; tamoxifen: 11.3% vs. 5.6%, $p=0.2$). **Discussion:** This study showed that although ALND significantly increased the number of positive nodes removed in the adjuvant and neoadjuvant setting, it had no relevant impact on rate and type of adjuvant systemic therapy.

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12/8/2022

5:00 PM - 6:15 PM

PD15-12

PD15-12 A pre-surgical window trial of oral tamoxifen versus transdermal 4-hydroxytamoxifen gel in women with estrogen receptor positive duct carcinoma in situ (DCIS)

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Background: Adjuvant oral tamoxifen (TAM) benefits women with DCIS, but toxicity concerns have limited its acceptance. Transdermal therapy with 4-hydroxy tamoxifen (4-OHT) gel applied to the breast skin is a possible solution. Previous pilot data suggest equivalent anti-proliferative efficacy of TAM and 4-OHT gel, but minimal systemic exposure with transdermal therapy. We report a prospective double blinded randomized phase 2 trial comparing TAM to 4-OHT gel in women with DCIS. Methods: 107 women with estrogen receptor positive ($\geq 10\%$) DCIS were randomized to TAM (20 mg/day + placebo gel) or 4-OHT gel (2mg 4-OHT gel/breast, bilaterally + oral placebo), for 4-10 weeks prior to surgery. The primary endpoint was reduction in DCIS Ki67 labeling index (LI). Secondary endpoints included the 12-gene DCIS Score assay (Exact Sciences), breast tissue and plasma concentrations of 4-OHT and endoxifen, TAM-responsive circulating proteins, and patient reported symptoms (Breast Eight Symptom Scale). We estimated that 80 evaluable participants would provide 80.5% power to establish non-inferiority of 4-OHT, defined as relative Ki67-LI decline $>35\%$ and absolute decline $>2.6\%$, with one-sided

$\alpha=0.10$. Non-inferiority of 4-OHT gel for Ki67-LI reduction was tested using an ANCOVA model. Statistical comparisons within- and between-arms were calculated with paired t-test and Welch Two Sample t-test, respectively. Results: 72 of 87 women adhered to the protocol, and were evaluable for the primary endpoint (39 TAM and 33 4-OHT gel). Mean treatment duration was 47 days for TAM and 44 days for 4-OHT gel ($p=0.2$). The median absolute decline in Ki67 labeling index was significant in the oral TAM (-3.7%, $p < 0.001$) but not in 4-OHT gel arm (-1.3%, $p=0.2$) ($p=0.002$). Ki67 results following menopausal stratification also favored the TAM arm: (-1.3%; $p=0.06$ in 37 premenopausal women and -3.7%; $p=0.02$ in 35 postmenopausal women). Similarly, DCIS score showed a significantly greater reduction in the TAM (-14, $p < 0.001$) but not in the 4-OHT gel arm (-4, $p=0.1$). Tissue 4-OHT concentrations were non-significantly higher in the TAM arm and were similar between superficial and deep sampling locations (superficial 6.1 and 4.2 ng/g for TAM and 4-OHT gel, respectively, $p=0.55$; deep 5.7 and 3.8 ng/g, respectively, $p=0.06$), whereas plasma 4-OHT concentration was markedly lower in the gel group (2 ng/mL and 0.24 ng/mL for TAM and 4-OHT gel, respectively, $P < 0.001$). Endoxifen was abundant in plasma (11 ng/mL) and deep tissue (13 ng/g) of the TAM arm, but present in trace amounts in the 4-OHT gel arm (undetectable in plasma and 0.31 ng/g in tissue; $p < 0.001$). Circulating TAM responsive markers (insulin like growth factor 1, sex hormone binding globulin, von Willebrand factor, and protein S total) and vasomotor symptoms were significantly and unfavorably modulated by TAM, but not by 4-OHT gel therapy. Conclusions: The non-inferiority of transdermal 4-OHT gel to Tam in terms of anti-proliferative effect in DCIS lesions was not demonstrated at the doses used for this study. DCIS Score analysis gave similar results. Tissue 4-OHT concentration in 4-OHT gel and Tam-treated subjects was roughly similar. However, endoxifen exposure was higher with oral TAM therapy and may partially explain the observed differences in major endpoints. In future studies, use of higher 4-OHT gel doses, longer duration of treatment, or different formulation may overcome these.

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12/9/2022

7:00 AM - 8:15 AM

P6-01-01

Validation of an Optical Imaging Platform to Identify Metabolic Vulnerabilities in Chemo-Resistant and Sensitive Tumors

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Less than 20% of Triple Negative Breast Cancer (TNBC) patients experience long-term responses to mainstay chemotherapy, as tumors develop chemo-resistance. While combinations of chemotherapies and targeted therapies show potential improvements in TNBC clinical outcomes, patient stratification and prediction of treatment response is critical. Spatio-temporal metabolic reprogramming holds promise as a biomarker of therapy response as resistant tumor subpopulations utilize alternate metabolic pathways to escape therapy, enter minimum residual disease (MRD) and recur. Currently, there are limited tools to temporally evaluate heterogeneous changes along distinct metabolic axes in vivo at a spatial resolution capable of resolving vulnerabilities of residual tumor subpopulations. Here, we utilized an optical imaging-based platform to identify in vivo, longitudinal differences in metabolic reprogramming between a resistant and sensitive tumor model at high resolutions along three metabolic axes of TNBC chemoresistance (oxidative phosphorylation, glycolysis, and fatty acid oxidation). Xenografts were established by orthotopic cell injection and mice were treated with Paclitaxel (PTX), a commonly used chemotherapeutic drug in TNBC treatment, under a conventional maximum dose density regimen once the tumor reached a volume ~150mm³. MDA-MB-231 xenografts were resistant to PTX, defined as an initial response to PTX, a period of minimal residual disease, and a resurgence in tumor volume at ~60 days post drug withdrawal (n=3). HCC-1806 xenografts were sensitive to PTX, defined as an initial response to PTX in all mice and a complete cure in 7/10 mice. A separate cohort of mice for each tumor line was implanted with window chambers and imaged longitudinally at distinct stages of the tumor's lifecycle with previously validated fluorophores 2-NBDG, TMRE, and Bodipy to directly report on glucose uptake, mitochondrial membrane potential, or fatty acid uptake, respectively. Wide field fluorescence imaging of MDA-MB-231 mice showed a significant increase in TMRE as early as two days after the 3rd PTX dose (n=5, p< 0.05), a significant decrease in 2-NBDG as early as two days after the 5th PTX dose (n=5, p< 0.05) and no significant changes in bodipy uptake. This increase in non-glucose-driven mitochondrial respiration was sustained during

MRD. An increase in heterogeneity of TMRE uptake was seen during disease regression, MRD, and recurrence (n=5, p< 0.05). HCC-1806 tumors showed increased glucose uptake, decreased fatty acid uptake, and no significant changes in mitochondrial membrane potential during acute treatment. Metabolic changes were transient, with no significant changes in probe uptakes after drug withdrawal and during MRD. Unlike the MDA-MB-231 tumors, no significant changes in the heterogeneity of TMRE uptake were seen following paclitaxel withdrawal in HCC-1806 tumors (n=5, p>0.05). Our results point towards a metabolic switch from glycolysis to non-glucose, non-fat-driven mitochondrial respiration in MDA-MB-231 mice, possibly suggesting amino acid catabolism as a fuel during MRD. In the sensitive HCC-1806 line, we observed changes in glucose and fatty acid uptake during acute treatment, but no significant changes in metabolism during MRD. Consistent with the literature, our results point toward an increase in metabolic plasticity and heterogeneity in a chemo-resistant model compared to a chemo-sensitive one. Together, our results show the potential of using metabolic changes following therapy as a biomarker of therapy response, while highlighting the importance of tracking the change (or lack of change) in metabolism longitudinally. We aim to use this system to visualize and exploit early, in vivo metabolic vulnerabilities of disease regression that accompany local and distal recurrences.

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7:00 AM - 8:15 AM

P6-01-02

Using MammaPrint on Core Needle Biopsy to Guide Neoadjuvant Chemotherapy for Invasive Breast Carcinoma

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Introduction:

MammaPrint, a 70-gene assay used to predict breast cancer recurrence, is typically obtained on the surgical specimen to guide the use of adjuvant chemotherapy. However, MammaPrint results obtained at the time of diagnosis on core biopsy specimen could allow consideration of neoadjuvant chemotherapy (NAC), particularly for tumors that may not traditionally be considered for NAC such as invasive lobular carcinoma (ILC). We hypothesized that MammaPrint scores correlate with pathologic complete response (pCR) and can predict NAC response independent of histology type.

Methods:

The National Cancer Database was used to identify patients with AJCC Stage I-III unilateral HR+/HER2- breast cancer with MammaPrint scores treated 2010-2018. Patients were stratified by histology: invasive ductal carcinoma (IDC) and ILC; and by MammaPrint score for 5-year breast cancer recurrence: Low Risk (1%) and High Risk (12%). Descriptive statistics identified clinical and treatment differences between groups. Logistic regression was used to identify factors associated with chemotherapy receipt and sequence. A subset analysis of patients receiving NAC compared pCR rates by MammaPrint score and histology type.

Results:

Of 10,999 patients, 9,351 (85%) were diagnosed with IDC and 1,648 (15%) with ILC. ILC were larger at presentation: 40% of ILC were cT2 or greater vs. 29% of IDC ($p < 0.001$). However, 90% of patients in both groups had cN0 disease. The majority of ILC were grade II (67% ILC vs. 52% IDC, $p < 0.001$). High Risk MammaPrint scores were significantly more common in IDC tumors: 44% IDC vs 25% ILC ($p < 0.001$). Mastectomy and axillary lymph node dissection (ALND) were performed more often for ILC than IDC (unilateral mastectomy 32% vs. 21%, bilateral mastectomy 17% vs. 12%, ALND 29% vs. 24%; all $p < 0.001$). Conversely, chemotherapy (38% vs. 30%, $p < 0.001$) and radiation (69% vs. 64%, $p < 0.001$) were more frequently used to treat IDC than ILC. In the subset analysis of patients who received NAC ($n = 715$), tumors with High Risk MammaPrint scores had more favorable in-breast and axillary responses than those with Low Risk scores for both ILC and IDC (Table 1). Furthermore, only tumors with High Risk MammaPrint scores achieved an overall pCR: 7% IDC and 5% ILC. There were no significant differences in pCR rates by histology type. On multivariable logistic regression, High Risk MammaPrint score was positively associated with the receipt of NAC (OR 4.3, $p < 0.001$) and adjuvant chemotherapy (OR 24.8, $p < 0.001$). NAC, adjuvant chemotherapy, and any chemotherapy were also strongly associated with node-positive disease and tumor size $>2\text{cm}$, but not IDC vs. ILC histology.

Conclusions:

Superior response to NAC was observed in tumors with High Risk MammaPrint score regardless of histology type, indicating a correlation between pCR rates and genomic assay results. Greater use of NAC guided by High Risk MammaPrint score obtained on core needle biopsy may allow patients with invasive breast cancer to undergo less extensive breast and axillary surgery. Further prospective studies using MammaPrint testing on core biopsy specimens could validate these findings in clinical practice.

Histology	Invasive Ductal Carcinoma			Invasive Lobular Carcinoma		
	MammaPrint Score	Low Risk	High Risk	p-value	Low Risk	High Risk
In Breast Response						
	n = 575			n = 103		
Downstage	56 (46.3%)	225 (49.6%)	<0.001	15 (27.8%)	19 (38.8%)	0.195
pCR*	6 (5.0%)	49 (10.8%)	0.053	1 (1.9%)	3 (6.1%)	0.263
Axillary Response						
	n = 287			n = 47		
Downstage	4 (5.6%)	62 (28.7%)	0.340	4 (16.7%)	6 (26.1%)	0.597
pCR*	2 (2.8%)	54 (25.0%)	<0.001	3 (12.5%)	5 (21.7%)	0.400
Combined Response						
	n = 281			n = 46		
pCR*	0 (0.0%)	15 (7.1%)	0.021	0 (0.0%)	1 (4.5%)	0.291

*pCR = pathologic complete response

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7:00 AM - 8:15 AM

P6-01-03

Tumor-infiltrating lymphocytes (TILs) and 21-gene recurrence score in 1,883 patients with ER+/HER2- breast cancer

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Background: In ER+/HER2- breast cancer, several lines of evidence suggest that tumors with high level of tumor-infiltrating lymphocytes (TILs) have a greater chance of obtaining a pathological complete response (pCR) after neoadjuvant chemotherapy. In addition, high 21-gene recurrence score (RS) is associated with an increasing rate of pCR in luminal tumors. We investigated the relationship between TIL and RS in 1,883 patients with early ER+/HER2- breast cancer.

Method: In 1,883 ER+ breast cancer patients with 21-gene assay, TIL level was evaluated. Correlation between continuous TIL and RS was investigated. Logistic-regression analysis was performed to identify risk factors for high RS (≥26). The cut-off for high TIL was 50%. Recurrence-free survival (RFS) was investigated.

Results: A weak positive correlation between TIL level and RS was observed (correlation coefficient=0.283, $p < 0.001$) in all patients. Average TIL level of the high RS tumors was significantly higher. Two parameters were positively correlated in both two groups classified by age 50 years (correlation coefficient=0.281 in the age ≤50; correlation coefficient=0.288 in the age >50). Either continuous TILs or binary high TIL level was demonstrated to be an independent factor for high RS. When all patients were divided into 4 groups using TIL and RS (low-RS/low-TIL, low-RS/high-TIL, high-RS/low-TIL, and high-RS/high-TIL), the RFS was worst in the low-TIL/high-RS group ($p < 0.001$).

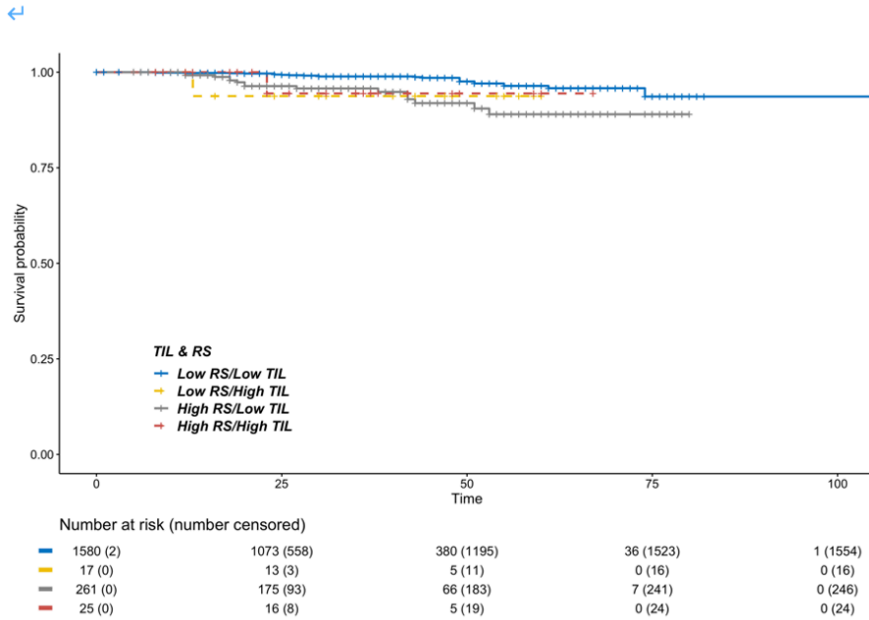
Conclusions: Our findings show that TIL level is correlated with RS in ER+ breast cancer regardless of age and suggest that high TIL level can be regarded as a risk factor for high RS. Multigene assay could be integrated in designing clinical trials evaluating immune-check point

blockades in luminal breast cancer.

Recurrence-free survival according to RS and TIL

Table 1. 5-years RFS according to TIL and RS

	5-years RFS	95% CI
RS-Low/TIL-Low	96.4	94.8-98.1
RS-Low/TIL-High	93.8	82.6-100.0
RS-High/TIL-Low	89.0	83.3-95.2
RS-High/TIL-High	94.4	84.4-100.0



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The Hierarchy of Biomarkers

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Background: Biomarkers with robust analytical and clinical validity can help optimize therapy decisions within clinical trials for patients with breast cancer, particularly if some data on clinical utility also exist. However, little is known about how physicians enrolling in clinical trials view them. Physician comfort with the integral use of conventional and investigational biomarkers for reducing chemotherapy intensity within clinical trials is explored in this study. Method: A convenience sample of academic and community oncologists from across the United States were invited to participate in qualitative interviews that explored their perspectives on the use of biomarkers for the de-escalation of chemotherapy in patients with breast cancer. Purposive sampling techniques were used to identify participants, ensuring even distribution of gender, work setting, and time practicing medical oncology. Interviews were audio-recorded and transcribed. Transcripts were analyzed by two independent coders to identify major themes and exemplary quotes in NVivo. A framework for understanding how providers conceptualize biomarkers was created. Results: There was a total of 39 physicians with a median age of 50; 51% of physicians were academic and 49% were community-based. 44% of oncologists have been in practice for less than 15 years, and 36% and 20% of oncologists were in practice for

15-30 years and over 30 years, respectively. The model on physician level of comfort for biomarker use consisted of 1) standard of care biomarkers, 2) standard biomarkers in newer contexts, and 3) experimental biomarkers with inclusion of additional related subthemes. There was a shared theme among physicians that historical experience with a biomarker made them more comfortable in de-escalation of chemotherapy. The greatest level of physician comfort with biomarker for de-escalation of chemotherapy came with biomarkers used in standard of care (e.g., MammaPrint, Oncotype DX). Themes related to these biomarkers included: strong level of evidence, agreement with NCCN guidelines, and widespread use in the community. For example, one physician stated, "for me to use a prognostic biomarker ... typically it's going to have to at least be within the NCCN guidelines or out there". Secondly, physicians expressed reasonable confidence with some reluctance in the use of standard of care biomarkers in contexts that differ from where they were initially tested (i.e., use of biomarker in patients with different features or disease biology). These themes included the use of biomarkers in specific subtypes of cancer and when there is less supportive evidence. One physician commented, "It's just hard to analyze and really know whether [pathCR in ER+ setting] actually holds like it does for other tumor biologies". There was more hesitation and least comfort with experimental biomarkers (e.g., tumor-infiltrating lymphocytes, circulating tumor DNA). For experimental biomarkers, physicians were primarily concerned with the quality and quantity of evidence supporting their use. Prospective trials were favored over retrospective; however, physicians were accepting if the retrospective study included a large sample, other biomarkers were used in conjunction, or multiple studies confirmed the results. Other themes that emerged regarding experimental biomarkers were their testing in diverse populations and reproducibility. Physicians expressed contentment with experimental biomarkers that were proven in "multiple big enough studies", were "reproducible and not subjective", and "demonstrate utility in the patient population that's relevant". Conclusion: Biomarkers can be divided into 3 successive levels: 1) standard of care biomarkers, 2) standard biomarkers in newer contexts, and 3) experimental biomarkers. Level of comfort concerning the use of biomarkers for de-escalation of chemotherapy is related to level of evidence for experimental biomarkers.

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P6-01-05

Platelet-derived growth factor-CC expression in primary triple-negative breast cancer is associated with the basal-like molecular subtype and increased immune infiltrate

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Around 10-15% of all breast cancers are categorized clinically as triple-negative breast cancer (TNBC). TNBC is defined by lack of protein expression or over expression of treatment targets such as the Estrogen Receptor α (ER) and Human Epidermal Growth Factor Receptor-2 (HER2), and the prognostic factor PR (Progesterone Receptor). The negative definition of TNBC results in a heterogeneous mix of tumors with variable molecular characteristics and prognosis. Defining TNBC molecular subtypes in detail is of importance to improve prognostication and find new treatment options. Expression of Platelet-derived growth factor-CC (PDGF-CC) has previously been correlated with the TNBC subtype, and paracrine PDGF-CC signaling has been reported to be of importance for maintaining TNBC tumor cell phenotype. We aimed to characterize PDGF-CC expression within the TNBC patient population by combining studies of PDGF-CC in tissue microarrays (TMAs) with matching RNAseq data and clinical follow-up; all variables originating from the SCAN-B (Sweden Cancerome Analysis Network – Breast) clinical study (ClinicalTrials.gov: NCT02306096). TMAs constructed of primary TNBC patient samples were stained for PDGF-CC using the Dako PT Autostainer system. Tumor cell-specific expression of PDGF-CC intensity was scored as either absent (N=11), weak (N=86), intermediate (N=81) or strong (N=70), and the scores were used to

create corresponding TNBC PDGF-CC subgroups. We then explored associations of these subgroups with clinicopathological variables and time-to-event outcomes. Intermediate and strong PDGF-CC scores were associated with Nottingham Histological Grade 3 ($p=0.001$), increased proliferation ($p<0.001$) and younger patient age at diagnosis ($p=0.002$). RNAseq data corresponding to tumors included in the TMAs was then retrieved, and differentially expressed genes were identified and used to perform Gene Set Enrichment Analysis (GSEA) comparing the TMA-derived PDGF-CC subgroups. Immune-related signatures were found to be enriched in the strong PDGF-CC subgroup vs. intermediate. Interestingly, strong PDGF-CC intensity was associated with a decreased risk of recurrence in the chemotherapy treated patient group (HR 0.28, 95% CI 0.10-0.80, $p=0.017$). Finally, patient samples were assigned a PAM50 subtype and a TNBC molecular subtype by the TNBCtype algorithm. Ninety-four percent of tumors in the strong PDGF-CC subgroup were classified as basal-like, whereas the corresponding number in the weak and intermediate PDGF-CC subgroups were 51% and 84%, respectively. The TNBC molecular subtype termed 'Immunomodulatory' was more frequently represented in the strong PDGF-CC subgroup compared to weak and intermediate (33% vs. 13% and 16%, respectively). In conclusion, strong PDGF-CC protein expression identified basal-like TNBCs, with an increase in immune cell infiltrate shown by RNAseq analysis. Whether or not PDGF-CC has a direct effect on influx of immune cells into tumors remains to be investigated. Analyses are currently ongoing to better understand the improved outcome associated with strong PDGF-CC intensity and on the contrary, the worse outcome associated with weak and intermediate PDGF-CC intensity, and if paracrine PDGF-CC signaling may explain the discrepancy observed.

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P6-01-06

Multi-Parametric MRI-Based Radiomics Models from Tumor and Peritumoral Regions as Potential Predictors of Treatment Response to Neoadjuvant Systemic Therapy in Triple Negative Breast Cancer Patients

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PURPOSE Triple negative breast cancer (TNBC) is an aggressive and heterogeneous subtype of breast cancer. Pathologic complete response (pCR) to neoadjuvant systemic therapy (NAST) predicts better survival. Early prediction of the treatment response can potentially triage non-responding patients to alternative protocol treatments, spare them of the unneeded toxicity, and improve pCR. We evaluated the ability of radiomic textural analysis of intratumoral and peritumoral regions on the dynamic contrast enhanced (DCE) and diffusion-weighted imaging (DWI) MRI images obtained early during NAST to predict pCR. **MATERIALS AND METHODS** This IRB-approved prospective study (NCT02276443) included 182 patients with biopsy proven stage I-III TNBC who had multiparametric MRIs at baseline (BL), post 2 cycles (C2), and post 4 cycles (C4) of NAST before surgery. Tumors and peritumoral regions of 5 mm and 10 mm in thickness were segmented on the 2.5 minutes DCE subtraction images and on the b=800 DWI images. Ten histogram-based first order texture features including mean, minimum, maximum, standard deviation, kurtosis, skewness, 1st, 5th, 95th, and 99th percentile, and 300 radiomic Grey Level Co-occurrence matrix (GLCM) features along with their absolute and relative differences between the 3 imaging time points were extracted from the tumors and from the peritumoral regions with an in-house Matlab toolbox. Treatment response at surgery (pCR vs non-pCR) was documented. The samples were divided into training and testing datasets by a 2:1 ratio. Area under the receiver operating characteristics curve (AUC ROC) was calculated for univariate analysis in predicting pCR. Logistic regression with elastic net regularization was performed for texture feature selection. Parameter optimization was performed by using 5-fold cross-validation based on mean cross-validated AUC in the training set. **RESULTS** Of 182 TNBC patients, 88 (48%) had pCR and 94 (52%) did not achieve pCR. Eight multivariate models combining radiomic features from both DCE and DWI tumoral and peritumoral regions had AUC > 0.8 (0.807-0.831) with p-value < 0.001 in both training and testing sets. The highest AUC=0.831 was obtained from a model consisting of 15 radiomic features: tumor DWI (5 GLCM features) at C2, peritumoral region on DCE (skewness) at C2, tumor DCE (1st, 5th percentile) at C4, tumor DWI (3 GLCM features) at C4, peritumoral region DWI (1 GLCM feature) at C4, and the relative difference between C4/C2 on DCE (5th, 95th percentile and mean). **CONCLUSION** Multi-parametric MRI-based radiomics models from the tumor and the peritumoral regions showed high accuracy as potential early predictors of NAST response in TNBC patients.

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7:00 AM - 8:15 AM

P6-01-08

Gene signatures provide independent prognostic information in elderly breast cancer patients

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Background: Elderly breast cancer patients (≥ 70 years old) are under-represented in clinical trials and remain an undertreated population. Gene expression signatures have been shown to add additional prognostic information beyond that of routine clinicopathological factors, however their utility in elderly breast cancer patients remains unclear. As such, the main aim of this study is to determine if gene signatures can provide prognostic information that may help to aid treatment decisions for elderly breast cancer patients.

Material and methods: Research versions of the genomic grade index (GGI), 70-gene, 21-gene recurrence score (RS), cell cycle score (CCS), PAM50 and PAM50 Risk of Relapse score - Proliferation (ROR-P) signatures were applied to 39 open access breast cancer datasets totalling 9583 patients. After filtering based on age ≥ 70 years old, the presence of Estrogen Receptor (ER) and survival information availability 871 patients remained. The prognostic capacity of signatures was tested in all (N=871), Estrogen Receptor positive/ Lymph node positive (ER+/LN+, N=335) and Estrogen Receptor positive/ Lymph node negative (ER+/LN-, N=374) patients using Kaplan-Meier and multi-variable Cox proportional hazard modeling. Models were adjusted for tumor size, grade, ER and lymph node status in all patients, and tumor size and grade in the ER+/ LN+ and ER+/ LN- subgroup analyses. Recurrence Free Survival (RFS) censored at 10 years was used as clinical endpoint and defined as the time from date of curative surgery to the time of recurrence or death. Both loco-regional recurrences and distant metastatic events were included in this endpoint.

Results: Tumours from patients ≥ 70 years of age showed high levels of ER (87%), were large (69% ≥ 20 mm) and were of intermediate or high grade (82%). All gene signatures were statistically significant in Kaplan-Meier analysis of all and ER+/LN+ patients (Logrank $P < 0.001$). This significance remained in multi-variable analysis (Cox proportional hazards, $P \leq 0.05$) with the exception of PAM50 which showed a trend ($P \leq 0.1$) in ER+/LN+ patients. In ER+/LN- patients the GGI, 70-gene, PAM50, ROR-P, and CCS signatures were significant in Kaplan-Meier analysis (Logrank $P \leq 0.05$) but only the 70-gene, PAM50, ROR-P, and CCS signatures remained so in multi-variable analysis (Cox proportional hazards, $P \leq 0.05$).

Conclusions: In general, we found that gene signatures provide statistically significant prognostic information in Kaplan-Meier and multi-variable analyses of all, ER+/LN+ and ER+/LN- breast patients over the age of 70.

Table 1: Multivariable proportional hazard (Cox) analyses for all gene signatures for patients above age of 70.

Signature	All patients ^a (N = 871)			Patients (ER+/LN+) ^b (N = 335)			Patients (ER+/LN-) ^b (N = 374)		
	N (%)	HR (95% CI)	P	N (%)	HR (95% CI)	P	N (%)	HR (95% CI)	P
PAM50									
Luminal A (ref)	396 (49)	1 (-)	-	157 (50)	1 (-)	-	208 (61)	1 (-)	-
Luminal B	244 (31)	1.6 (1.1 - 2.2)	0.01	117 (37)	1.4 (0.9 - 2.2)	0.09	102 (30)	1.8 (1 - 3.1)	0.05
Her2	84 (10)	1.8 (1.1 - 2.9)	0.02	30 (9)	1.8 (0.9 - 3.4)	0.07	20 (6)	1.6 (0.6 - 4.2)	0.39
Basal	84 (10)	1.2 (0.7 - 2.4)	0.58	12 (4)	4.1 (0.9 - 6.4)	0.06	11 (3)	0.4 (0.06 - 3.1)	0.4
RORP									
Low proliferation (ref)	177 (20)	1 (-)	-	64 (19)	1 (-)	-	96 (26)	1 (-)	-
Intermediate proliferation	485 (56)	1.6 (1 - 2.51)	0.04	202 (60)	2.1 (1 - 4.2)	0.03	219 (59)	1 (0.5 - 2)	1
High proliferation	209 (24)	2.6 (1.61 - 4.39)	< 0.001	69 (21)	3.8 (1.8 - 7.9)	< 0.001	59 (15)	2.3 (1 - 4.9)	0.04
GGI									
GG1 (ref)	453 (52)	1 (-)	-	169 (50)	1 (-)	-	204 (63)	1 (-)	-
GG3	418 (48)	1.6 (1.1 - 2.2)	0.005	166 (50)	1.8 (1.2 - 2.7)	0.004	140 (37)	1.3 (0.8 - 2.5)	0.22
70-gene									
Low risk (ref)	479 (55)	1 (-)	-	186 (55)	1 (-)	-	249 (67)	1 (-)	-
High risk	392 (45)	1.7 (1.3 - 2.4)	< 0.001	149 (45)	1.6 (1.1 - 2.5)	0.01	125 (33)	1.9 (1.1 - 3.2)	0.01
Cell cycle score									
Low (ref)	329 (38)	1 (-)	-	118 (35)	1 (-)	-	166 (44)	1 (-)	-
Intermediate	283 (32)	1.8 (1.2 - 2.6)	0.003	128 (38)	1.7 (1 - 2.7)	0.04	130 (35)	1.9 (1 - 3.6)	0.04
High	259 (30)	2.3 (1.5 - 3.5)	< 0.001	89 (27)	2.7 (1.6 - 4.6)	< 0.001	78 (21)	2.1 (1 - 4.5)	0.02
21-gene RS									
Low risk (ref)	199 (23)	1 (-)	-	75 (23)	1 (-)	-	106 (28)	1 (-)	-
Intermediate risk	211 (24)	1.1 (0.6 - 1.8)	0.42	98 (29)	1.2 (0.6 - 2.3)	0.52	102 (27)	1.2 (0.6 - 2.6)	0.57
High risk	461 (53)	1.7 (1 - 2.5)	0.001	162 (48)	2.5 (1.4 - 4.3)	0.002	166 (45)	1.6 (0.8 - 3.2)	0.17

NOTE: Bold values indicate P < 0.05.

^a Adjusted for tumor size, tumor grade, estrogen receptor status, and lymph node status.

^b Adjusted for tumor size and tumor grade.

NOTE: Bold values indicate P < 0.05.

a Adjusted for tumor size, tumor grade, estrogen receptor status, and lymph node status.

b Adjusted for tumor size and tumor grade.

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P6-01-09

Efficacy of platinum-based chemotherapy and germline mutational status in early-stage triple-negative breast cancer: a unicenter retrospective analysis with long-term follow-up

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BACKGROUND: In early-stage triple negative breast cancer (TNBC), the addition of carboplatin (CBDCA) to neoadjuvant chemotherapy (CT) increases pathologic complete response (pCR) and relapsed-free survival. However, it is unclear whether CBDCA improves overall survival (OS). In addition, the prognostic and/or predictive role of pathogenic germline variants (PGV) in BRCA1/2 genes and other cancer risk in this setting is not fully understood. Here, we assessed the efficacy of (neo)adjuvant CBDCA and the prognostic and predictive role of a panel of 14 genes in patients (pts) with eTNBC.

METHODS: This is a retrospective study on 117 pts diagnosed with early-stage TNBC between 2000-2021 at Hospital Clinic of Barcelona. Eighty-one pts (69%) were candidates for PGV testing. Overall, 14 genes (PGV) (BRCA1, BRCA2, PALB2, BRIP1, CHEK2, TP53, ATM, RAD51C, RAD51D, BARD1, MLH1, MSH2, MSH6 and PMS2) were assessed using the TruSight hereditary cancer panel (Illumina MySeq platform) according to local guidelines. Univariable and multivariable logistic regression and Cox regression analyses were performed to identify clinical and molecular predictors of pCR and relapse-free survival (RFS), respectively. Chi-squared or Fisher's exact tests were used to assess characteristics' distribution as appropriate.

RESULTS: Of 117 pts, 83 (71%) received CT in the neoadjuvant setting and 28 (24%) in the adjuvant setting. CBDCA was added to standard CT in 68 pts (82%) in the neoadjuvant cohort and 7 pts (6%) in the adjuvant cohort. Among pts with germline testing, 32/81 (39%) harbored PGV. BRCA1 was the most frequently mutated gene (18/32, 56%), followed by BRCA2 (5/32, 16%), PALB2 (4/32, 13%), BRIP1 (2/32, 6%), CHEK2, TP53 and PMS2 (3/32, 6%). Percentages of pts receiving CBDCA were similar between patients with and without PGV (14/16, 87% and wild type (53/67, 79%) (p=0.120). In the neoadjuvant cohort (n=83), CBDCA was the only variable significantly associated with pCR at both univariate (pCR rates of 58.5% with CBDCA and 14.3% without CBDCA; odds ratio [OR]=8.2 [95% CIs 2.0-55.7], p=0.008) and remained statistically significant after adjusting for PGV, tumor size and nodal status (OR=6.9 [95% CIs 1.4-53.0], p=0.028). pCR rates according to PGV are reported in Table 1. In terms of RFS, addition of CBDCA to neoadjuvant therapy (hazard ratio [HR]=0.2 [0.1-0.45], p< 0.001), PGV (HR=0.2 [0.05-0.9], p=0.048), pCR (HR=0.2 [0.1-0.6], p=0.004) and nodal status (HR=5.1 [1.7-15.2], p< 0.003) were significantly associated with RFS in univariate analyses. In a multivariable model, CBDCA remained an independent predictor of improved RFS along with pCR. When the neoadjuvant and adjuvant cohort were pooled together (n=117), platinum-based CT remained significantly associated with better RFS (HR=0.2 [0.14-0.86], p=0.021) regardless of time of administration (i.e., neoadjuvant or adjuvant). With a median follow-up of 5 years, CBDCA use was not found associated with OS (HR=0.7 [0.3-1.8], p= 0.560).

CONCLUSIONS: The addition of CBDCA to standard CT was significantly associated with pCR and RFS but not OS, consistent with the phase III data. The benefit in terms of RFS was

independent of the presence and the type of pathogenic germline alterations.

Table 1. pCR rates according to PGV

Pathogenic germline variants (PGV)	n _{total}	pCR rate
<i>BRCA1</i>	18	8/11 (73%)
<i>BRCA2</i>	5	1/1 (100%)
<i>PALB2</i>	4	1/1 (100%)
<i>BRIP1</i>	2	2/2 (100%)
<i>CHEK2/TP53/PMS2</i>	3	0/1 (0%)
Wild Type/ Unknown	86	28/67 (42%)

Table 1. pCR rates according to PGV

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12/9/2022

7:00 AM - 8:15 AM

P6-01-11

A UK prospective multicentre decision impact, decision conflict and economic evaluation of the use of Oncotype DX® to guide chemotherapy in 680 women with hormone receptor positive, HER2 negative breast cancer and 1 to 3 nodes involved.

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Introduction: For a test to be of value, it needs to demonstrate that it is changing clinical decisions, improving clinical confidence and of economic benefit.

This trial looked at the use of Oncotype DX Breast Recurrence Score ® (RS) assay against these criteria in 680 women with hormone receptor positive (HR+), HER2 negative early breast cancer with 1 to 3 lymph nodes positive (LN+) in the UK National Health Service (NHS) (5 teaching and 9 district general hospitals) between 2017 and 2022.

Methods: Patients with LN+ early breast cancer who were willing and fit to receive chemotherapy (CT) were consented to join the trial. At the initial oncologists' appointment, physicians were asked to state their preference for or against CT and their level of confidence in their decision on a scale of 1 to 5. Following receipt of the RS result physicians were asked to make a final decision for or against CT and similarly record their level of confidence.

Descriptive analyses were used to characterize (1) patient and tumour characteristics, (2) change in treatment recommendations post-RS testing (by RS result and nodal status), and (3) change in physicians' level of confidence post-RS testing (by RS result and nodal status). Average cost for chemotherapy and RS test price were used to estimate overall cost savings.

Results: A total of 680 patients were recruited. 16 patients were excluded (5 failed samples, 5 withdrew consent, 3 HER2 positives, 2 with advanced disease, and 1 specimen delayed in transit), leaving 664 assessable patients. The median age was 58 years and 77.1% of women were post-menopausal. Most patients had a RS of 0-17 (n=400, 60.2%); while 206 (31%) had a

RS of 18-30 and 58 (8.7%) had a RS of 31-100. Using post-RxPONDER cutoffs, 566 (85.2%) had an RS of 0-25; 98 (14.8%) had an RS of 26-100.

Decision impact results:

The decision impact results broken down by RS result and nodal status are detailed in Table 1. Of the 662 patients with complete decision impact data, in 359 (54.2%) the recommendation by the physician changed from CT+ hormone therapy (HT) to HT alone. In 286 (43.2%) cases the decision was unchanged and in 17 (2.6%) the recommendation changed from HT alone to CT+HT. Overall 342 (51.7%) cases were spared chemotherapy.

Decision conflict results:

The change in the physicians' level of confidence by RS result and nodal status are detailed in Table 2. Of the 660 cases with complete decision conflict data, physicians reported an increase in confidence in their recommendations after receiving the RS in 363 (55.0%), confidence was unchanged in 219 (33.2%) and decreased confidence in 78 (11.8%) cases.

Economic analysis:

Using the estimates of Burdanov et al, the average costs of a course of chemotherapy in the UK is £6,000 to £7,000. An estimate of the overall cost saving of 342 courses is £2,064,00 to £2,408,000 and the overall cost of 664 RS assays at the list price of about £2580 (although an undisclosed discount applies to the NHS) is £1,713,120. This suggests that the use of RS assay represents a significant saving to the NHS.

Conclusion:

The use of Oncotype DX assay in node positive early breast cancer leads to about half of women being spared chemotherapy, a significant improvement in clinical confidence for oncologists and an economic saving to the health care system.

Table 1 Pre- vs Post-Oncotype DX Treatment Recommendation by Physician According to Recurrence Score and Nodal Status

Table 1 Pre- vs Post-Oncotype DX Treatment Recommendation by Physician According to Recurrence Score and Nodal Status

	Recurrence Score Categories, N (%)												Overall		
	0-17				18-30				31-100						
	Nodal Status Category												Overall		
	N1	N2	N3	Mic	N1	N2	N3	Mic	N1	N2	N3	Mic			
CT+HT to HT	151 (65.9)	85 (70.8)	28 (84.8)	10 (55.6)	52 (42.6)	22 (40.7)	8 (32.0)	2 (40.0)	1 (3.0)	0	0	0	274 (68.5)	84 (40.8)	1 (1.7)
HT to CT+HT	3 (1.3)	0	0	0	11 (9.0)	0	0	1 (20.0)	1 (3.0)	0	0	1 (33.3)	3 (0.6)	12 (5.8)	2 (3.4)
No change	75 (32.8)	35 (29.2)	5 (15.2)	8 (44.4)	59 (48.4)	31 (57.4)	16 (64.0)	2 (40.0)	31 (93.9)	17 (100)	5 (100)	2 (66.7)	123 (30.8)	108 (52.4)	55 (94.8)
Missing	0	0	0	0	0	1 (1.9)	1 (4.0)	0	0	0	0	0	0	2 (1.0)	0

HT = Hormone Therapy, CT = Chemotherapy, N1 = 1 node, N2 = 2 nodes, N3 = 3 nodes, Mic = Micromets

Table 2 Change in Physicians' Level of Confidence Post-Oncotype DX Testing According to Recurrence Score and Nodal Status

Table 2 Change in Physicians' Level of Confidence Post-Oncotype DX Testing According to Recurrence Score and Nodal Status

	Recurrence Score Categories, N (%)												0-17	18-30	31-100	0-17	18-30	31-100
	Nodal Status Category																	
	N1	N2	N3	Mic	N1	N2	N3	Mic	N1	N2	N3	Mic	Overall					
Increased Confidence	139 (60.7)	62 (51.7)	18 (54.5)	11 (61.1)	56 (45.9)	31 (57.4)	6 (24.0)	4 (80.0)	23 (69.7)	9 (52.9)	3 (60.0)	1 (33.3)	230 (57.5)	97 (47.1)	36 (62.1)			
Decreased Confidence	23 (10.0)	18 (15.0)	3 (9.1)	1 (5.6)	20 (16.4)	8 (14.8)	4 (16.0)	0	0	1 (5.9)	0	0	45 (11.3)	32 (15.5)	1 (1.7)			
No Change	67 (29.3)	40 (33.3)	12 (36.4)	6 (33.3)	44 (36.1)	14 (25.9)	14 (56.0)	1 (20.0)	10 (30.3)	7 (41.2)	2 (40.0)	2 (66.7)	125 (31.3)	73 (35.4)	21 (36.2)			
Missing	0	0	0	0	2 (1.6)	1 (1.9)	1 (4.0)	0	0	0	0	0	0	4 (2.9)	0			

HT = Hormone Therapy, CT = Chemotherapy, N1 = 1 node, N2 = 2 nodes, N3 = 3 nodes, Mic = Micromets

Disclosure(s):

Simon D. Holt, MBE MA MB BChir FRCS: Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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12/9/2022

7:00 AM - 8:15 AM

P6-01-12

Predictive value of immune genomic signatures from breast cancer cohorts containing data for both response to neoadjuvant chemotherapy and prognosis after surgery

Presenting Author(s) and Co-Author(s):

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Country: United States

Abstract Background Previous studies of immune-related gene signatures (IGSs) in breast cancer have attempted to predict the response to chemotherapy or prognosis and were performed using different patient cohorts. The purpose of this study was to evaluate the predictive functions of various IGSs using the same patient cohort that included data for response to chemotherapy as well as the prognosis after surgery. **Methods** We applied five previously described IGS models in a public dataset of 508 breast cancer patients treated with neoadjuvant chemotherapy. The prognostic and predictive values of each model were evaluated, and their correlations were compared. **Results** We observed a high proportion of expression concordance among the IGS models ($r: 0.56-1$). Higher gene expression scores of IGSs were detected in aggressive breast cancer subtypes (basal and HER2-enriched) ($P < 0.001$). Four of the five IGSs could predict chemotherapy responses and two could predict 5-year relapse-free survival in cases with hormone receptor-positive (HR+) tumors. However, the models showed no significant differences in their predictive abilities for hormone receptor-negative (HR-) tumors. **Conclusions** IGSs are, to some extent, useful for predicting prognosis and chemotherapy response; moreover, they show substantial agreement for specific breast cancer subtypes. However, it is necessary to identify more compelling biomarkers for both prognosis and response to chemotherapy in HR- and HER2+ cases.

Disclosure(s):

Yidan Zhu, phd student: No financial relationships to disclose

12/9/2022

7:00 AM - 8:15 AM

P6-01-13

Identification of Protein Biomarkers for Early Detection and Stratification of Triple Negative Breast Cancer

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Breast cancer (BC) is the most frequent malignancy in women worldwide. Breast cancer affects roughly 3,000,000 people worldwide, with triple negative breast cancer (TNBC) accounting for 10-15% of all cases. In comparison to other types of breast cancer, TNBC stands out for its heterogenous disease, poor prognosis and aggressive behaviour. In the early stages of TNBC, neoadjuvant chemotherapy (NAC), which is given to the patient before surgery, has been considered a viable treatment strategy. Pathological complete response (pCR), which has been shown to increase estimates of disease-free (the amount of time following treatment during which there are no signs of malignancy), distant recurrence-free (the cancer has spread to far-off regions of the body) and overall survival, has been linked to NAC in 30% of patients. The objective of this study was to apply mass-spectrometry-based proteomics to serum samples from TNBC patients who have received NAC to identify i) biomarkers that might predict response to NAC, ii) biomarkers that might correlate with the extent of residual disease. These biomarkers will potentially inform treatment decisions such as the escalation/de-escalation of chemotherapy dosage for early TNBC patients. In this study, two proteomic approaches have been used to identify and measure protein candidate biomarkers: un-biased LC-MS/MS and targeted proteomics respectively. The discovery approach led to the identification of 17 unique proteins and 118 unique peptides that were differently expressed. The developing of a multiple reaction monitoring (MRM) assay for biomarker evaluation will be based on the prioritization of the potential signature proteins and other proteins obtained from public resources. Subject to successful evaluation and subsequent validation the candidate biomarkers may be beneficial for identifying TNBC patients who will achieve residual disease after NAC.

Disclosure(s):

Essraa metwali, phd: No financial relationships to disclose

Stephen Pennington, n/a: No financial relationships to disclose

12/9/2022

7:00 AM - 8:15 AM

P6-01-14

Genomic characterization and oncology outcomes of a locally advanced ER+/HER2-breast cancer cohort treated with neoadjuvant chemotherapy

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Background: Locally advanced ER+/HER2- breast cancer (LABC) is an aggressive condition often requiring multidisciplinary management. While early and metastatic breast cancer are well characterized, LABC is largely underrepresented in clinical trials and genomic studies. Herein we present comprehensive molecular profiling of an ER+/HER2- LABC cohort and their oncology outcomes. Method: The clinical records of locally advanced ER+/HER2- LABC (EC IIIA or higher) patients diagnosed and treated with neoadjuvant chemotherapy at Hospital de

Base (Sao Jose do Rio Preto, Brazil) were reviewed. Comprehensive genomic profiling was performed on formalin-fixed paraffin-embedded (FFPE) tumor samples using capture-based hybrid next-generation sequencing (NGS) by targeting 425 cancer-related genes. The status of patients' homologous recombination deficiency (HRD) and tumor mutation burden (TMB) were also measured. Survival outcomes were estimated using the Kaplan-Meier method. Univariable and multivariable analyses were performed to assess the association between oncology outcomes with clinicopathological and molecular characteristics. A p-value of 0.05 was considered statistically significant. FDR was utilized for multiple comparisons adjustment. Result: From May 2010 and December 2019, after inclusion and exclusion criteria, 90 patients were included. The median age of the cohort was 54 (24 – 88) years old. There were 21 (23%), 65 (72%), and 4 (5%) patients with stage IIIA, IIIB, and IIIC, respectively. A majority of the patients had tumors Grade 2 (72%, 65/90), with 10 (11%) Grade 1, 12 (13%) Grade 3, and the remaining 3 (4%) being undetermined. Most patients were postmenopausal, 58% (52/90). All patients received chemotherapy-based neoadjuvant treatment, and 6 (7%) achieved pathological complete response (pCR). After a median follow-up of 63 months, the median recurrence-free survival (RFS) of the entire cohort was 80.4 months and the median overall survival (OS) was not reached yet. A lower tumor grade was strongly associated with better RFS ($p = 0.00058$) and OS ($p = 0.00028$), while the pCR subgroup did not show significantly better RFS or OS. In terms of genomic profiling, *PICK3CA* (32/90, 35.6%) and *TP53* (27/90, 30.0%) were the most frequently mutated genes. The median TMB was 4.1 muts/Mb, ranging from 0 to 29.7 muts/Mb. Altered NOTCH pathway was a negative prognostic factor (HR: 2.6; 95%CI: 1.0 - 6.5, $p = 0.042$) while NRF2 pathway aberrations demonstrated poorer RFS compared to their wildtype counterparts (HR: 3.1; 95%CI: 1.1 - 8.9, $p = 0.035$). Of note, mutated *CUL3*, a key player of the NRF2 pathway, was correlated with poor RFS (HR: 42.8; 95%CI: 7.0 - 262.5, adjusted $p = 0.0004$) and OS (HR: 48.4; 95%CI: 8.0 - 294.0, adjusted $p = 0.0003$) although the sample size was restricted. Furthermore, patients carrying NOTCH2 mutations ($N = 2$) showed significantly shorter RFS (HR: 14.9; 95%CI: 3.0 - 74.2, adjusted $p = 0.004$) and OS (HR: 28.8; 95%CI: 5.2 - 160.2, adjusted $p = 0.0008$). TMB was not a predictor of either pCR or survival. Eight patients carried BRCA1/2 pathogenic mutations (8.9%), and ten out of 44 HRD evaluable patients (22.7%) were HRD-high (HRD score ≥ 38). However, neither BRCA1/2 mutations nor HRD-positivity was associated with pCR, RFS, or OS. Conclusion: Comprehensive genomic profiling of ER+/HER2- LABC patients revealed that altered NOTCH and NRF2 pathway genes were associated with poor survival outcomes. An analysis involving residual cancer burden (RCB) is currently ongoing.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-01-15

Breast cancer patients with different hormone receptor subtypes receiving neoadjuvant chemotherapy (NAC) experience differential overall survival according to their resistance to NAC

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Background:

Response to neoadjuvant chemotherapy (NAC) is an indicator of outcomes and can be quantified as achievement of pathologic complete response (pCR) (absence of residual invasive disease in breast and lymph nodes) and residual percent cellularity. However, the significance of residual tumor cellularity post-NAC is not well understood. We assessed the impact of NAC-induced reduction in tumor cellularity among hormone receptor subtypes and the effect of these reductions on overall survival (OS).

Methods: An IRB-approved retrospective review identified demographics, disease presentation, response to treatment, and outcomes. ER and PR status were categorized as low positive (1-9%), positive ($\geq 10\%$) and negative. Treatment response was noted as percent residual cellularity (complete 0%, almost complete $< 10\%$, good 10-30%, moderate $>30-80\%$ and poor $>80\%$) in the surgical specimen and pathologic stage. We examined measures of response to NAC within breast tumor subtypes and the effect of these responses on associations with OS among hormone receptor subtypes.

Results:

The clinical series comprised 384 patients who received curative intent NAC. This series was diverse in presentation, displayed considerable variability in response to NAC (Table 1). 88 (23.6%) patients did not experience tumor down staging, and of those presenting with clinical nodal Stage 1 or higher (n=197), 94 (47.7%) did not experience nodal down staging. Although

Triple Negative Breast Cancer (TNBC) status was not significantly associated with post-NAC residual tumor cellularity ($p=0.74$), ER, PR, and HER2 status were individually associated with this measure of response to NAC ($p=0.04$, 0.01 , and 0.01 , respectively). However, none of these associations explained more than 2.5% of the variability in this marker of treatment response. Median non-censored follow-up time was 4.26 years. Accounting for censoring, median survival was 13.65 years (lower 95% confidence limit was 11.79 years). Differential associations with OS were observed for three hormone receptor subtypes (ER: $p < 0.001$, HER2: $p=0.04$, and TNBC: $p < 0.001$) according to residual tumor cellularity, classified by percent residual cellularity categories of complete or almost complete response versus all others. Importantly, although ER negative patients with poor residual cellularity response had worse OS than ER positive patients with good response (Hazard Ratio [HR], 95% Confidence Interval [CI] = 4.74, 2.2-10.2), ER negative patients with good response did not have significantly worse OS than ER positive patients with good response (HR, 95% CI = 1.37, 0.57-3.26). Similar patterns were seen for patients with HER2 negative breast cancer or TNBC. Chemo resistant TNBC patients had higher risks for mortality than if they were not chemo resistant (HR, 95% CI: 2.41, 1.02-5.71).

Conclusions:

Our data suggest that OS associated with different hormone subtypes differs according to response to NAC. Differential OS according to response to NAC is greatest for patients classified according to ER status influences, with good response eliminating much of the differential mortality risk between ER negative and positive patients. There is a similar difference according to TNBC, although the difference appears to be less complete. Further studies should focus on understanding the chemo resistance of ER negative tumors, and perhaps TNBC, to identify mechanisms that may ultimately drive treatment response and survival.

Table 1. Demographic and other characteristics

Table 1. Demographic and other characteristics

Characteristic	Mean	Standard Deviation
Age at Diagnosis	51.0	11.8
BMI	28.6	6.3
Characteristic	N	%
Race		
American Indian	25	6.7
Black	9	2.4
White	42	79.6
Other/Unknown	296	11.3
Hispanic Ethnicity	196	53.7
Clinical Stage III or higher	120	32.3
Clinical T Stage		
1	38	10.2
2	196	52.7
3	108	29.0
4	30	8.1
Clinical N Stage		
0	175	47.0
1	129	34.7
2	44	11.8
3	24	6.5
ER		
Negative	159	42.7
Low-Positive	31	8.3
Positive	182	48.9
PR		
Negative	175	47.0
Low-Positive	51	13.7
Positive	146	39.2
HER2 positive	131	35.2
Triple Negative	93	25.0
Invasive Ductal Carcinoma	344	92.5
Received Standard of Care Chemotherapy	370	99.5
Completed NAC	290	78.2
Pathologic Response (PR)		
None	10	2.7
Partial PR	249	67.5
pCR	110	29.8
Percent Cellularity Response		
Poor	27	7.3
Moderate	77	20.7
Good	45	12.1
Almost Complete	79	21.2
Complete	111	29.8
Unknown	33	8.9

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Sangeetha Prabhakaran, MD: Biotheranostics: Consulting Fees (e.g., advisory boards)

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12/9/2022

7:00 AM - 8:15 AM

P6-01-16

Circulating Tumour DNA (ctDNA) Detection and Dynamics in Patients with Early Breast Cancer (EBC): Results of the Neoadjuvant TRACER cohort

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Background: ctDNA dynamics are associated with treatment response, and ctDNA detection following treatment is associated with disease recurrence in early breast cancer (EBC). Highly sensitive assays may permit effective risk stratification and guide interventional strategies.

RaDaR, a bespoke assay using deep sequencing of tumour-specific variants, has been shown to detect recurrence in the postoperative setting. We quantified ctDNA using RaDaR in serial samples from a large prospective cohort of EBC patients who received standard neoadjuvant chemo- (+/- HER2- targeted) therapy.

Methods: Patients with EBC of all receptor subtypes receiving neoadjuvant therapy were enrolled in the TRACER cohort from 2015. Plasma samples (Streck) were collected at baseline, during treatment, perioperatively, and during follow-up. RaDaR was performed on all available timepoints for patients with tissue available for exome sequencing (assay requirement). Clinical and pathologic characteristics, treatment, and recurrence outcomes were collected.

Results: 145 patients were recruited as of April 2021, and over 700 plasma samples were collected through December 2021 (patient characteristics, Table 1). 115 (79%) tissue samples were retrieved for assay design. Data are presented for the initial 43 patients and 265 samples analyzed, including 82 post-surgical time points. Median time since diagnosis was 3.5 years (range, 1.5-5.0). Exome sequencing and assay generation were successful in all patients (n=43), yielding assays targeting a median of 48 (range 22-50) variants. 88% (38/43 patients) had ctDNA detected at baseline, with median variant allele frequency (eVAF) in positive patients of 0.15% (range, 0.0019-4.9%). ctDNA levels fell rapidly with treatment: 19/37 (51.3% ; median eVAF in positive patients: 0.0098% , range 0.001-0.156%) had ctDNA detected prior to cycle 2, and 4/32 (12.5%) had ctDNA detected at cycle 4 or 5 (mid treatment ; median eVAF in positive patients: 0.001% , range, 0.0007-0.011%). In the perioperative period, 17/18 (94%) of patients with available pre-operative specimens and 27/28 (96%) of patients with available post-operative samples had clearance of ctDNA. In adjuvant follow up, ctDNA was detected in 4 of the 43 analyzed patients, with ctDNA clearance observed following planned switch of endocrine therapy in one. Clinical follow-up continues, and analysis of the remaining samples (72 patients and over 425 samples) is underway.

Conclusion: RaDaR demonstrated high sensitivity for ctDNA prior to treatment in patients receiving neoadjuvant therapy for EBC, permitted dynamic monitoring of treatment effect, and identified patients with persistent ctDNA after curative-intent therapy, as well as ctDNA emergence prior to clinical recurrence. Full results for the TRACER cohort and analysis of clinical covariates will be presented at the meeting. ClinicalTrials.gov NCT03702309.

Table 1

Table 1:

	Results (n=43)
Age (Median [Range])	49.0 [24-71]
Pre-menopausal (%)	65.1
HR+/HER2- (%)	27.9
HR+/HER2+ (%)	20.9
HR-/HER2+ (%)	18.6
TNBC (%)	32.6
Taxane-based (%)	9.3
Sequential Anthracycline + Taxane (%)	90.7
IDC (%)	95.4
pCR - YES (%)	32.6
cT1/2 (%)	62.8
cT3/4 (%)	37.2
cNO (%)	46.5
cN1 (%)	53.5

Patient Baseline Characteristics

Disclosure(s):

Mitchell J. Elliott, MD: No financial relationships to disclose

Zachary Veitch, MD: No financial relationships to disclose

Philippe Bedard, MD: Amgen: Contracted Research (Ongoing); AstraZeneca: Contracted Research (Ongoing); Bicara: Contracted Research (Ongoing); BristolMyersSquibb: Contracted Research (Ongoing); Genentech/Roche: Contracted Research (Ongoing); Lilly: Contracted Research (Ongoing); Medicenna: Contracted Research (Ongoing); Merck: Contracted Research (Ongoing); Novartis: Contracted Research (Ongoing); SeaGen: Contracted Research (Ongoing); Zymeworks: Contracted Research (Ongoing)

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12/9/2022

7:00 AM - 8:15 AM

P6-01-17

A single-center prospective cohort study to evaluate circulating tumor cells as a monitoring tool in women with breast cancer treated with neoadjuvant chemotherapy

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Background The presence of circulating tumor cells (CTCs) among women before and/or after completion of neoadjuvant chemotherapy (NAC) for breast cancer may be associated with an increased risk of recurrence, but limited data is available. **Objectives** To use the Epic Sciences platform to detect and enumerate CTCs in blood samples from women with a new diagnosis of non-metastatic breast cancer of any subtype both i) prior to commencing NAC, and ii) after completion of NAC and surgery. **Methods** Inclusion criteria included women of any age with non-metastatic breast cancer of any subtype who have not yet commenced NAC. Those diagnosed with prior invasive cancer at any site (apart from non-melanoma skin cancer diagnosed more than five years prior to enrollment) were excluded. Blood samples were obtained to measure CTCs prior to NAC and after NAC and surgery, respectively. CTC identification was based on immunofluorescence analysis using Epic Sciences platform as previously described (Ueno et al 2017). The presence of CTCs was correlated with clinical/pathological data and treatment response, which were abstracted from patients' medical records. The association between the presence of CTCs and clinical/pathologic characteristics was tested using Fisher's exact test for categorical variables and t-test or Wilcoxon rank sum tests for numerical variables. All analyses were performed using the R software package. An

ad-hoc preliminary analysis was conducted among the first 34 of 50 participants. Results 41 patients (out of an intended 50) have been recruited to-date. 34 participants have a pre- and/or post-treatment CTC measurement available, but 1 was excluded because it was identified to have metastatic disease shortly after enrollment. Among 33 evaluable patients without metastatic disease, 6 (19%) had triple negative breast cancer (TNBC), 13 (39%) had HER2+ and 13 (39%) had hormone receptor (HR)+/HER2- breast cancer. Most (94%) received anthracycline and taxane-based NAC. The median age of breast cancer diagnosis was 50 (29-75). A total of 53 samples were tested for CTC enumeration (5 mL per sample) including 33 pre-treatment and 20 post-treatment samples. CTCs were detected in 32 samples (n=32/53, 60%), including 24 pre-NAC (n=24/33, 73%) with a median of 0.9 CTCs per mL (0.2-19) and 8 post-NAC and surgery (n= 8/20, 40%) with a median of 0.6 CTCs per mL (0.3-3.3). Among the 24 patients (73%) who had detectable CTCs pre-NAC, 10 had HR+/HER2- (41.7%), 9 had HER2+ (37.5%) and 4 (16.7%) had triple negative disease. Among the 20 patients for whom matched pre- and post-treatment CTC results were available, 16 (80%) had detectable CTCs pre-treatment and 8 (40%) had detectable levels post-NAC and surgery. Among the 8 patients (40%) for whom CTCs were detectable post NAC and surgery, 4 (50%) had HR+/HER2-, 2 had HER2+ (25%) and 2 (25%) had triple negative disease. 3 of these patients had numerically higher CTC levels after completion of NAC and surgery compared to pre-NAC levels, 2 of whom had HR+/HER2- breast cancer and one of whom had TNBC. A total of 7 of 33 patients achieved a pathological complete response (PCR) to NAC, among whom 3 had matched pre- and post-treatment CTC results available; none of these 3 patients had detectable CTCs post-treatment. Conclusions Approximately 3 in 4 women with non-metastatic breast cancer who undergo NAC have detectable CTCs pre-treatment using the Epic Sciences Platform. Of 20 patients with matched pre-/post-treatment results, a high proportion (40%) have persistently detectable CTCs. Hence, CTCs may represent an additional measure of minimal residual disease for patients undergoing NAC for breast cancer.

Disclosure(s):

Rania chehade, MD, MSc: No financial relationships to disclose

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Veronika Moravan, Msc: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-01-18

Predicting response of triple negative breast cancer to neoadjuvant chemotherapy using a deep convolutional neural network-based artificial intelligence tool

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Background: Triple-negative breast cancer (TNBC) is commonly treated with neoadjuvant chemotherapy (NAC). Pathologic complete response (pCR) to NAC is associated with improved patient outcomes. The ability to predict which patients have high likelihood to achieve pCR has important clinical implications. We developed and validated a deep convolutional neural network (CNN)-based artificial intelligence (AI) model to extract morphometric features of TNBC to predict response to NAC. Methods: Whole-slide images (WSIs) of hematoxylin and eosin-stained core biopsies of 165 (pathologic complete response [pCR] in 60 and non-pCR in 105) and 78 (pCR in 31 and non-pCR in 47) TNBC patients, respectively, were used for training and validation of the model. The model extracted morphometric features from WSIs in an unsupervised way and transformed the image tiles from WSIs into high-dimensional vectors, generating clusters of morphologically similar patterns. Downstream ranking of clusters using neural networks provided regions of interest with high or low predictive value for NAC response. Morphometric scores combined with clinical TNM stage gave AI prediction scores; a low score close to 0 and high score close to 1, respectively, represented a high or low probability of pCR, respectively. Results: The predictive ability of the AI score for the entire cohort of 78 TNBC patients ascertained by receiver operating characteristic (ROC) analysis demonstrated area under the curve (AUC) of 75.5%. The AUC for stage I, II, and III disease was 88.1%, 73.7%, and 74.7% respectively. The performance of the AI scores was also analyzed based on their distribution into quartiles. Patients in the highest score quartile were predicted to not have pCR and those in the lowest score quartile were predicted to have pCR. Of the 20 patients in the lowest score quartile, 15 experienced pCR yielding a positive predictive value of the AI score for pCR of 75%. Of the 20 patients in the highest score quartile, 16 did not have pCR, yielding a negative predictive value of 80%. Conclusions: This is the first demonstration of using an AI tool to predict response to NAC in patients with TNBC. These results if validated in subsequent studies, could inform individualized decisions regarding intensity of NAC, including options to de-escalate NAC in patients with TNBC who are likely to achieve pCR.

Disclosure(s):

Savitri Krishnamurthy, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Caliber ID: Contracted Research (Ongoing); PathomiQ Inc.: Contracted Research (Ongoing); Perimeter Imaging: Contracted Research (Terminated, November 30, 2021)

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12/9/2022

7:00 AM - 8:15 AM

P6-01-19

Multiparametric MRI-based Longitudinal-radiomics Analysis for Early Prediction of Treatment Response of Breast Cancers to Neoadjuvant Chemotherapy: A Multicenter Study

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Purpose: We evaluated the performance of the longitudinal-radiomics of multi-parametric magnetic resonance imaging (MRI), developed and validated based on a multicenter dataset adopting a radiomic strategy, for prediction of treatment response to neoadjuvant chemotherapy (NAC) in breast cancer.

Methods and materials: We analyzed clinical and pathological data of patients with breast cancer and compared machine-learning classification algorithms in predicting treatment response following NAC from four hospitals (primary cohort and external validation cohort 1-3) between July 2015 and December 2021. Patients were monitored with MRI before (pretreatment) and after (mid-treatment) three or four cycles of NAC. Longitudinal-radiomics analysis was performed at pre- and mid-treatment dynamic contrast-enhanced, T2-weighted imaging, and diffusion-weighted imaging mapping by using 3D Slicer software. Radiomics features were extracted from original and filtered images using PyRadiomics (V3.0.1) filtered images were generated using Laplacian of Gaussian and wavelet filters. The stacking strategy including LR, LDA and SVM (radial basis function) were used to combined the results of the base models, and gave a secondary prediction result.

Results: In total, 1048 cases were enrolled in the study. In identifying the residual cancer burden (RCB) 0 v.s. RCB 1-3, longitudinal-radiomic models achieved the highest area under the receiver operating characteristic curve (AUC) of 0.909 and 0.893 in the training and test sets. The accuracies of the stacking-SVM classifier were 84.3% (86/102), 75.6% (205/271) and

77.9% (265/340) in the external validation set. In identifying the RCB 3 v.s. RCB 0-2, longitudinal-radiomic models achieved the highest AUC of 0.981 and 0.923 in the training and test sets. In the external validation set, the performance was with accuracy=91.2%-92.2%. The cascade model also stratified 78.9%, 69.1% and 76.1% of the RCB 1-2 patients into RCB 1-2 prediction group to receive suitable NAC and feasible breast-conserving surgery. Our findings showed high predictive ability and reproducibility across multicenter dataset. By two-step prediction results of cascade models, the patient could be assigned to one of the three groups corresponding to three RCB status: RCB 0, RCB 1-2, or RCB 3. In this way, using the cascade models, some of RCB 3 patients may allow treatment to be tailored for optimal outcomes. RCB 0 and RCB 1-2 groups could receive suitable NAC and feasible breast-conserving surgery.

Conclusion: In conclusion, our study had good predictive ability for RCB assessment, which could help clinicians guide individualized treatment options for breast cancer patients in NAC. The application of stacking cascade model may have the potential to further reduce unnecessary NAC and economic costs associated with current breast cancer management.

Figure 1. The flowchart of the study. This was a multicenter study with patients retrospectively enrolled from four medical centers in different cities of China. Pretreatment and midtreatment multi-parametric MRI (DCE, T2WI, and DWI) and clinical information were proposed to predict treatment response to NAC in patients with primary invasive breast cancer. The data from Foshan was used as the primary cohort (PC), and the other three data sets were used as independent validation cohorts (VC). This study included radiomic feature engineering, model building, model comparison and clinical application.

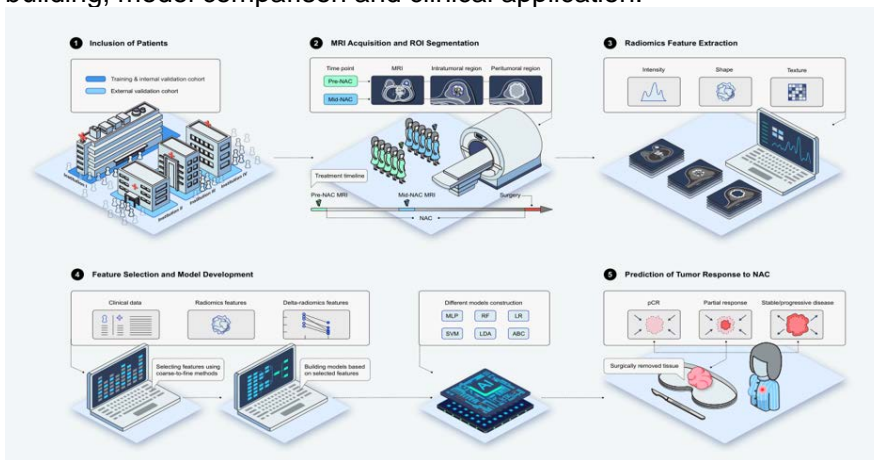


Figure 2. ROC curves among different radiomic signatures and among different models in identifying the RCB 0 vs RCB 1-3. RCB, residual cancer burden; ROC, receiver operating characteristic; SVM, support vector machine; RF, random forest; MLP, multilayer perceptron; LR, logistic regression.

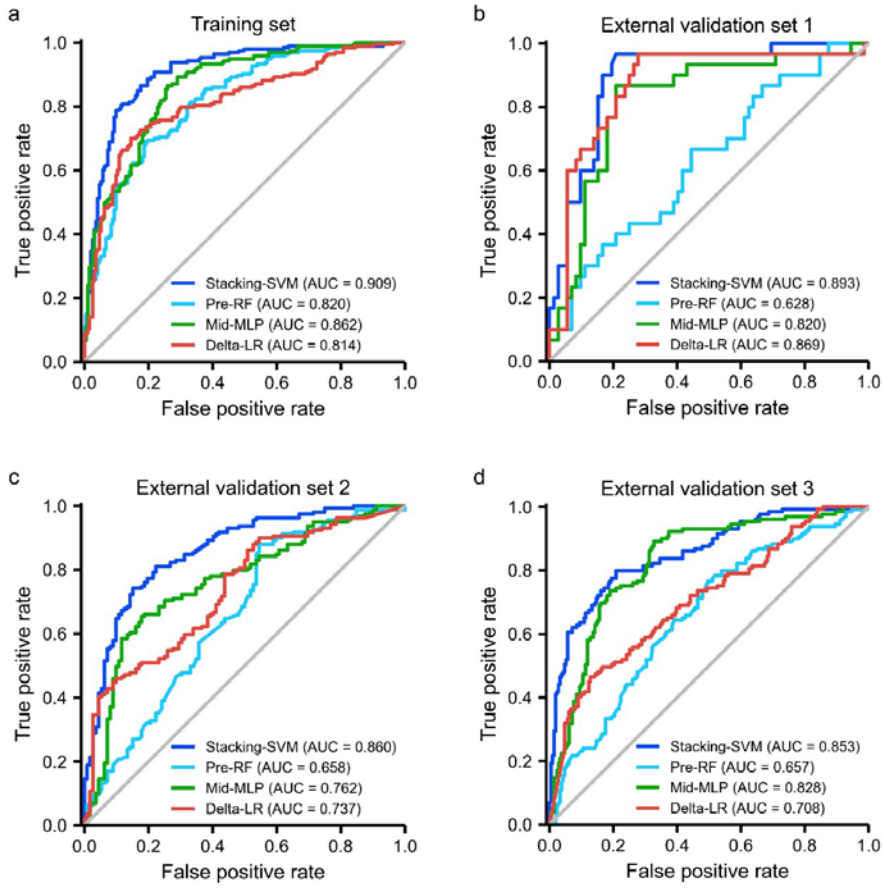
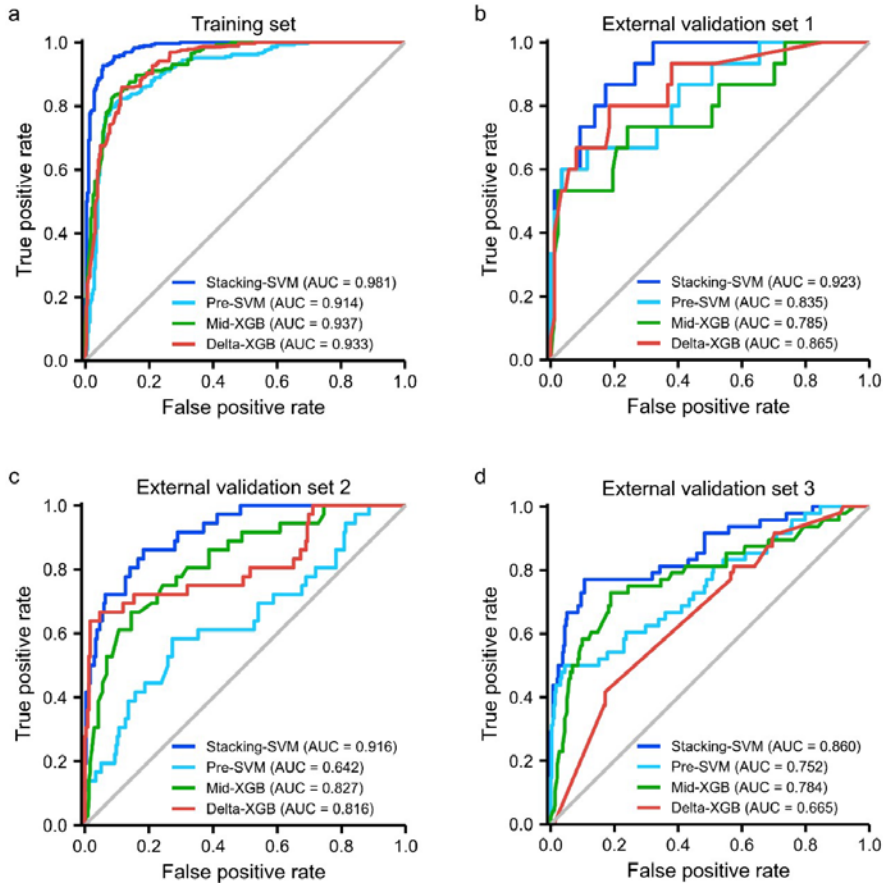


Figure 3. ROC curves among different radiomic signatures and among different models in identifying the RCB 3 vs RCB 0-2. RCB, residual cancer burden; ROC, receiver operating characteristic; SVM, support vector machine; RF, random forest; MLP, multilayer perceptron; LR, logistic regression.



Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-01-20

Luminal androgen receptor subtype and M2 macrophage signatures strongly associate with low pathological complete response rates and poor outcomes in patients with triple negative breast cancer receiving neoadjuvant chemotherapy

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Background: Triple negative breast cancers (TNBC) are a heterogeneous group of cancers and it is difficult to predict which patients will respond to neoadjuvant chemotherapies (NACT). Achieving pathologic complete response (pCR) to NACT is prognostically favorable, whereas lack of pCR is associated with high rates of recurrence and death from TNBC. Currently, there is no universally accepted biomarker to predict TNBC response to NACT. Methods: We analyzed 25 in-house TNBC biopsies that were treated with neoadjuvant adriamycin (A), cyclophosphamide (C) and paclitaxel (T) and 31 residual TNBC after NACT-ACT using RNA-seq data from macro-dissected tumor tissues from formalin fixed paraffin embedded (FFPE) blocks. Raw reads were mapped to the Human reference genome GRCH38 using the kallisto aligner v0.46.1. Immune infiltrate fractions were estimated using the Cibersort algorithm derived from the LM22 gene-signature matrix of 22 hematopoietic cell types. TNBCtype-4 classification of samples was determined calculating the enrichment of gene-sets for: Luminal Androgen Receptor (LAR), Basal-like 1 and 2 (BL1, BL2), Mesenchymal(M). Overall immune-infiltrate analysis and cancer-intrinsic subtyping were conducted independently on each transcriptional profile. Results were validated by running our novel analyzing protocol in independent cohorts including 182 TNBC cases treated with NACT-ACT from a published Vanderbilt cohort and 179 TNBC cases from the TCGA database. Results: Twenty one (68%) of the 31 residual TNBC after neoadjuvant ACT were luminal androgen receptor (LAR) subtype and significantly enriched in M2 macrophage signature. The LAR subtype and monocyte or M2 macrophage signatures strongly associated with lack of pCR in the 25 TNBC biopsy cases and 182

Vanderbilt TNBC cases treated with NACT-ACT. Survival analysis of 179 TNBC cases from the TCGA database showed a significant association of LAR subtype and M2 macrophage signature with worse survival. Conclusions: We developed a novel RNA-seq analyzing protocol that combines tumor subtype and immune profile. The LAR subtype and M2 macrophage signatures strongly associated with lack of pCR and worse survival in TNBC patients when treated with NACT-ACT. Both tumor subtype and immune profile should be considered in biomarker development and further studied in specimens from patients treated with modern chemoimmunotherapy regimens.

Disclosure(s):

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7:00 AM - 8:15 AM

P6-01-22

Age, Ki-67, Nodal pCR and overall survival following Neoadjuvant Chemotherapy for Node Positive ER+/Her2- Breast Cancer

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Background

The role of chemotherapy in node positive (N+) luminal breast cancer (BC) is often debated, given low total pathologic complete response (pCR) rates following neoadjuvant chemotherapy (NAC) and discrepancy in adjuvant chemotherapy benefit. A prior single institution study of cN+ luminal BC showed that pts age < 50 and tumor Ki-67 \geq 20% had high nodal pCR (> 35%). This study's goals were 1) to validate Ki-67 and age in relation to nodal pCR and 2) evaluate the prognostic impact of nodal pCR on overall survival (OS).

Methods

We queried the National Cancer Database 2010-2019 for pts with cN+ ER+/HER2- BC treated with NAC and surgery. Breast pCR was defined as ypT0/ypTis and nodal pCR as ypN0/ypN0i+. Ki-67 was available in 2018 & 2019 only and was used to evaluate Ki-67 and nodal pCR. 2010-2018 data were used to evaluate nodal pCR and OS. OS was analyzed using multivariable Cox proportional hazards regression.

Results

In 2018-2019, 4,801 pts were identified and 2,473 (51.5%) had Ki-67 available. Nodal pCR was 23.7% and was higher in pts < 50 years old (28.1% vs 21.1%) and in those with Ki67 \geq 20% (28.4% vs 12.7%), both $p < 0.001$. Pts < 50 with Ki67 \geq 20% had the highest nodal pCR at 31.7%, followed by age \geq 50 with Ki67 \geq 20% at 26.3%. With Ki67 < 20%, nodal pCR was

15.4% (in age < 50) and 11.3% (in age ≥ 50).

From 2010-2018, we identified 20,084 cN+ ER+/HER2- BC pts treated with NAC. Total pCR was 7.4%, 14.3% had nodal pCR only, 3.8% had breast pCR only, and 74.5% had residual disease in breast and nodes. OS at 5 years was 79.1% and varied by NAC response: 90.8% with total pCR, 83.8% with nodal pCR only, 80.7% with breast pCR only, and 76.9% with residual disease in breast and nodes. Specifically nodal pCR (with or without breast pCR) was seen in 22.0% and was associated with 5-year OS rate of 86.4% compared to 77.1% without nodal pCR, $p < 0.001$. On multivariable analysis adjusted for other clinical and treatment factors, nodal pCR was associated with better OS (adjusted HR 0.56, 95% CI: 0.50-0.61, $p < 0.001$) in all ages combined and within both the age < 50 and age ≥ 50 subgroups (see Table).

In a subgroup of pts approximating RxPonder entry criteria (defined as cT1-3, N1, Grade I or II, ER+/PR+), results were consistent with the overall cohort: nodal pCR varied by both age (17.5% in age < 50 and 13.6% in age ≥ 50, $p < 0.001$) and by Ki67 ≥ 20% vs < 20% (16.8% vs 7.9%, $p < 0.001$) and nodal pCR remained prognostic for OS with adjusted HR 0.63 (95% CI: 0.50-0.81, $p < 0.001$).

Conclusion

In cN+ ER+/HER2- BC treated with NAC, nodal pCR is more common in pts < 50 and those with high Ki-67 and is highly prognostic for OS. These data strongly suggest that NAC chemotherapy benefit should not be evaluated using total pCR rates in isolation, but for N+ pts to also consider nodal response. Given that nodal pCR is highly prognostic for OS, future neoadjuvant strategies should consider nodal pCR as a potential intermediate biomarker for long term survival.

Multivariable analysis of factors associated with overall survival, including the adjusted effect of nodal pCR

Variable*	Overall		Age <50		Age 50+	
	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value
Nodal pCR, Yes vs No	0.56 (0.50, 0.61)	<0.001	0.56 (0.47, 0.66)	<0.001	0.55 (0.49, 0.63)	<0.001
Grade						
Moderately vs well differentiated	1.49 (1.28, 1.73)	<0.001	1.76 (1.31, 2.35)	<0.001	1.39 (1.17, 1.65)	<0.001
Poorly vs well differentiated	2.40 (2.07, 2.78)	<0.001	3.14 (2.35, 4.19)	<0.001	2.09 (1.76, 2.49)	<0.001
PR Status, Positive vs Negative	0.55 (0.51, 0.59)	<0.001	0.52 (0.45, 0.59)	<0.001	0.57 (0.52, 0.62)	<0.001
Pathologic T Category						
ypT1 vs ypT0/ypTis	1.39 (1.21, 1.60)	<0.001	1.93 (1.52, 2.46)	<0.001	1.14 (0.96, 1.35)	0.149
ypT2 vs ypT0/ypTis	1.82 (1.58, 2.10)	<0.001	2.56 (2.00, 3.28)	<0.001	1.46 (1.23, 1.74)	<0.001
ypT3 vs ypT0/ypTis	2.72 (2.34, 3.16)	<0.001	4.37 (3.37, 5.66)	<0.001	2.08 (1.73, 2.50)	<0.001
ypT4 vs ypT0/ypTis	3.31 (2.81, 3.89)	<0.001	5.16 (3.81, 6.98)	<0.001	2.55 (2.10, 3.10)	<0.001
Receipt of Endocrine Therapy, Yes vs No	0.66 (0.60, 0.73)	<0.001	0.62 (0.52, 0.73)	<0.001	0.68 (0.61, 0.77)	<0.001

*Additionally adjusted for age, race, ethnicity, insurance, breast surgery, axillary surgery, adjuvant, radiation, and year of diagnosis. Unknown levels of some variables were included in the model but not reported in the table.

Disclosure(s):

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7:00 AM - 8:15 AM

P6-01-23

Role of tumor infiltrating lymphocytes and PD-L1 expression in the response to eribulin and pembrolizumab in metastatic triple negative breast cancer (mTNBC) on the ENHANCE1 trial

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Background Treatment with combination chemo-immunotherapy has become the front-line standard for eligible patients with PD-L1 positive mTNBC. PD-L1 is the only approved biomarker for pembrolizumab in metastatic breast cancer for response to combination chemo-immunotherapy, however given that it is not predictive of response in all cases additional biomarkers are needed. Tumor infiltrating lymphocytes (TILs) have been shown to be both predictive and prognostic in operable TNBC, but there are fewer data regarding the role of TILs in mTNBC. In this study we report the associations between TILs and outcomes in patients treated prospectively on the ENHANCE-1 study with eribulin and pembrolizumab. Methods ENHANCE-1 was a single arm phase Ib/II trial which evaluated the efficacy and safety of eribulin and pembrolizumab in 167 patients (pts) with mTNBC who had received 0-2 prior lines of therapy (66 pts in the first line setting [stratum 1] and 101 pts with 1-2 prior lines of therapy [stratum 2]). Objective response rate (ORR) was defined as percentage of pts with either

complete response (CR) or partial response (PR) by RECIST 1.1. The ORR was 25.8% in stratum 1 and 21.8% in stratum 2. Stromal TILs (sTIL) and intratumoral TILs were evaluated on whole slide H&E sections from biopsy specimens used for enrollment on ENHANCE-1 by breast pathology according to the International TILs Working Group guidelines. PD-L1 positivity was determined via immunohistochemistry using the Agilent 22C3 antibody. We also assessed TIL density digitally using machine learning classifiers to identify tumor/stromal tissue areas and individual lymphocytes. Results We found that there was statistically significant increase in sTIL counts in responders compared to non-responders in stratum 1 ($p=0.002$) but not in stratum 2 ($p=0.99$). We did not find any associations between intratumoral TILs and response. Quantitative PD-L1 scoring via combined proportion score (CPS) was also positively associated with response in stratum 1 ($p=0.01$) but not in stratum 2 ($p=0.34$). We also find that sTIL counts are most correlated to CPS scores (continuous) for non-responders within stratum 1 ($R^2=+0.55$, $p<0.01$). Conclusion In this population of patients with mTNBC treated prospectively with eribulin and pembrolizumab, sTILs and PDL1 CPS were each individually associated with a positive response in patients treated with front-line combination chemo-immunotherapy. Neither was predictive for patient response in stratum 2. One important caveat is the biopsies were not required immediately prior to enrollment, possibly confounding the tumor microenvironment (TME) at the time of analysis. Our data contribute to emerging data that sTILs can act as a biomarker for response to immune checkpoint inhibition when utilized in the front-line setting for mTNBC. Further characterization of the TME via quantitative immunofluorescence is ongoing. This study was funded by Eisai IIS-E7389

Disclosure(s):

Mathew Kearney, MD: No financial relationships to disclose

Hua Guo, MD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P6-01-24

Long-term outcome data using Endopredict® as risk stratification and chemotherapy decision biomarker in hormone receptor positive, HER2-negative early breast cancer

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Background: The Endopredict test is used for estimating risk of distant recurrence for women presenting with early-stage breast cancer with a positive estrogen receptor (ER) and negative human epidermal growth factor receptor 2 (HER2) status. The current ASCO Guideline Update on biomarkers confirms the value of the Endopredict test to guide decisions of adjuvant endocrine and chemotherapy. This study shows prospective long-term outcome data of early breast cancer patients whose chemotherapy decision was guided by the Endopredict test result (EPclin). Methods: ER-positive and HER2-negative early breast cancer patients with 0-3 positive lymph nodes treated between March 2012 and March 2015 were included in this single institution study. The Endopredict® test was carried out on all tumour samples. Demographic, clinical and pathological data were assessed for each patient at baseline. Treatment compliance, local recurrence, distant metastases and survival was evaluated. Risk estimates were obtained by the Kaplan-Meier method and cumulative risk functions in case of competing risks. Group comparisons were performed by Cox proportional hazards regression models and quantified through hazard ratios. Median Follow-Up was estimated by the inverse Kaplan-Meier

method. Exploratory hypothesis testing was conducted at two-sided 5% significance levels. Results: In a cohort of 368 consecutive cases the median follow-up time was 8.2 years. Endopredict allocated 238 pts (64%) in the EPclin low risk and 130 pts (34%) in the EPclin high risk group. The 5-year distant metastasis free survival (DMFS) in the EPclin low risk group was 96.6% (95% CI 0.943-0.989) and 85.5% (95% CI 0.796-0.920) in the EPclin high risk group. With a hazard ratio (HR) of 2.21 (95% CI: 1.27-3.88; p=0.005) the risk for distant metastasis in EPclin high risk patients was more than two-fold higher in comparison with EPclin low risk patients. 87 pts. (66.9%) of the EPclin high risk group underwent chemotherapy (compliant), whereas 43 pts (33.1 %) opposed the recommended chemotherapy (non-compliant). Kaplan-Meier plots in the EPclin high risk subgroups compliant vs non-compliant showed a significant disease-free survival (DFS) benefit towards the patients following the chemotherapy recommendation (HR 0.46; 95%CI 0.23-0.95; p=0.036). The 5-year DFS for the high risk compliant subgroup was 89.1% (95% CI: 0.827-0.961) vs. the high risk non-compliant subgroup with 68.9% (95% CI: 0.562-0.845). Regarding the subgroups pre- and postmenopausal, patients with a EPclin high risk test result were at significant higher risk of experiencing distant metastases than patients with a EPclin low risk test result in both subgroups (premenopausal: HR 3.55; 95%CI 1.17-12.32; p=0.025; postmenopausal: HR 1.19; 95%CI 0.99-3.7; p=0.054). We analyzed the EPclin categorization in context of the ki67 subtypes luminal A (low; 0-10%) and luminal B (high; 25-100%). The EPclin-based risk stratification was significantly associated with improved DFS in both ki67 subtypes (ki67 low: HR 4; 95%CI 1.25-12.04; p=0.021 and ki67 high: HR 3.77; 95%CI 1.19-18.93; p=0.022). 33.3% (21 pts) of all tumor samples classified as luminal B (63 pts), were reclassified towards the low risk group via Endopredict, sparing chemotherapy recommendation. Contrary 19.2% (14 pts) of all luminal A (73 pts) were categorized to high risk EPclin. Conclusion: These first long term prospective outcome data confirm, that Endopredict can guide decisions on adjuvant chemotherapy in early ER positive, HER2 negative breast cancer. Pts categorized as EPclin high risk benefitted from an adjuvant chemotherapy. Our results show that Endopredict risk stratification is also applicable in premenopausal women. Furthermore the Endopredict test showed a better classification accuracy in comparison to ki67 subtypes, resulting in a more precise estimation of prognosis.

Disclosure(s):

Evelyn Klein, n/a: No financial relationships to disclose

Adriana Josipovic, n/a: No financial relationships to disclose

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Johannes Ettl, n/a: Amgen, Celgene, Eisai, Myriad, Teva.: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer, Pierre Fabre, Lilly, Roche, AstraZeneca, Daiichi, Gilead, Seagen: Consulting Fees (e.g., advisory boards) (Ongoing)

12/9/2022

7:00 AM - 8:15 AM

P6-01-25

Evaluation of Multigene Assays as Predictors for Response to Neoadjuvant Chemotherapy in Early-Stage Breast Cancer Patients

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Background: Oncotype DX (ODX) and MammaPrint (MP) are gene-expression assays that have been established to predict distant cancer recurrence in the adjuvant chemotherapy setting. However, they have not been validated to predict pathologic complete response (pCR) to neoadjuvant chemotherapy (NACT). We sought to examine the ability of the ODX and MP assays to predict the likelihood of pCR to NACT in early-stage breast cancer patients. Methods: Data from breast cancer patients diagnosed between 2010 and 2019 were obtained from the National Cancer Database. All patients who received NACT (at least 30 days of treatment) and had pathologic response data and ODX or MP results were included. Analysis of ODX was limited to patients with hormone receptor (HR)+/HER2- stage I-III disease, while analysis of MP included both HR+/HER2- and HR-/HER2- stage I-III patients. ODX scores were modeled both

as a continuous variable and a categorical variable classified as low (0-25) and high (≥ 26) per the TAILORx trial cutoff, whereas MP results were modeled as a dichotomous variable (i.e., low risk and high risk) because numeric values were unavailable. Multivariable logistic regression models were used to assess the relationship between pCR (defined as ypT0/Tis ypN0) and ODX or MP results, adjusting for age, race/ethnicity, clinical T and N stages, tumor grade, and progesterone receptor status. Adjusted odds ratios (AOR) and 95% confidence intervals (CI) were calculated. Results: A total of 2,219 patients, treated at 630 institutions, who received NACT with an ODX recurrence score were included in the ODX cohort. Of 1,181 patients with a high ODX score, 11.2% achieved pCR, while only 1.6% of 867 patients with a low ODX score did. In the adjusted model, having a high ODX score was associated with greater odds of pCR (AOR = 4.48, 95% CI: 2.44-8.22). There was a significant monotonic increasing trend of pCR by continuous ODX score. The mean ODX score was 42.5 (SD = 15.5) in patients who achieved pCR, compared to 27.9 (SD = 13.7) in patients who did not; the discriminating capacity of ODX was moderate to strong (area under the ROC curve = 0.767). A total of 1,349 patients, treated at 337 institutions, who received NACT and had MP test results were included in the MP cohort. Of 1,141 patients with MP high risk disease, 11.8% achieved pCR, compared to < 4.8% of 208 patients with MP low risk disease. In the adjusted model, having MP high risk disease was associated with greater odds of pCR (AOR = 2.21, 95% CI: 1.02-4.77). A similar association between MP results and pCR was also found in the subset of patients who were HR+/HER2- (AOR = 2.25, 95% CI: 0.99-5.15). Conclusions: Both ODX and MP were independently associated with likelihood of pCR after NACT for early-stage, high-risk breast cancer. These findings suggest a potential role for ODX or MP testing as a predictive biomarker in the NACT setting, and can facilitate clinical decision making between physicians and patients.

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7:00 AM - 8:15 AM

P6-01-27

Utilization of the Oncotype Dx Assay for Young Patients with Early Stage, Hormone-Receptor Positive, HER2-Negative Breast Cancer in an Integrated Health System

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Background: Oncotype Dx (ODX) is one of the most widely used prognostic multigene expression assays for early-stage, hormone receptor-positive (HR+), HER2-negative (HER2-) breast cancer. Previous studies demonstrated reduction in chemotherapy in patients with a low ODX Recurrence Score (RS). Over recent years, utilization of this tool has increased in young breast cancer (YBC) patients (age \leq 40 years), a population often underrepresented in randomized clinical trials. The purpose of this retrospective study was to assess the utilization of this assay over time in an integrated health system and whether ODX RS results altered

clinical practice. Methods: YBC patients with T1-T2N0 HR+HER2- breast cancer were retrospectively evaluated. Descriptive analysis examined the association between tumor characteristics, year of diagnosis, ODX testing, treatment, and recurrence outcomes. ODX risk categories were defined as: low risk 0-15; intermediate risk 16-25; high risk > 25. Recurrence was determined by the date of confirmation on pathology or imaging. Bivariate analysis compared characteristics between groups using Fisher exact tests for categorical variables and t-tests and nonparametric tests for continuous variables. Results: From 2008-2018, 1,436 Stage I-III YBC patients were diagnosed with invasive breast cancer, and 455 met eligibility criteria for ODX testing. Median follow-time (interquartile range, IQR) was 4.9 (2.8, 7.9) years for the 255 women who were tested and 5.7 (3.5, 8.7) years for the 200 women who were not tested ($p < 0.05$). Prior to 2018, 52.1% of patients were tested; after 2017, ODX testing rate increased to 88%. Overall, there were 255 patients who underwent ODX testing (55.9%). The median age (IQR) of patients who had an ODX test was 38.0 (35.0, 39.0). Of 225 tested patients, 42.0% ($n=107$) were White, 6.3% ($n=16$) Black, 33.7% ($n=86$) Asian/Pacific Islander, 15.7% ($n=40$) Hispanic, and 2.3% ($n=6$) identified as Other. There was no overall difference in testing based on ethnicity ($p=0.42$). More patients with grade 1 versus grade 3 disease were tested, 61.5% vs 45.2% ($p=0.02$ from overall Fisher exact test). Adjuvant chemotherapy was administered to 61.0% (122/200) patients who were not tested, whereas 38.4% (98/255) of those tested received chemotherapy ($p < 0.001$). In tested patients, 6% of low-risk (RS 0-15), 37% of intermediate risk (RS 16-25), and 92% of high risk (RS >25) patient received adjuvant chemotherapy. Among patients with T2 lesions, a higher proportion not tested (90.8% [59/65]) received adjuvant chemotherapy compared with those not tested (57.1% [40/70]). There were no differences in recurrence based on ODX testing, 11.0% (22/200) not tested vs. 9.4% (24/255) tested ($p=0.26$). Conclusions: Utilization of ODX testing increased after 2017. A significantly lower proportion of women who underwent ODX testing received chemotherapy, compared with women not tested for ODX. A higher percent of women with T2 cancer received chemotherapy if testing was not completed, which may reflect a greater fear of recurrence in younger patients. Further investigation is needed to better understand this potential risk of overtreatment in the YBC population.

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7:00 AM - 8:15 AM

P6-01-28

Tangling the clinicopathological significance of MRE11-RAD50-NBS1 complex in sporadic breast cancers

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The MRE11–RAD50–NBS1 (MRN) complex is critical for genomic stability. Although germline mutations in MRN may increase breast cancer susceptibility, such mutations are extremely rare. Here, we have conducted a comprehensive clinicopathological study of MRN in sporadic breast cancers. We have protein expression profiled for MRN and a panel of DNA repair factors involved in double-strand break repair (BRCA1, BRCA2, ATM, CHK2, ATR, Chk1, pChk1, RAD51, γ H2AX, RPA1, RPA2, DNA-PKcs), RECQ DNA helicases (BLM, WRN, RECQ1, RECQL4, RECQ5), nucleotide excision repair (ERCC1) and base excision repair (SMUG1, APE1, FEN1, PARP1, XRCC1, Pol β) in 1650 clinical breast cancers. The prognostic significance of MRE11, RAD50 and NBS1 transcripts and their microRNA regulators (hsa-miR-494 and hsa-miR-99b) were evaluated in large clinical datasets. Expression of MRN components was analysed in The Cancer Genome Atlas breast cancer cohort. We show that low nuclear MRN is linked to aggressive histopathological phenotypes such as high tumour grade, high mitotic index, oestrogen receptor- and high-risk Nottingham Prognostic Index. In univariate analysis, low nuclear MRE11 and low nuclear RAD50 were associated with poor survival. In multivariate analysis, low nuclear RAD50 remained independently linked with adverse clinical outcomes. Low RAD50 transcripts were also linked with reduced survival. In contrast, overexpression of hsa-miR-494 and hsa-miR-99b microRNAs was associated with poor survival. We observed large-scale genome-wide alterations in MRN-deficient tumours contributing to aggressive behaviour. We conclude that MRN status may be a useful tool to stratify tumours for precision medicine strategies.

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Adel alblihy, n/a: No financial relationships to disclose

Ahmed Shoqafi, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

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Serial genomic analysis of circulating free DNA and change of immune-related gene signature in triple negative and HER2 positive advanced, metastatic breast cancer

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Background: Circulating tumor cells (CTCs) and circulating free DNA (cfDNA) have a promising role for detecting early response and progression in breast cancer. Furthermore, change of immune-related gene signature during systemic treatment influence the treatment response of breast cancer. Herein we report the outcome of serial genomic analysis of CTC, cfDNA and change of immune-related gene signature in advanced, metastatic triple negative breast cancer (TNBC) and HER2 positive breast cancer (BC). Methods: Serial whole blood were prospectively collected in 18 early or advanced, and 10 metastatic BC patients periodically during systemic chemotherapy. CTC was isolated from whole blood through EpCAM positive bead selection, and ctDNA was isolated from plasma. For genomic profiling of CTC and ctDNA, OncoPrint™ Comprehensive Assay Plus and OncoPrint™ Pan-Cancer cfDNA assay (included BRCA1, BRCA2 and MYCN customized panel) was performed and analyzed, respectively. Total RNA was extracted using whole blood and analyzed using Nanostring Pancancer Immunology Panel. Results: Total 61 serial samples were obtained from 28 patients during the study. At baseline, FGFR4 mutation was the most commonly detected (10 patients, 76.9%) with median variant of allele frequency (VAF) of 54.5% (range 20.87~99.8%) in advanced and metastatic TNBC based on CTC analysis. In case of cfDNA, 11 patients (84.6%) showed TP53 mutation with low VAF (median 1.8%, range 0.1~12.3%). In HER2 positive BC, FGFR4 was also the most common mutation (5 patients [62.5%]; median VAF 57.9%) in CTC analysis and TP53 was most frequently detected (5 patients, [62.5%]; median VAF 3.0%) in cfDNA analysis. In three pathogenic gBRCA1 mutated patients, BRCA1 was identically detected in 2 patients based on CTC analysis and in 3 patients based on cfDNA analysis with VAF of approximately 50%. There were no significant changes of VAF in target mutations of CTC and cfDNA during systemic treatment, irrespective of tumor response and subtype. However, in one patients who harbored 13 mutations detected based on baseline CTC analysis, showed disappearance of 12 mutations in final CTC analysis with partial response based on radiologic findings. In contrary,

there was another patient who gained multiple mutations during CTC analysis during neoadjuvant chemotherapy (NAC) with gain of tumor mutational burden (TMB). She did not achieve pathologic complete response and RCB score was 3 after completion of NAC. Most TNBC patients who received NAC and showed partial response, TMB showed gradual decrease during treatment. Baseline immune-related gene signatures were compared between HER2(+) BC and TNBC, and type 1 interferon signaling pathway was upregulated in HER2 (+) BC compared to TNBC. Conclusions: Our study suggest that serial follow up CTC and ctDNA, immune-related gene signature is feasible and reflect the general characteristics of baseline characteristics and dynamic molecular alteration of breast cancer. Further analysis with larger patient sample and correlation with tumor tissue is warranted in the future.

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7:00 AM - 8:15 AM

P6-01-30

PgR levels and Ki67 expression of Lobular Carcinomas of the Breast might indicate OncotypeDX testing to evaluate Chemotherapy benefit.

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AIM: The majority of invasive lobular carcinomas (ILC) of the breast are luminal A tumors of good prognosis, having a low or intermediate OncotypeDX Recurrence Score (RS). They are usually treated with hormonal therapy only and some have doubted the relevance of the RS for patients with ILC. However, in a number of ILC cases a high RS can be found, indicating chemotherapy benefit. The aim of the present analysis was to explore in our database of lobular carcinomas analyzed with OncotypeDX, the percentage of tumors with a RS >25 and test the hypothesis if Progesterone Receptor (PgR) and/or Ki-67 expression could be an indicator to have patients evaluated with OncotypeDX. PATIENTS AND METHODS: Among 2.946 patients analyzed with Oncotype DX, we found 397 patients with pure lobular carcinomas (13.47%). Ki-67 expression was obtained from 315 patients and 13 of them (4%) had a high Ki-67 value of >30%. PgR expression was negative in 56 out of 397 patients (14%). We analyzed the possible relationship of RS values with PgR levels and Ki-67 expression. RESULTS: Overall, 94% of patients with ILC had a Recurrence Score ≤ 25 and only 6% (24/397) had a RS ≥ 26 . There was a wide distribution of RS among patients with different values of PgR; however, there was a negative trend of Recurrence Score values and PgR expression levels. This trend was more obvious in the 56 patients with negative PgR expression. Although there were high RS values across all levels of Ki-67 expression, there was a trend towards high RS with higher Ki-67 expression; 5 out of 13 patients (38%) with ki-67 >30% had a RS ≥ 26 . CONCLUSION: Our analysis shows that the majority of lobular carcinomas of the breast have a low OncotypeDX RS, suggesting that can be treated only with hormonal therapy. However, negative or low PgR levels and high Ki-67 expression might predict a high RS and thus chemotherapy benefit and those two parameters could be used as indicators for OncotypeDX evaluation of lobular carcinomas of the breast.

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7:00 AM - 8:15 AM

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Evaluation of pathologic response and residual tumor cellularity following neo-adjuvant chemotherapy predict prognosis in breast cancer patients

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Introduction: Treatment of early-stage breast cancer (BC) has changed since recent evidence showed that neoadjuvant chemotherapy (NAC) can reduce residual tumor cellularity (RTC) and improve patient outcomes. Achieving a pathologic complete response (pCR) has been associated with significantly improved disease-free survival (DFS), distant disease-free survival (DDFS), and overall survival (OS). However, among patients treated with NAC, few experience pCR, while approximately 60-80% of them achieve a pathologic partial response (pPR). In previous studies, BC patients with different grades of pPR have been usually grouped and analyzed together, with inconsistent results and unclear prognostic significance. Objectives: The primary aims of this study were to describe the clinical and treatment characteristics of BC patients treated with NAC, to identify independent predictive factors of pCR, and to compare the oncologic outcomes between patients achieving pCR or pPR. The secondary aim of this study was to measure the RTC of BC patients with pPR and to compare the outcomes of

patients with different RTC in order to improve prognostic information. Methods: All the consecutive BC patients undergoing NAC at the Breast Unit of IRCCS Humanitas Research Hospital (Milan, Italy) between October 2006 and April 2020 and their corresponding post-operative pathology slides were reviewed. The following exclusion criteria were used: excisional biopsy or debulking surgery as first BC operation, patients with a previous BC diagnosis or other prior or synchronous malignancies, male patients, unknown NAC regimen, disease progression during NAC, and follow-up ≤ 12 months. Results: A total of 495 BC patients received NAC. Overall, 148 (29.9%) patients achieved pCR, while 347 (70.1%) had pPR, and median RTC was 40%. At multivariable analysis, 3 independent factors predicting pCR were identified. Tumor stage pre-NAC (cT1-2 84.5% versus cT3-4 15.5%, odds ratio (OR)=0.119, 95% confidence interval (95%CI)=0.048-0.189, $p=0.001$), BC sub-type (HER2-enriched 54.7% versus triple-negative 29.8% versus luminal-like 15.5%, OR=2.178, 95%CI=2.055-2.301, $p=0.001$), and vascular invasion (absence 98.0% versus presence 2.0%, OR=0.022, 95%CI=0.004-0.090, $p=0.001$). Patients with BC undergoing NAC and achieving pCR presented statistically significant longer DFS, DDFS, and OS ($p < 0.001$). Patients with RTC $< 40\%$ presented statistically significant better DFS and DDFS ($p = 0.033$, $p = 0.015$, respectively). However, no statistically significant difference in terms of OS was observed between RTC $< 40\%$ and RTC $\geq 40\%$ groups ($p = 0.148$). Conclusions: Tumor stage pre-NAC, BC sub-type, and vascular invasion are significantly and independently associated with pCR. Patients with pCR present a better prognosis compared to patients with pPR in terms of DFS, DDFS, and OS. Measurement of RTC in BC patients with pPR improves the prognostic information that can be obtained from the assessment of the pathologic response. Different patterns of residual disease play an important role in predicting the risk of subsequent loco-regional and distant recurrence, and patients with RTC $< 40\%$ present significantly better DFS and DDFS.

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7:00 AM - 8:15 AM

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Diffusion-weighted magnetic resonance imaging for subtype-specific prediction of pathologic complete response in neoadjuvant chemotherapy

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Background: The apparent diffusion coefficient (ADC) presents a biomarker that is sensitive to tumor cellularity. ADC maps can be calculated from non-contrast diffusion-weighted magnetic

resonance imaging (DW-MRI) measurements. ACRIN 6698, a sub-study of clinical trial I-SPY 2, investigated mean ADC – averaged over the whole tumor – as a marker to predict pathologic complete response (pCR) [1]. This work compares a group of histogram-based ADC metrics in addition to mean ADC for early prediction of pCR in patients stratified by breast cancer subtype.

Methods: We performed a retrospective analysis of DW-MRI, dynamic-contrast enhanced (DCE) MRI, and clinical outcome (i.e., pCR at surgery) in a cohort of 79 female patients who were diagnosed with high-risk, stage II/III breast cancer. Patients underwent neoadjuvant chemotherapy (NAC) with paclitaxel (12 weeks), followed by doxorubicin plus cyclophosphamide (12 weeks). The included population represents a subset of the I-SPY 2 cohort and comprises 48 patients with hormone receptor [HR]+/HER2-, and 31 patients with HR-/HER2-. DW- and DCE-MRI acquisitions were performed according to the I-SPY 2 protocol at pretreatment (T0) and after three weeks (T1) and were analyzed to find early treatment percentage (%) change (T0 to T1) in any metric M; where %-change = $100 \times (M(T1) - M(T0))/M(T0)$. Histogram analysis provided nine region-of-interest (ROI)-based ADC metrics (Table 1). ROIs were manually delineated by expert observers in three-dimensional ADC maps, focusing on diffusion-restricted regions [2]. DCE-MRI was analyzed for the integral I-SPY 2 imaging marker of %-change in functional tumor volume (FTV) between T0 and T1. Statistical analysis compared the predictive power of ADC metrics and FTV, including: the receiver-operating-characteristic (ROC) curve from a logistic regression model to predict pCR as 'positive', area-under-the-curve (AUC) assessment, and rank-sum Wilcoxon test ($p < 0.05$: statistically significant).

Results (Table 1): 16 out of 79 (20.3%) patients reached pCR at surgery, with 18.8% pCR among HR+/HER- and 22.6% among HR-/HER2- groups. For all nine computed ADC statistics (listed as median [Q1, Q3], across all patients), %-change was higher in patients who reached pCR than patients with non-pCR (highest value for metric 'MIN': 23.9% [-0.9%, 52.5] vs. 16.6% [0.4%, 27.6%], though without statistical significance: $p=0.237$). Likewise, %-change of FTV was also stronger in pCR patients than non-pCR patients (-58.8% [-80.6%, -22.5%] vs. -28.2% [54.2%, -2.7%], with statistical significance: $p=0.036$). For all patients combined ($n=79$), among the various reported ADC metrics, %-change in 'PCTL_95' (95th percentile of histogram) yielded the highest AUC (0.7; 95% CI = [0.56, 0.83]; $p=0.012$). %-change in FTV showed the second highest AUC (0.67; 95% CI = [0.52, 0.82]; $p=0.036$). By subtype, AUC was highest for %-change of 'PCTL_95' (0.69; 95% CI = [0.5, 0.87]; $p=0.072$) in the HR+/HER2- subgroup; and highest for both %-change of 'MEAN' (AUC = 0.73; 95% CI = [0.49, 0.94]; $p=0.065$) and 'PCTL_75' (AUC = 0.73; 95% CI = [0.49, 0.94]; $p=0.073$) triple negative (HR-/HER2-) subgroup. By comparison, %-change of FTV yielded AUCs of 0.64 (95% CI = [0.41, 0.85]; $p=0.191$) and 0.71 (95% CI = [0.51, 0.9]; $p=0.098$) in the HR+/HER2- and triple-negative subgroups, respectively.

Conclusion: Various tumor ADC metrics from non-contrast DW-MRI demonstrate potential biomarkers for assessing responsiveness to NAC at an early treatment timepoint. ADC may have predictive performance that is comparable to FTV, depending on the breast cancer subtype. Observations for %-change in 'MEAN' ADC at T1 differed from previous reports [1], which may be explained by the small sample size and single (paclitaxel) drug arm. Additional studies are warranted to include patients of experimental arms and of HER2+ subtypes.

[1] Partridge et al., *Radiology* 289(3):618-27 (2018)

[2] Nu et al., *Tomography* 8: 1208-20 (2022)

Results of statistical analysis of ADC-based and FTV markers for predicting treatment response at 3 weeks into NAC.

	ADC statistics retrieved DW-MRI % -change from T0 to T1									DCE-MRI metric % -change T0-T1
	MEAN	MIN	PCTL_05	PCTL_15	PCTL_25	PCTL_50	PCTL_75	PCTL_95	MAX	FTV
all patients (n=79, pCR=20.3%)										
pCR, median	18.1	23.9	18.6	14.7	16	16.7	17	19.4	10.8	-58.8
[Q1, Q3]	[3.9, 25.2]	[-0.9, 52.5]	[-5.7, 34.1]	[1, 26.7]	[2.1, 25.4]	[1.2, 24.2]	[1.1, 24.8]	[8.9, 21.5]	[2.8, 14.1]	[-80.6, -22.5]
non-pCR, median	10.4	16.6	10.1	10.5	10.3	10.8	8.5	7.3	7.3	-28.2
[Q1, Q3]	[3.9, 16.1]	[0.4, 27.6]	[0, 19.7]	[3.9, 17.8]	[3.9, 16.9]	[3.8, 16.5]	[2.8, 15.4]	[0.9, 13.7]	[-3.6, 11.8]	[-54.2, -2.7]
AUC	0.64	0.6	0.59	0.57	0.61	0.59	0.62	0.7	0.59	0.67
95% CI [LL, UL]	[0.47, 0.79]	[0.43, 0.75]	[0.42, 0.74]	[0.41, 0.72]	[0.45, 0.76]	[0.43, 0.74]	[0.46, 0.78]	[0.56, 0.83]	[0.45, 0.72]	[0.52, 0.82]
p-value	0.085	0.237	0.278	0.376	0.192	0.267	0.135	0.012 **	0.262	0.036 **
HR+/HER2- (n=48, pCR=18.8%)										
pCR, median	12.3	24.3	18.2	14	15.7	12.1	10.2	20.5	11.5	-57.7
[Q1, Q3]	[1.6, 25.2]	[-7, 47.1]	[-8.2, 32.1]	[-10.4, 30]	[-7.1, 27.7]	[-2.2, 23.5]	[1, 22]	[5.9, 24.7]	[5.8, 13.4]	[-73.8, 2.6]
non-pCR, median	9.4	17.8	9.4	8	8.3	10.1	8.3	7.5	7.6	-28.2
[Q1, Q3]	[3.9, 15.8]	[3.6, 26.1]	[1.5, 19.7]	[3.9, 18.5]	[4.3, 16.9]	[3.9, 16.8]	[2.4, 15]	[0.4, 11.2]	[-2.7, 12.8]	[-50.2, -6.6]
AUC	0.56	0.53	0.5	0.49	0.53	0.53	0.54	0.69	0.6	0.64
95% CI [LL, UL]	[0.35, 0.78]	[0.31, 0.76]	[0.27, 0.76]	[0.26, 0.75]	[0.29, 0.78]	[0.31, 0.76]	[0.34, 0.76]	[0.5, 0.87]	[0.42, 0.78]	[0.41, 0.85]
p-value	0.552	0.761	0.968	0.947	0.782	0.792	0.682	0.072	0.335	0.191
HR-/HER2-, 'triple-negative' (n=31, pCR=22.6%)										
pCR, median	20.5	23.4	19.1	14.9	16.4	20.1	19.3	18.6	6.8	-59.9
[Q1, Q3]	[14.3, 22.9]	[17.1, 53]	[11.6, 33.5]	[10.6, 26.7]	[13, 23.2]	[13, 23.5]	[13.3, 25.3]	[12.3, 20.2]	[1.8, 13.6]	[-88.2, -44.3]
non-pCR, median	11.4	13.5	11.2	11.9	12.4	13.1	10.3	7	6	-30.6
[Q1, Q3]	[5, 16.2]	[0.8, 29.9]	[-2.3, 18.9]	[2.5, 16.8]	[2.4, 16]	[3.8, 16]	[5.4, 16.1]	[1.5, 14.9]	[-4, 9.3]	[-60.5, 1.6]
AUC	0.73	0.7	0.7	0.65	0.7	0.66	0.73	0.7	0.59	0.71
95% CI [LL, UL]	[0.49, 0.94]	[0.48, 0.89]	[0.49, 0.9]	[0.43, 0.87]	[0.48, 0.89]	[0.42, 0.88]	[0.49, 0.94]	[0.48, 0.9]	[0.4, 0.8]	[0.51, 0.9]
p-value	0.065	0.119	0.119	0.219	0.119	0.202	0.073	0.108	0.479	0.098

Median [Q1, Q3] values represent the median and interquartile range over the respective patient population regarding the % -change of the respective ADC (FTV) metric from T0 to T1. T0: pretreatment, T1: 3-week timepoint, ADC: apparent diffusion coefficient, MRI: magnetic resonance imaging, DW: diffusion-weighted, DCE: dynamic-contrast enhanced, pCR: pathologic complete response, AUC: area under the ROC curve, 95% CI [LL, UL]: confidence interval lower and upper limit, PCTL_x: xth-percentile of tumor ADC histogram, MEAN: mean of ADC within ROI, MIN: minimum of ADC within ROI, MAX: maximum of ADC within ROI, FTV: functional tumor volume, **: statistically significant.

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Longitudinal DCE-MRI Radiomic Models for Early Prediction of Response to Neoadjuvant Systemic Therapy (NAST) in Triple Negative Breast Cancer (TNBC) Patients

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Background and Purpose Early prediction of neoadjuvant systemic therapy (NAST) response in triple negative breast cancer (TNBC) patients could potentially aid in the selection of alternative therapies and avoid unnecessary toxicity in patients unlikely to achieve pathologic complete response (pCR) with NAST. In this study, we investigated the radiomic features of the peritumoral and the tumoral regions from dynamic contrast enhanced (DCE) MRI acquired at different time points of NAST for early treatment response prediction in TNBC. **Methods and Materials** This study included 182 biopsy-confirmed stage I-III TNBC patients enrolled in an IRB approved prospective clinical trial (NCT02276433). All patients underwent DCE-MRI on a GE 3T MRI scanner at baseline (BL), after two (C2) and four (C4) cycles of doxorubicin/cyclophosphamide based chemotherapy and before surgery. The peritumoral and the tumoral regions were segmented manually by two fellowship-trained radiologists using early phase (2.5 min) DCE-MRI subtraction images. Ten first order radiomic features, 300 grey-level-co-occurrence matrix (GLCM) features along with their absolute and relative differences (C4/BL, C2/BL, C4/C2) between the 3 imaging time points were extracted from the peritumoral and the tumoral regions. Patients were randomly divided into training and testing sets in a 2:1 ratio. For univariate analysis, area under the receiver operating characteristics curve (AUC ROC) was measured to determine the features most predictive of pCR/non-pCR. Wilcoxon Rank Sum test was used to test the statistical significance of predictive performance. In multivariate analysis, radiomic models were established using logistic regression with elastic net regularization followed by 5-fold cross validation for performance assessment. **Results** Eighty-eight (48%) patients had pCR (59 training, 29 testing) and 94 (52%) patients had non-pCR (63 training, 31 testing). Twenty-five radiomic features (4 from peritumoral C4, 5 from tumoral C4, 4 from peritumoral C4/BL, 6 from tumoral C4/BL, 2 from peritumoral C4/C2 and 4 from tumoral C4/C2) were statistically significant with $AUC \geq 0.75$ in both the training and the testing sets at the univariate analysis. The significant features at C4 had AUCs of 0.75-0.79 for the training set and 0.76-0.81 for the testing set. Changes measured between C4 and BL or C2 showed AUC of 0.76-0.84 in the training and 0.75-0.81 in the testing datasets. Eleven multivariate regression models comprised of radiomic features at BL, C2, C4 and their changes (C4/BL, C4/C2 and C2/BL) showed an AUC of 0.80-0.84 for cross validation and an AUC of 0.80-0.82 for independent testing. **Conclusions** Radiomic models using longitudinal DCE MRI parameters of peritumoral and tumoral regions during NAST have the potential to predict pCR in TNBC patients undergoing NAST.

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A Pre-operative Dynamic Contrast Enhanced MRI-Based Radiomics Models as Predictors of Treatment Response after Neoadjuvant Systemic Therapy in Triple Negative Breast Cancer Patients

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Background and Purpose Triple negative breast cancer (TNBC) is a biologically aggressive tumor and a refractory subtype of breast cancer due to the lack of therapeutic targets, such as estrogen receptors, progesterone receptors, and human epidermal growth factor receptor 2. In this study, we investigated the accuracy of radiomic models based on the dynamic contrast enhanced (DCE) MRI images obtained after the completion of NAST as discriminators of treatment response in TNBC patients. **Materials and Methods** This IRB-approved prospective study (ARTEMIS trial, NCT02276443) included 181 patients with biopsy proven stage I-III TNBC who had MRIs after completion of NAST and before surgery. Patients were classified as pathologic complete response (pCR) and non-pCR at the surgery. Tumors were segmented on the 2.5 minutes DCE subtraction images. Regions with necrosis or clip artifacts were excluded from the contour. If tumors were not visible, the tumor bed was contoured. Whole-tumor histogram-based first order texture features ($p=10$) including mean, minimum, maximum, Standard deviation, kurtosis, skewness, 1st, 5th, 95th, and 99th percentiles, and radiomic ($p=300$) Grey Level Co-occurrence matrix (GLCM) features were extracted with an in-house Matlab toolbox. The samples were split into training and testing data sets by a 2:1 ratio. For univariate analysis area under the receiver operating characteristics curve (AUC ROC) was performed for pCR status prediction. For texture feature selection logistic regression with elastic net regularization was performed. Parameter optimization was performed by using 5-fold cross-validation based on mean cross-validated AUC in the training set. A P-value less than 0.05 was considered statistically significant. **Results** Of the total 181 patients, 88 (49%) had pCR and 93 (51%) had non-pCR. Univariate analysis identified 7 statistically significant first order imaging features (Minimum, Maximum, Mean, 1st Percentile, 5th Percentile, 95th Percentile, and 99th Percentile) with $AUC \geq 0.7$ ($p < 0.001$), in both training and testing data sets. Percentile 5 showed highest $AUC = 0.78$ ($p < 0.001$). Two multivariate models were statistically significant at cross-validation with $AUC \geq 0.7$. The first model combined 2 first order data (Percentile 1 and

Percentile 5) with AUC = 0.73 (p< 0.001). The second model combined 8 first order features (Percentile 1, 5, 95, 99, Mean, Minimum, Maximum, and Skewness) and 24 GLCM features with AUC = 0.7 (p=0.003). Conclusion DCE-MRI radiomic features from tumor and tumor bed regions in TNBC may be helpful imaging biomarkers for predicting treatment response after NAST.

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7:00 AM - 8:15 AM

P6-01-36

Validation of prognostic platform to further refine identification High Risk Patients indicated for Chemotherapy Free Treatment in Early-Stage Breast Cancer

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Use of prognostic assays and clinical features to further risk stratify patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) breast cancer has become standard of care. Stratification of patients into low/mid risk of disease recurrence enables physicians to decide which patients can safely forgo chemotherapy. Yet there exists a subpopulation of patients who tend to have recurrences following endocrine therapy alone. Complicating the issue, recent data has shown these proliferation-based markers assessed from a single site tissue biopsy may not be reliable for minority populations, potentially owing to spatial heterogeneity of tumors. To address this, we used a novel 2-parameter pharmacokinetic modeling framework that allows biosignatures to be extracted from dynamic contrast enhanced (DCE) magnetic resonance imaging (MRI) studies that contain 3-6 timepoints spaced 60-90 seconds apart. These parameters, referred to as P1 and P2, represent leakiness from vessels into the extravascular space and vice versa. This approach was previously developed in a study of 111 breast cancer patients where the 21-gene

recurrence score and DCE-MRIs were available. Low P1 showed better outcomes in low- and mid- patients (n=88, $p \leq 0.028$; log-rank test). Patients with a high P1 had a 20.2% chance recurrence at six years. The same trend was observed in mid-recurrence score patients only (n=23, $p \leq 0.058$). No recurrences were observed in patients with low P1 in either the RS-low or RS-mid categories. There were no recurrences in the high P1, RS-low/-mid category that received chemotherapy, suggesting that chemotherapy could be beneficial in this category of patients, although the trend was not statistically significant (n=10, $p=0.46$). Here we present an independent, single site validation of these prognostic markers in patients who received only neoadjuvant endocrine therapy and had corresponding pre-treatment MRIs. Two hundred ninety-eight patients with early-stage breast cancer and pre-treatment MRIs were identified via chart review. Of the patients assessed, 33 patients were treated with neoadjuvant endocrine therapy and qualified for the analysis. Consistent with the previous analysis, the 5-year event-free survival rate in low P1 population was 100% while that in the high P1 population was 45.8% ($p=0.053$). Overall, we find strong support that these markers could help physicians further fine tune their decision-making when determining who to forgo chemotherapy.

Disclosure(s):

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7:00 AM - 8:15 AM

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Tumor microenvironment subtype influence the response of neoadjuvant chemotherapy in breast cancer

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Introduction Recent transcriptome analysis developed a holistic tumor microenvironment (TME) classification platform based on immune and fibrotic markers. This TME classification had four categories, immune enriched, fibrotic (IE/F); immune enriched, non-fibrotic (IE); Fibrotic (F); and Immune Desert (D). And these four TME subtypes are a predictive biomarker to immunotherapy in multiple cancer and four subtypes have been changed during treatment. Previously our study suggested baseline immune features and dynamic immune response on-treatment were predictive of treatment outcome in BC with neoadjuvant chemotherapy (NAC). In this study, we evaluated the impact of TME classification and dynamic change of TME classification on treatment outcome in BC with NAC. **Methods** Early and locally advanced BCs which would be planned to receive standard NAC (four cycles of anthracycline plus cyclophosphamide and four cycles of docetaxel or docetaxel plus trastuzumab for human epidermal growth factor receptor 2[HER2+] disease or six cycles of docetaxel, carboplatin, trastuzumab and pertuzumab for HER2+ disease) followed by curative surgery. We prospectively collected tumor tissue and matched blood three times for each patients: at BC diagnosis (T1), three weeks after the first cycle of NAC (T2), and curative surgery (T3). RNASeq was performed to classify TME subtype. In terms of clinical variables, clinical stage

and IHC subtype at diagnosis, pathologic complete response (pCR), distant recurrence free survival (DRFS) and overall survival (OS) were used. Generalized logistic regression was used for predicting RCB class and pCR with clinical and genomic characteristics at T1. Kaplan-Meier analysis were performed to analysis DRFS and OS. Results In total, 210 patients who were treated with scheduled NAC were enrolled. Finally, RNASeq in 240 BC tissues (T1:119, T2:91 and T3:30) were conducted from 142 patients. In 119 BCs which was performed RNASeq at T1, hormone receptor(HR)+, HER2- BC was 32 (26.9%), 29 of HR+HER2+ BC (24.4%), 18 of HR-HER2+ BC (15.1%) and 44 of triple negative BC (TNBC) (37.0%). In TME classification, immune desert (D) was most frequently observed (45.3%), followed by IE (35.3%), F (10.1%) and IE/F (9.2%). The association between BC subtype and TME subtype suggested that HR+HER2- BC was frequently categorized into D (22 of 32, 68.8%) whereas TNBC was into IE (24 of 44, 54.5%) ($p < 0.001$). TME subtype has been dynamically changed during NAC. At T2, IE subtype was most frequently observed (27.5%) followed by D (25.3%), IE/F (24.2%) and F (23.1%). The inclination of TME change were different according to NAC response. In BC achieved pCR, IE/F subtype had increased (4 at T1 and 10 at T2) and decrease of D subtype (15 at T1 and 3 at T2). In BC with non-pCR, IE/F subtype had slightly increased at T2 (7 at T1 and 12 at T2) but there was no IE/F subtype at T3 point. Contrarily, D subtype had decreased at T2 but increased at T3 (39 at T1, 20 at T2 and 24 at T3). The impact of TME subtype was different according to pCR status. In BC with pCR, F subtype had poor prognosis in DRFS and OS compared to other subtype ([5year DRFS rate for F vs. others: 66.7% vs. 93.2%, $p=0.028$], [5year OS rate for F vs. others: 70.7% vs. 100%, $p < 0.001$]). In BC without pCR, there was no different DRFS and OS according to TME subtypes. Conclusion Our data suggested that TME subtype has been changed during NAC and the subtype switching was affected by the NAC response. Moreover, TME subtype may have prognostic role in DRFS and OS according to pCR status.

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7:00 AM - 8:15 AM

P6-01-38

Predictive efficacy biomarker for chemotherapy agents against triple-negative breast cancer bioprinted organoid tumors (BOTs) using solid tumor biopsy-on-a-chip

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Background: Despite \$90 billion in preclinical research and clinical trials every year, 90% of cancer clinical trials are unsuccessful. Thus, there is considerable interest in predicting clinical efficacy of preclinical formulations early in discovery using patient derived ex vivo platforms. However, extracting adequate tissue for such models can be difficult depending on tumor type and site. Dominant mechanisms for expanding patient tissue include xenografts and organoids. However, the former imposes a large time window to establish while the latter is constrained in space by sizescales. Here, we present a novel approach for expanding TNBC tissue, specifically for use in ex vivo models, that addresses these constraints with 3D bioprinted organoid tumors (BOTs). Objective: The aim of this study is to generate TNBC BOTs that mimic core biopsy tissue for use in ex vivo precision and personalized predictive biomarkers for chemotherapies. Methods: BOTs were generated using alginate-based bioink prepared with MDA-MB-231 TNBC cells. Briefly, specially prepared fresh TNBC bioink was deposited layer-by-layer using a Cellink BIO X6 bioprinter in geometrical configurations to mimic 14- to 18-gauge tumor biopsies. These were chemically cross-linked and cured in stages to allow cells and matrix to self-assemble with limited degrees of freedom. Fully cured BOTs were loaded in our ex vivo solid tumor biopsy-on-a-chip and treated with chemotherapy agents to evaluate sensitivity and resistance, with outcomes determined using immunofluorescent live and dead cell staining methods. Results: A 3-minute crosslinking time with calcium chloride provided a stable and functional sodium alginate medium for treating cellular BOTs. Two layers of TNBC bioink was determined to be the optimal size and shape for compatibility with our ex vivo

biopsy-on-a-chip predictive efficacy biomarker platform. TNBC cells were verified to be evenly distributed within the cured sodium alginate matrix using live cell nuclear stains. Successful diffusion of multiple agents to spatially distinct regions of the bioprinted tissue was verified with fluorescently labeled small molecules and nucleic acid stains up to 200 μ M deep. Impact: Patient derived BOT core mimics and other configurations could be used in ex vivo breast cancer chemotherapy screening models to obtain sensitivity and resistance profiles as predictive functional biomarkers both on the bedside for personalized treatment strategy development and on the bench to uncover new therapeutic targets. Due to their potential to replicate biophysical and biochemical characteristics of a tumor and its microenvironment, BOT based precision and personalized medicine platforms can provide more accurate drug efficacy readout compared to in vitro cancer models.

Disclosure(s):

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P6-01-39

The impact of the 21-gene Recurrence Score® assay upon physician treatment recommendations in the neoadjuvant setting in lymph node-negative breast cancer patients in a multicenter prospective study in Quebec

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Background: Although the role of the 21-gene Breast Recurrence Score® assay is well established to predict response to adjuvant chemotherapy in the setting of node-negative hormone receptor (HR)-positive, HER2-negative breast cancers (BC), fewer studies have evaluated the assay in the neoadjuvant setting. Due to the correlation between a high Recurrence Score® (RS) result and pathological complete response (pCR), the Breast Recurrence Score assay has been used to aid in selecting between chemotherapy (CT) or endocrine therapy. We wanted to further understand the impact of the assay upon physician treatment recommendations and the use of chemotherapy in this patient cohort. Methods: We conducted a multicenter, prospective, observational study in patients with clinically node-negative HR-positive, HER2-negative BC with T2-T3 disease being considered for neoadjuvant therapy. Physicians were required to complete two questionnaires indicating treatment choice, including CT, endocrine therapy, or surgery, prior to and post availability of RS result. Patients were followed up for 6 months after commencement of neoadjuvant therapy. The primary objective was to evaluate the change in the physician's recommendation for neoadjuvant CT prior to and post assay results. As a secondary objective, we also evaluated the impact of the RS result on physician's expressed level of confidence. Results: A total of 70 patients were enrolled between April 2018 and November 2021 at five hospital centers, as part of the McPeak Sirois Group of Quebec. The median age of the cohort was 60 years (range, 30 to 79 years). 24.3 % (n=17) of the cohort consisted of patients aged < 50 years, and 75.7% (n=53) were ≥ to 50 years. 29.0% (n=20) of the patients had a RS < 16, 39.1% (n=27) had a RS between 16-25, and 31.9% (n=22) had a RS > 25. For the entire cohort, the RS result led to a net reduction in

chemotherapy recommendation by 33.3% (OR (odds of having CT post-RS recommendation versus pre-RS recommendation) = 0.23 [95% CI: 0.12-0.44]; P< 0.0001), and 39.2% net reduction in the use of chemotherapy at 6-month follow-up (OR = 0.18 [95% CI: 0.09-0.35]; P< 0.0001). Furthermore, the RS result led to a 35.3% net reduction in physician recommendation of CT for patients < 50 years (OR = 0.19 [95% CI: 0.04-0.83]; P=0.027) and a 32.7% net reduction for patients ≥ 50 years (OR = 0.24 [95% CI: 0.11-0.50]; P=0.0001). For patients with a RS < 16, there was a reduction in CT recommendation by 75.0%, and by 44.4% for patients with a RS between 16 - 25 (OR = 0.15 [95% CI: 0.06-0.38]; P< 0.0001). Moreover, RS results led to an increase in confidence in physician treatment decisions for 59.4% of patients (OR = 12.53 [95% CI: 5.46-28.78]; P< 0.0001). Conclusion: We determined that the 21-gene Breast Recurrence Score assay altered neoadjuvant treatment decisions, leading to a reduction in the use of chemotherapy by about one-third, regardless of age. Additionally, the assay increased physician confidence in their treatment recommendation for about 60% of patients. This demonstrates the potential clinical utility of the assay to decrease the use of CT in the neoadjuvant setting amongst HR-positive, node-negative BC patients in Quebec.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-01-40

Integrative transcriptomic analysis and cohort validation identify key genes in chemotherapy treatment response in Latino breast cancer patients.

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Purpose: Breast cancer (BC) is one of the most frequent invasive cancers and one of the main causes of cancer mortality in women. Effective treatment interventions for BC are urgently required to improve survival rate and quality of life. Chemotherapy has been widely applied in BC treatment; however, therapeutic resistance remains an unresolved issue. Currently, only a minority of patients benefit from chemotherapy, emphasizing the need to identify more effective hub genes associated with therapy response. The overarching goal of this study is to assess hub genes correlated with BC chemotherapy treatment response via multiple databases and validate the workflow in an independent cohort of Hispanic/Latino (Colombian) women diagnosed with invasive Luminal B BC candidates for neoadjuvant chemotherapy. Design: Screening and multistep filtering of common genes correlated with chemotherapeutic response was performed by integrating differentially expressed genes between responders and non-responders in publicly available datasets. For each database, the differentially expressed genes (DEGs) between non-responders and responders were identified using GEO2R and LIMMA. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses were conducted for the identified common genes using Metascape and

DAVID. Functional enrichment analysis and protein-protein interaction (PPI) network for DEGs were constructed using (STRING) database. Hub genes were identified from PPI network by Cytoscape software analysis. The mRNA expression of hub genes in BC and normal tissues was subsequently explored by UALCAN. Evaluation of the effect of hub genes on survival was performed using Kaplan-Meier plotter. Hub genes were imported into the DGIdb to obtain the potential for BC chemotherapy-associated treatment drugs. The previous workflow was then applied/validated to an Illumina high-throughput RNA sequencing of 50 Luminal B cases (HER2+ and HER2-) of Hispanic/Latino patients. Results: 490 DEGs were obtained from the intersection of five public databases. Pathway enrichment analysis revealed DEGs were associated with cell cycle, estrogen response, adaptive immune response, and regulation of kinase activity, among others. Thirty-two hub genes were identified from PPI network analysis with high degree nodes and betweenness centrality. Significant differential expression of hub genes between BC tissue and normal tissues was observed in UALCAN. These genes were significantly associated with survival probability. Fifteen potential targeted therapeutic drugs were identified through DGIdb database. Validation workflow in independent Luminal B cohort showed 238 DEGs, 90 hub genes with high degree and enrichment in the regulation of hormone levels, cellular response to EGFR, signaling by ERBB2 and MAPK. GATA3 was the hub gene found in both databases and the validation set. Both databases and validation set show hub genes, enriched pathways, and drugs that indicate their close association with tumorigenesis and would contribute to acting an important role in therapy response prediction. Conclusions: This workflow was created using public databases and applied to a patient's cohort of different ancestries. This methodology can successfully provide potential biomarkers that correlate with therapy response. Genes were selected from PPI network. Most of them were independent biomarkers of BC treatment response, including that in underrepresented patients. Moreover, these genes may exert critical function in non-response and progression.

Disclosure(s):

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7:00 AM - 8:15 AM

P6-01-41

Influence of HER2 expression status in the distribution of recurrence score from the OncotypeDx assay among women with early-stage estrogen-receptor-positive/HER2-negative breast cancer

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BACKGROUND: The OncotypeDX assay analyzes the expression of 21 genes, including HER2 and Grb7, to assess the predictive effect of chemotherapy in breast cancer recurrence among women with early-stage estrogen-receptor (ER) positive/HER2-negative breast cancer. In this study, we evaluate the distribution of recurrence score from the OncotypeDX assay based on the HER2 expression status by immunohistochemistry (IHC). **METHODOLOGY:** Utilizing the National Cancer Database, we identified adult women with a diagnosis of stage I – III ER+/HER2- invasive ductal carcinoma of the breast between the years 2010 and 2018. Recurrence scores were classified into low (< 11), intermediate (11-26), and high risk (>26); and the distribution of these recurrence scores cross-tabulated with different IHC scores of HER2 expression (0, 1+, and 2+) by IHC. Women with an IHC score of 2+ had to be negative for HER2 gene amplification by FISH. Multivariate logistic regression model adjusting for age, race, origin, progesterone receptor status, grade, and cancer stage was used to assess the odds of receiving a high OncotypeDx Score (≥ 26). **RESULT:** Among 198,931 women with ER+/HER2 negative breast cancer, 59,632 (30.0%) had HER2 IHC score of 0, 102,170 (51.4%) had IHC score of 1+, and 37,129 (18.6%) women were with IHC score of 2+. The median age at diagnosis of breast cancer among all three categories of HER2 expression was 59 years. The median recurrence score for women with IHC scores of 0, 1+, and 2+ was 15, 15, and 16 respectively ($p < 0.001$). A higher proportion of women with HER2 IHC score of 2+ had a high recurrence score compared to women with an IHC score of 0 (15.2% vs. 13%, $p < 0.001$). In multivariate analysis, compared to women with HER2 IHC score of 0, women with HER2 IHC score of 2+/FISH negative were observed to have higher Odds (OR: 1.16; 95% CI: 1.11 – 1.20, $p < 0.001$) of receiving high recurrence score. There was no significant difference in the odds of receiving a high recurrence score between women with IHC 0+ and 1+(OR: 0.99; 95% CI: 0.96 – 1.03, $p 0.82$). **CONCLUSION:** Women with a HER2 IHC score of 2+ were observed to have a higher odds of receiving high-risk recurrence scores as compared to women with IHC score of 0. This needs to be further correlated with the response to chemotherapy and the risk of recurrence.

Disclosure(s):

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BASELINE 18FDG-PET METABOLIC TUMOUR VOLUME (MTV) AS A POTENTIAL PREDICTIVE FACTOR OF RESPONSE TO METRONOMIC CHEMOTHERAPY (mCHT) IN HR+/HER2- METASTATIC BREAST CANCER (MBC) PATIENTS (pts). PRELIMINARY RESULTS OF THE METRO-PET STUDY

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Background:

MBC is an incurable disease and chemotherapy (CHT) represents one option of treatment upfront, in TNBC pts, or at failure of an endocrine therapy + targeted agents in HR+ ones. mCHT was extensively studied in different types of ABC pts and is largely used in clinical practice. 18FDG-PET is often used as a tool for disease staging at baseline and for disease restaging during treatment. Different quantitative and semi-quantitative 18FDG-PET parameters have been investigated as predictive and prognostic biomarkers in NSCLC and other tumours. Aim of the present study is to evaluate the role of baseline SUVmax, global SUVmean, SUVpeak, Metabolic Tumour Volume (MTV) and Total Lesion Glycolysis (TLG) as predictive factors of response to mCHT.

Patients and Methods

We identified 36 MBC pts treated with mCHT between 2014 and 2021, with at least two separate 18FDG-PET evaluations. Patients and biological tumour characteristics, previous treatments, site of relapse as well as quantitative pre-treatment 18FDG-PET parameters have been collected. Tumour response was assessed using PERCIST Criteria. Median and mean \pm SD 18FDG-PET parameters have been reported according to the type of response. Complete and Partial responses have been grouped together with Stable Disease.

Results

Median age was 69 (33-82). Luminal pts were 25 (67.6%), TNBC pts were 16.2%; most were heavily pre-treated for their metastatic disease (≥ 3 lines: 14, 37.8%) and presented ≥ 3 metastatic sites (14, 37.8%). All pts received mCHT, 26 (70.3%) as combination therapy (VRL+CAPE or VRL+CAPE+CTX), or single agent (VRL, 11). Bone was the commonest metastatic site (62.2%). ORR was 43.2%; 7 pts had SD (18.9%), the remaining developed PD (37.8%). Similar values have been observed between the 2 groups in terms of SUVmax, global SUVmean and SUVpeak. Mean MTV was higher in responder (n=22) vs non responder (n=14) pts, as TLG. Details are reported in Table 1.

Conclusions

High mean baseline MTV and TLG seem to be related to response to mCHT in MBC pts. Our

observation is in contrast to what is described for other cancer types, especially NSCLC, and for standard neoadjuvant treatment of BC. Considering the peculiar mechanisms of action of mCHT, our preliminary findings warrant further exploration in a larger series of BC pts.

Table 1 - Baseline 18FDG-PET uptake values in responder and non responder patients

	SUV _{max}	global SUV _{mean}	SUV _{peak}	MTV	TLG
RESPONDER					
Mean	12.42	4.97	9.51	129.33	524.48
Median	9.98	3.75	7.50	38.17	119.75
SD	7.98	2.82	6.94	211.28	838.84
NON RESPONDER					
Mean	10.20	4.09	6.81	38.92	154.75
Median	10.17	3.54	6.89	22.31	126.33
SD	3.95	1.63	2.44	37.49	140.82

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Predictors of Response to Neoadjuvant Chemotherapy in Breast Cancer: OncotypeDX versus MammaPrint versus Liquid Biopsy

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Background: OncotypeDX (ODX) is a 21-gene recurrence score (RS) assay that is predictive of the benefit of adjuvant chemotherapy in early-stage hormone receptor-positive and HER2-negative (HR+/HER2-) breast cancer. MammaPrint (MP) is a 70-gene signature validated to prognosticate distant metastasis and survival. We have previously presented data suggesting that the presence of circulating tumor cells (CTCs) evaluated via liquid biopsy may also have prognostic and predictive utility in HR+/HER2- breast cancer. In this study, we compare the value of ODX, MP and liquid biopsy evaluating CTCs and disseminated tumor cells (DTCs) in predicting pathologic complete response (pCR) following neoadjuvant chemotherapy (NAC). Methods: This retrospective analysis used the National Cancer Database (NCDB) 2004-2017 breast cancer dataset to identify a cohort of patients with HR+/HER2-, AJCC clinical stage I-III breast cancer who received NAC. A series of multiple logistic regression models were used to assess the value of a. ODX (RS < 26 versus ≥26), b. MP, c. the presence of CTCs, and d. the presence of DTCs in predicting pCR to NAC. Each model controlled for age, race, Charlson/Deyo comorbidity scoring, disease histology, grade, and nodal status. Results: A total of n=52,463 patients with stages I-III HR+/HER2- breast cancer received NAC. The patient characteristics of this cohort were as follows: the majority were White (n=42,826, 81.6%), between 50-70 years of age (n=27,683, 52.8%), and with invasive ductal carcinomas of the breast (n=40,197, 76.6%). N=6,111 (11.6%) had Grade I or well-differentiated disease, n=23,546 (44.9%) Grade II or moderately-differentiated disease, and n=2,605 (43.5%) had Grade III or poorly-differentiated disease. N=3,823 have documented recurrence scores based on ODX: with n=2,653 having RS < 26 (69.4%) and n=1,170 (30.6%) having RS ≥26. After controlling for age, race, comorbidity scoring, disease histology, grade and nodal status, RS ≥26 was found to be significantly associated with pCR to NAC (OR 1.85, 95% CI 1.46-2.35, p< 0.001). High-risk scoring per MP was also correlated with pCR but this relationship was not

statistically-significant (OR 1.68, 95% CI 0.93-3.03, $p=0.084$), possibly due to the smaller size of this sample ($n=828$ patients underwent MP testing). Liquid biopsy data was also limited, with $n=250$ patients having documented CTC status and $n=211$ having documented DTC status. Neither the presence of CTCs (OR 0.96, 95% CI 0.44-2.09, $p=0.908$) nor DTCs (OR 0.61, 95% CI 0.25-1.50, $p=0.279$) was significantly associated with pCR to NAC. Conclusions: ODX is found to be predictive of pCR to NAC in early-stage, HR+/HER2- breast cancer. Utility of MP and liquid biopsy data in this context appears less robust, however, data is limited. More research is needed to validate existing data in a prospective trial setting, and explore for novel biomarkers across breast cancer subtypes.

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7:00 AM - 8:15 AM

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Alteration of DNA methylation landscape in breast patients treated with adjuvant chemotherapy

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Background Exposure to cytotoxic chemotherapy treatment may alter DNA methylation (DNAm) in treated patients. Methods We performed DNAm analysis in 1,244 and 897 breast cancer patients treated and not treated by adjuvant chemotherapy using the Illumina MethylationEPIC array (1,804 blood, 337 saliva). DNAm changes of 620,095 individual CpGs and 41,581 promoters were evaluated using linear regression models, adjusting for age at diagnosis, ethnicity, years between sample collection and diagnosis and cell-type heterogeneity. Results from datasets normalized separately were combined by meta-analysis (random effects model). Gene set enrichment analyses were conducted to identify key processes or pathways associated with chemotherapy treatment. Results A total of 425 differentially methylated CpGs and 20 promoters were significantly associated with chemotherapy treatment ($p < 5e-8$). Enriched gene sets among 3,495 chemotherapy-associated promoters (unadjusted $p < 0.05$, preranked by Z scores) included three suppressed Gene Ontology (GO) terms that survived Bonferroni correction (GO:0002376, immune system process; GO:0009605, response to external stimulus; and GO:1903034: regulation of response to wounding). Using meta-analysis regression coefficients for all promoters as a ranking metric, olfactory transduction (KEGG, hsa04740) was found to be significantly suppressed (unadjusted $p = 6.38e-06$, adjusted

p=0.002). Taste transduction (hsa04742, unadjusted p=1.73e-03, adjusted p=0.565) was the next most significantly suppressed pathway. Conclusion The enrichment of imprinted genes within biological processes and pathways suggests a biological mechanism by which chemotherapy treatment could affect immune response, wound healing and changes in the perceptions of smell and taste.

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P6-01-45

Correlation of an immune-related 8-gene panel with the efficacy of neoadjuvant chemotherapy for breast cancer

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Introduction: Neoadjuvant chemotherapy, one of systemic treatment of breast cancer, is employed for downstaging of inoperable tumor. Pathological complete response (pCR) after neoadjuvant chemotherapy is associated with good prognosis for breast cancer. The critical role of anti-tumor immune responses in conventional chemotherapy and targeted therapy has been reported. However, the pCR-associated immune genes are still ambiguous. Materials and Methods: Thirty-seven primary breast cancer patients receiving neoadjuvant chemotherapy as the first-line treatment for breast cancer were recruited in this VGH-TAYLOR study (NCT04626440). Total RNA of fresh tumor tissues was isolated and then reverse transcribed into cDNA. The OncoPrint Immune Response Research Assay was employed for examination of immune-related gene expressions. In silico analyses were performed using the public databases, including Gene Expression Omnibus, Kaplan-Meier plotter, ROC Plotter, Cancer Therapeutics Response Portal, and The Cancer Genome Atlas. Results: Patients achieved a

pCR were associated with lower tumor stage and HER2 expression. The next-generation sequencing-based analysis showed that the expression of eight genes were higher in tissues of patients with pCR than non-pCR, including KLRK1, IGJ, CD69, CD40LG, MS4A1, CD1C, KLRB1, and CA4. The 8-gene score was associated with better recurrence-free survival in patients receiving chemotherapy. Data from an ROC Plotter database showed that higher expressions of IGJ, CD69, and MS4A1 in patients respond to neoadjuvant chemotherapy compared to non-responders. In silico analysis revealed that the negative correlation between pCR-associated gene expressions and IC50 values suggesting the gene high expression was sensitive to the drugs. Moreover, the levels of pCR-associated gene were downregulated in breast tumor tissues and positively correlated with immune cell infiltrations. Conclusion: We identified eight immune genes which were associated with better prognosis and drug responses. The 8-gene score may serve as a prognostic marker for breast cancer patients who receiving neoadjuvant chemotherapy.

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Independent validation of the HER2DX genomic test in HER2-positive breast cancer treated with neoadjuvant docetaxel, carboplatin, trastuzumab +/- pertuzumab (TCH/TCHP): a correlative analysis from a multicenter academic study.

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Background: HER2DX (Prat et al. EBiomedicine 2022) is a 27-gene prognostic (risk-score) and predictive (pathological complete response [pCR]-score) assay in early-stage HER2+ breast cancer based on clinical data and the expression of 4 gene signatures (immune, proliferation, luminal differentiation and HER2 amplicon). Here, we aim to evaluate, for the first time, the ability of HER2DX to predict pCR following neoadjuvant TCH or TCHP in HER2+ disease. Methods: Standardized HER2DX was performed in a central lab on baseline pre-treatment FFPE tumor biopsies from the GOM-HGUGM-2018-05 study in Spain, a consecutive retrospective series of patients (pts) with newly diagnosed stage I-III HER2+ breast cancer eligible for neoadjuvant therapy. Pts received standard 6 cycles of docetaxel, carboplatin and trastuzumab (TCH) or TCH with pertuzumab (TCHP) regimens. Primary aim was to test the ability of HER2DX pCR score to predict pCR (ypT0/is ypN0). Secondary objectives were to test the ability of HER2DX pCR score to predict pCR independently of clinical-pathological variables and the PAM50 subtype (HER2-enriched versus not), and to evaluate the association of HER2DX pCR score with the HER2DX risk-score. Logistic regression and receiver-operator curve (ROC) analysis were assessed. Statistical analyses were performed in R code 4.0.5. Results: HER2DX was evaluated in 155 pts (97%) enrolled in the study with available RNA (as of June 2022). Mean age of pts was 50 (range 22-74) and 55.2% of pts (n=85) were pre-menopausal. Clinical T2-4 disease represented 77.4% of cases (n=120), clinical node-positive disease (cN1-3) represented 63.9% of cases (n=99), and 68.0% of tumors (n=105) were hormone receptor-positive. The overall pCR rate was 57.4% (95% confidence interval [CI] 50-65): 52.2% (95% CI 40-64) with TCH (n=67) and 61.4% (95% CI 50-72) with TCHP (n=88). The proportion of HER2DX low-, medium- and high-pCR groups was 34.2%, 34.8% and 31.0%, respectively. HER2DX pCR score (as a continuous variable from 0 to 100) was significantly associated with pCR (odds ratio [OR]=1.03, p=5.91e-07). The pCR rates in HER2DX pCR-high and pCR-low groups were 75.0% and 28.0% (OR=7.6, 95% CI 3.2-19.1, p=7.14e-06), respectively. In pts treated with TCHP, the pCR rates in HER2DX pCR-high and pCR-low groups were 85.7% and 27.3% (OR=16.0, 95% CI 4.3-59.01, p=3.2e-05), respectively. The AUC ROC of HER2DX pCR score (as a continuous variable) and pCR status was 0.746 (in all pts) and 0.812 (in pts treated with TCHP). HER2DX pCR score was significantly associated with pCR independently of hormone receptor status, Ki67, age, menopausal status, pertuzumab use, clinical stage and PAM50 HER2-enriched subtype. The proportion of HER2DX low- and high-risk of relapse disease was 32.0% and 68.0%, respectively. The correlation of HER2DX pCR score and HER2DX risk-score was weak (coefficient=-0.17), as previously described. Proportion of cases according to both HER2DX scores and absolute

difference of pCR rates between TCHP and TCH in each combined group is shown in Table. Conclusion: The HER2DX genomic test predicts pCR following neoadjuvant TCH or TCHP regimens independently of clinical-pathological variables and intrinsic subtype. The combination of both HER2DX scores might help better tailor systemic therapy in patients with newly diagnosed stage I-III HER2+ breast cancer.

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Stromal tumor infiltrating lymphocytes and pathological complete response in patients with inflammatory breast cancer treated with neoadjuvant chemotherapy

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Background: Inflammatory breast cancer (IBC) is a rare (1-5%), but aggressive form of breast cancer (BC), accounting for ~10% of BC mortality. In early setting (M0), standard of care is neoadjuvant chemotherapy (NACT), followed by surgery. Nevertheless, outcome is still relatively poor. Pathological complete response (pCR) after NACT is prognostic in BC in general, and can be predicted by a high percentage of stromal tumor infiltrating lymphocytes (sTIL) in the primary tumor. The predictive value of sTIL in IBC has only been sporadically investigated, often in smaller series. Our aim was to determine which variables, including sTIL, are associated with pCR and to determine the prognostic value of pCR in IBC in a large multicentric, retrospective cohort. Patients & Methods: We included patients with IBC treated with NACT+/- anti-Human Epidermal growth factor Receptor 2 (HER2) therapy, followed by surgery from 10/1996 to 10/2021 in 7 different European hospitals. Clinicopathological variables were collected and central pathological review was performed, including sTIL scoring. This study focused on M0 cases. Considered clinicopathological variables were: age, histology, tumor grade, estrogen receptor status (ER), HER2 status, focality (unifocal vs not), and baseline locoregional nodal status (Table 1). Associations between pCR, clinicopathological variables and sTIL were assessed using Firth's logistic regression models: Model 1 was adjusted for center, Model 2 additionally included all variables of interest. Similarly, linear regression was used to investigate the association between sTIL and clinicopathological features. Univariable and multivariable Cox regression was used to evaluate the role of pCR on disease free survival (DFS), distant recurrence free survival (DRFS) and overall survival (OS). DFS and DRFS were analyzed considering death without the respective event as competing risk. Results: 494 patients were included. The distribution according to receptor status was: ER-/HER2- (24.3%), ER+/HER2- (34.4%), ER+/HER2+ (13%) and ER-/HER2+ (20.2%). pCR rate was 26% and per receptor status: ER-/HER2- (28%), ER+/HER2- (10%), ER+/HER2+ (42%) and ER-/HER2+ (45%). pCR was associated with grade (G3 vs G1/2, OR = 2.79 (1.70 – 4.74), $p < .001$), ER-status (positive vs negative, OR = 0.39 (0.26 – 0.60), $p < .001$) and HER2 status (positive vs negative, OR = 3.74 (2.43 – 5.81), $p < .001$) in Model 1. Only the association with HER2 status remained significant in Model 2 (OR = 5.34 (2.83 – 10.47), $p < .001$). sTIL was scored for 385 patients. Median sTIL was 5.3% [IQR 2.0%;16.7%] and according to receptor status: ER-/HER2- (10%), ER+/HER2- (2.5%), ER+/HER2+ (6.7%) and ER-/HER2+ (8.3%). Higher sTIL was associated with NST ($p = .032$), grade 3 ($p = .015$), and ER-negativity ($p = .007$) in Model 1. This was no longer significant in Model 2, but the direction of the trends was preserved. sTIL was associated with pCR (5% increment, OR = 1.13 (1.05 – 1.22), $p = .002$), but no longer after adjustment. No association between pCR and sTIL was found stratifying by receptor status. The median FU was 9.4 years and multivariable Cox regression models revealed that ER+ and HER2+ status and achieving pCR were significantly associated with

better DFS, DRFS, and OS (Table1). Conclusion: Our results indicate that patients with HER2+ tumors have a higher probability of achieving pCR and that pCR has an independent prognostic role in IBC. This is the largest IBC study with centrally scored sTIL, demonstrating that sTIL is associated with pCR but its role as an independent predictor of pCR is still not certain.

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7:00 AM - 8:15 AM

P6-02-01

Frequency of pathogenic germline mutations beyond Germline BRCA gene mutations among Saudi patients with breast cancer

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Frequency of pathogenic germline mutations beyond Germline BRCA gene mutations among Saudi patients with breast cancer Mohammed Algarni*^{1,2,3}, Ashwaq Alolayan^{1,2,3}, Fouad Sabatin^{1,2,3}, Nadine Mabsout¹, Horya Zaher¹, Hussam Shehata¹, Saeed Alturki⁴, Abdulaziz alshalhoub¹, Fatimah Alturki¹, Sadal Refaea^{1,2,3}, Nafisah Abdelhafiz^{1,2,3}, Turki Alfayea^{1,2,3}, Mohammed Al Balwi^{1,2,3}, Kanan Alshammari^{1,2,3} ¹King Abdulaziz Medical City, Ministry of National Guard – Health Affairs, Riyadh, Saudi Arabia, ²King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia, ³King Abdullah International Medical Research Center, Riyadh, Saudi Arabia ⁴Anwa lab Riyadh, Saudi Arabia Background : Breast cancer is the

commonest cancer diagnosed in the kingdom of Saudi Arabia. Although the majority of breast cancer cases are sporadic , around 25-30% are related to hereditary and familial components. Germline BRCA gene mutations are most common mutations associated with hereditary breast cancer predisposition syndromes. In Saudi Arabia, the reported frequency of germline BRCA mutations is 11%^{1,2} . There is no data about the prevalence non BRCA pathogenic germline mutations in Saudi population. We aimed to study the prevalence of these mutations in Saudi patients with breast cancer. Methods : We analyzed all the confirmed breast cancer cases who were referred to the cancer genetic clinic at King Abdulaziz medical city in Riyadh, Kingdom of Saudi Arabia by using our cancer genetics database. Since November 2018 , a comprehensive hereditary cancer gene panel is offered to all referred breast cancer cases who meet the NCCN testing guidelines after obtaining a genetic counselling assessment and an informed consent. All testing was internally funded by the institution. The comprehensive panel tested genes are; ABRAXAS1, APC, ATM, AXIN2, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, DICER1, DIS3L2, EPCAM, FANCC, FH, FLCN, GALNT12, HNF1B, HOXB13, KIT, MC1R, MEN1, MET, MITF, MLH1, MLH3, MRE11, MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NTHL1, PALB2, PMS1, PMS2, POLD1, POLE, POT1, PRSS1, PTCH1, PTEN, RAD50, RAD51C, RAD51D, RECQL, RET, RNF43, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCA4, STK11, TGFBR2, TP53, TSC1, TSC2, VHL, WT1, XRCC2, XRCC3. Result : Between November 2018 and May 2022 , a total of 332 patients with breast cancer have been tested. The median age was 45 and 54 years for females and males , respectively. The majority of patients were females (n=322, 97%) . Most of the patients had stage III disease (n=183, 55%) followed by stage II(n=91 , 27%). Pathogenic variant(PVs) was reported in 16% (n= 52) , variant of uncertain significance (VUSs) was reported in 10% (n=32) while no mutation reported in the rest of the patients. TNBC was the most common phenotype among carriers of pathogenic mutation (50%). The PVs reported were BRCA1 (n= 19),BRCA2 (n= 21), PALB2(n= 2) ,PTEN (n= 2),ATM(n= 1),BARD1(n= 1),BLM(n= 1),BRIP1(n= 1),CDKN2A(n= 1), CHECK2(n= 1), MSH2(n= 1)and RECQL(n= 1) . Conclusion : This study shows that extended panel testing beyond BRCA gene increases the rate of detection of pathogenic germline mutations that has preventative and possibly therapeutic implications . In addition, to the best of our knowledge this is the first study that gives insight about the frequency of non germline BRCA mutations which represent unmet needs for breast cancer patients in Saudi Arabia. 1. J Glob Oncol. 2018 Aug;4:1-9. 2. Breast Cancer Res Treat. 2018 Apr;168(3):695-702

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7:00 AM - 8:15 AM

P6-02-02

Challenges and Dilemmas Following a Traceback Approach for Genetic Counseling and Genetic Testing for Pathogenic Germline Mutations among High-Risk Patients Previously Diagnosed with Breast Cancer

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Background: Accounting for almost 20% of all cancer cases, breast cancer continues to be the most common cancer and the leading cause of cancer-related deaths among females. In our region, almost 50% of breast cancer patients are diagnosed at age 50 or younger. Around 5-15% of breast cancers are hereditary and mostly related to BRCA1 or BRCA2 gene mutations. Risk-reducing interventions, like bilateral mastectomies and oophorectomies, are highly recommended for carriers of pathogenic variants. More recently, data had shown that specific breast cancer treatment may be informed by BRCA1 or BRCA2 mutation status. Until very recently, genetic testing and genetic counseling services were prohibitively expensive and were not available or routinely offered. Given the recently identified high prevalence of pathogenic

variants among our patients, and the wider availability and the lower cost of genetic testing, an opportunity exists to look back and offer such patients the chance to do genetic testing. Patients with positive tests can then be counseled, along with their close family members, for appropriate risk-reducing programs. Methods: Using our hospital-based cancer registry, we identified patients with breast cancer who fulfilled at least one of 3 approved indications for genetic testing but never had it. Eligible patients were those diagnosed at age 45 or younger, patients with triple-negative (TN) disease diagnosed at age 65 years or younger, and those with close blood relatives with breast or ovarian cancers. Patients were initially contacted over the phone and then seen by one of the investigators in our genetic counseling clinics. Testing was performed using next-generation sequencing (NGS)-based multi-gene panel (MGP) on a peripheral blood sample at a referral lab. Results: A total of 377 eligible patients were identified. The median age (range) was 48 (31-75) years. Genetic testing was performed on 198 (52.5%) and results were reported on 192. Age \leq 45 years (n= 157, 79.3%) and TN-disease (n= 59, 29.8%) were the most common indications for testing. In total, 20 (10.4%) patients were found to have pathogenic/likely pathogenic variants; mostly in BRCA2 (n=9) and BRCA1 (n=7). An additional 4 patients had TP53, PALB2, and ATM. Variants of uncertain significance (VUS) were identified in 53 (27.6%) patients. Following the visit to the genetic counseling clinic, an additional 41 (22.9%) patients agreed to test. The remaining 136 (36.1%) failed to be tested because of lack of updated contact information (n=54, 39.7%), living outside the country (n=19, 14.0%) or lack of insurance coverage (n=36, 26.5%). Fear of social stigma, lack of interest, or emotional stress were the reason for refusal among 24 (17.6%) patients. Conclusions: The Traceback approach may provide an opportunity to diagnose pathogenic/likely pathogenic variants among previously diagnosed patients with breast cancer. The high percentage of patients couldn't be tested for manageable reasons while fear of social stigma and emotional stress continued to be important barriers, especially in societies like ours. Given the important implications of genetic testing and its availability and affordability, reaching out to untested high-risk patients raises an ethical and professional dilemma that needs to be addressed from the physician, patients, and insurance perspectives.

Disclosure(s):

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7:00 AM - 8:15 AM

P6-02-03

Breast Health Assessment: A family health history tool using the electronic health record and clinical decision support to facilitate guidelines-driven hereditary breast cancer genetic testing at the time of screening mammogram

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Title: Breast Health Assessment: A family health history tool using the electronic health record and clinical decision support to facilitate guidelines-driven hereditary breast cancer genetic testing at the time of screening mammogram Background: Genetic testing (GT) is recommended for women who have a personal or family history of breast cancer and are at increased risk of carrying an inherited breast cancer risk gene pathogenic variant (PV) as defined by the National Comprehensive Cancer Network (NCCN) guidelines. Data shows that traditional GT workflows do not reach a large proportion of women eligible for GT. NorthShore University HealthSystem previously implemented the Genetic Wellness Assessment, a family health history (FHH) screening tool utilizing the electronic health record (EHR) and clinical decision support, to identify individual and familial risks to health conditions and personalize screening and prevention practices in primary care. To increase access to hereditary breast cancer GT, we implemented a similar FHH screening tool called the Breast Health Assessment (BHA) for patients completing routine screening mammogram. We describe uptake and results from implementation of the BHA in conjunction with routine screening mammogram. Methods: Patients scheduled for screening mammogram were assigned the BHA prior to their mammogram via the EHR portal. BHA questions addressed personal and family history of breast cancer and other cancer types associated with hereditary breast cancer syndromes. Upon completion of the BHA, patients who screened positive, i.e. identified as having a high-risk personal or family cancer history based on NCCN guidelines, were offered a comprehensive hereditary cancer panel (HCP). HCP included 38 genes associated with common cancer types, including all high and moderate risk breast cancer genes for which there are NCCN management guidelines. Individuals who were not identified as high-risk were offered a genetic health screen, which consisted of 148 genes associated with common cancer types, genetic forms of heart disease, medication response, and other health conditions. Saliva sample collection for GT occurred at the time of the patient's screening mammogram appointment. Results: From August 2021 through May 2022, 32,438 patients were assigned the

BHA prior to screening mammogram. Of these patients, 14,128/32,438 (44%) completed the BHA questionnaire. Based on BHA response, 3,490/14,128 (25%) screened positive and met NCCN criteria for GT for hereditary breast cancer risk genes and 529/3,490 (15%) completed GT. Additionally, 713/10,638 (7%) patients who screened negative on the BHA completed testing. In total, 1,242/14,128 patients (9%) completed GT and 78/1,242 (6%) were found to carry an inherited PV in a cancer risk gene, 35 of which were in an NCCN guidelines breast cancer risk gene. Of the 78 patients with a positive GT result, 57/78 (73%) had not been previously recommended for a genetics evaluation and/or received a genetics referral. Conclusion: The BHA is a novel FHH tool which increases access to hereditary breast cancer GT at the time of screening mammogram. Nearly half of women who completed screening mammogram completed the BHA and learned valuable information about their breast cancer risk and were invited to complete GT. Genetic testing completed through the BHA identified 78 patients with an actionable inherited PV in a cancer risk gene. This invaluable information will lead to potentially lifesaving personalized cancer screening and risk reduction and help identify additional at risk family members. Notably, 73% of patients who carried an inherited PV had not been previously recommended by their medical teams for genetic counseling and/or testing. The BHA has the potential to help close the care gap in GT for women at increased risk of breast cancer.

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Allison DePersia, MD: No financial relationships to disclose

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Katharine Yao, MD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P6-02-04

Use of breast surveillance between women with pathogenic variants and variants of uncertain significance in breast cancer susceptibility genes

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Background: Surveillance is a fundamental tool in the early detection and secondary prevention of many cancers. For women at increased genetic risk of breast cancer, mammography and breast magnetic resonance imaging (MRI) serve as the standard screening modalities. Use of surveillance mammography and MRI has been understudied among women with variant of uncertain significance (VUS) compared to pathogenic and likely pathogenic variants (P/LP). To address this gap, we examined the use of breast cancer surveillance and breast surgery in women who underwent multiple gene sequencing in a multicenter cohort of patients. We also expanded the surveillance literature by assessing correlates of breast MRI and mammography among women with VUS and investigating how rates of imaging changed over time after genetic testing. Methods: Using data from two cancer settings, we calculated use of risk reducing mastectomy (RRM) and surveillance for all women at genetically elevated risk of breast cancer, regardless of their personal history of breast cancer, with VUS or P/LP variants in a breast cancer susceptibility gene of high penetrance (BRCA1, BRCA2, PALB2, PTEN, TP53) and moderate penetrance (ATM, CDH1, CHEK2, NBN, NF1, STK11). The primary

outcome was longitudinal use of surveillance mammography and breast MRI for women during the 13-month span after genetic testing, and each subsequent 13-month period up to 6 years afterwards. Results: Of 889 women, those with and without personal history of breast cancer were similar with regards to race/ethnicity, marital status, and high- or average-risk status. However, women with a personal history of breast cancer were on average older (54.1 vs 48.2 years), had longer follow-up time since genetic testing (3.4 vs 3.0 years), and were more likely to have VUS (62.5% vs 37.7%) compared to those without personal history of breast cancer. VUS carriers were less likely to undergo RRM compared to those with P/LP (HR=0.17, p=< 0.001) and high-risk women were more likely to undergo RRM than average-risk women (HR=3.91, p=0.005). Longitudinally, surveillance use among unaffected women decreased from 49.8% in the first year to 31.2% in the sixth year after genetic testing. In comparison, a greater proportion of women with a personal history of breast cancer underwent surveillance, which increased from 59.3% in the first year to 63.6% in the sixth year after genetic testing. Mammography rates did not differ between women with P/LP and VUS within the first 13 months after genetic testing and up to 4 years afterwards. Over the first four years after genetic testing, women with VUS were less likely to undergo annual MRIs compared to P/LP. This observation was true for women without a personal history of breast cancer (OR=0.34, p=0.003; OR=0.37, p=0.03; OR=0.19, p=0.004 for years 1, 2, and 3 respectively) as well as for women with a personal history of breast cancer (OR=0.31, p<=0.001; OR=0.33, p=0.002; OR=0.37, p=0.012; OR=0.3, p=0.14 for years 1, 2, 3, and 4 respectively). Conclusion: In this study of surveillance mammography and breast MRI use among women at elevated risk of breast cancer, we found that women with P/LP variants in breast cancer susceptibility genes are more likely to undergo annual breast MRI compared to those with VUS, whereas there was no difference between the groups in their use of annual surveillance mammography. This study is one of the first to examine maintenance of breast surveillance in a sample of women at elevated risk of breast cancer with non-negative genetic test results in BRCA1/2 as well as non-BRCA1/2 genes, while adjusting for personal and family history of cancer. In addition, we found that VUS, whether in high or moderate penetrance breast cancer susceptibility genes, was associated with lower use of annual breast MRI compared to P/LP variants, and equivalent use of annual mammography. These results add important evidence to dispel the myth of VUS-associated mismanagement of care.

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Sukh Makhnoon, PhD, MS: No financial relationships to disclose

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Susan K. Peterson, PhD, MPH: No financial relationships to disclose

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7:00 AM - 8:15 AM

P6-02-05

Prevalence of non-BRCA germline pathogenic variants in Mexican women with breast cancer referred for genetic cancer risk assessment

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Background: The prevalence of germline pathogenic variants in Mexican women with breast cancer who met the reference criteria for genetic cancer risk assessment (GCRA) has been previously reported as close to 20%. However, information regarding the spectrum of gPVs in genes other than BRCA in this population is limited. Methods: This prospective study included

Mexican women who were diagnosed with BC and met international criteria for GCRA. Participants were enrolled in the Clinical Cancer Genomics Community Research Network (CCGCRN) registry and at two referral breast cancer centers in Mexico, the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City and at the Hospital Zambrano Hellion TecSalud, Monterrey. Participants underwent multigene panel testing (MGPT) for 37 cancer susceptibility genes. For this analysis, only the results of pathogenic and likely pathogenic variants in the index cases were reported. The demographic and molecular characteristics of the variants are described here. Results: From August 2017 to September 2021, 1020 Mexican women with BC underwent MGPT, with a median age at diagnosis of 41 y (range 20-86), of whom 206 (20.2%) were carriers. 208 gPVs were identified with BRCA1/2 representing 70% (145/208) of the gPVs (BRCA1 n=89, BRCA2 n=56). 63 (30%) of gPVs were identified in genes other than BRCA (CHEK2 n=21, PALB2 n=13, TP53 n=7, RAD51C n=5, ATM n=4, NF1 n=3, PTEN n=2, MUTYH homozygous n=2, RAD50 n=1, BRIP1 n=1, CDH1 n=1, NBN n=1, MSH2 n=1 and MSH6 n=1). The recurrent variants previously proposed as founders in the Hispanic population were frequent among those identified in their respective genes: CHEK2 c.707T>C 81% (17/21), PALB2 c.2167_2168delAT 46% (6/13) and BRCA1 del(exons 9-12) 18% (16/89). As a group, the 4 most frequent genes where gPVs were identified (BRCA1, BRCA2, CHEK2 and PALB2) represented 86% (179/208) of the positive results. Conclusion: Among the variants identified in this population of Mexican women with BC, the proportion of gPVs in genes other than BRCA was significant (about 1 out of 3 pts), which justifies the use of MGPT in the assessment of our population. However, a tailored panel (sequencing of BRCA1/BRCA2/CHEK2/PALB2 and MLPA for BRCA1) could be proposed in areas of Mexico with limited medical resources, including the analysis of other genes in selected patients according to clinical suspicion and family history of cancer.

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Yanin Chavarri-Guerra, n/a: No financial relationships to disclose

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P6-02-06

Implementation and outcomes of population-based hereditary cancer testing across a diverse multi-location breast imaging center

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Introduction: Up to 10% of all breast cancers (BC) are attributed to inherited pathogenic variants (PV) in BC susceptibility genes, and genetic testing at the time of breast imaging may identify more patients who could benefit from enhanced surveillance and/or risk reduction interventions. Data are limited on the yield of PVs in the setting of a breast imaging center. Hypothesis: Hereditary cancer gene screening at the time of breast imaging may identify patients and families who could benefit from cancer risk management. Methods: This retrospective cohort study included de-identified clinical data and commercial multi-cancer panel (40 genes) test results from sequential patients undergoing breast imaging at 3 centers in Texas over a 17 month period. Patients of providers who elected not to participate were excluded from this cohort. PV prevalence was quantified and stratified based on level of risk for BC and other cancers: high-risk (relative risk >4) for BC, moderate-risk (relative risk 2-4) for BC, high-risk for other cancers, moderate-risk or undefined risk for other cancers. Results: A total of 1,943 patients undergoing breast imaging chose to have genetic testing during the study period. Median age was 66 yrs (range 18-89 yrs). Self-reported race/ethnicity: White (34.5%), Hispanic (27.7%), African American (17.9%), Asian (4.5%), Ashkenazi Jewish (0.6%), Other (3.5%) and unreported (13.0%). A personal history of breast or ovarian-related cancers was reported in 4% (n=78) and a family history of these cancers was reported in 38.9% (n=835) of

patients. Among those tested, 44/1,943 (2.3%) had one or more PV in an autosomal dominant clinically actionable gene, further categorized as: high-risk BC gene (36.3%), moderate-risk BC gene (34.1%), high-risk gene for other cancers (13.6%), moderate-risk gene for other cancers (6.8%), or uncertain level of increased risk for other cancers (9.1%). A heterozygous PV in an autosomal recessive gene was present in 31/1943 (1.6%) patients. Overall, 354/1943 (18.2%) patients met current NCCN guidelines for hereditary breast and ovarian cancer (HBOC) gene testing. Only 15/44 (34.1%) patients with an autosomal dominant clinically actionable PV met current NCCN guidelines for HBOC testing. Genetic education was provided to 20/44 (45.5%) patients by lab-based genetic counselors and/or the patient's healthcare provider. Conclusions: Offering genetic testing in a diverse breast imaging center population was associated with a significant yield (4%) of both dominant and recessive clinically actionable PVs. Of note, almost 2/3 of PVs in hereditary cancer genes were among women who did not meet NCCN testing guidelines. Identification of a PV enables risk stratification, cascade testing of family members and an opportunity to access enhanced surveillance and risk reduction interventions.

Disclosure(s):

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7:00 AM - 8:15 AM

P6-02-07

Uptake of Breast Cancer MRI Screening in Patients After Multiplex Gene Panel Testing

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Purpose: Multiplex gene panel testing (MGPT) is used to identify individuals with an inherited susceptibility to cancer. However, little is known about the uptake of screening and surveillance among patients after MGPT and genetic counseling. The purpose of this study was to measure the uptake of guideline-concordant breast cancer screening after genetic testing and counseling.

Patients and Methods: 2,000 patients who met NCCN testing guidelines or had $\geq 2.5\%$ probability of a pathogenic/likely pathogenic variant (PV) were recruited at three cancer genetics clinics (University of Southern California (USC) Norris Comprehensive Cancer Center, Los Angeles County + USC Medical Center, Stanford Cancer Institute) from July 2014 through November 2016. All patients had 25- or 28-gene MGPT and results were disclosed by a genetic counselor, who provided screening recommendations to patients based on their risk. Post-test surveys were administered at three months, six months, one year, two years, and three years. Results: 1,614/2,000 (80.7%) patients were female and 1,147/1,614 (71.7%) completed at least one survey regarding MRI screening for breast cancer over the three years of longitudinal follow-up. Of these, 94/1,147 (8.2%) patients tested positive for at least one PV in a breast cancer risk gene; 58/94 (61.7%) tested positive for PVs in a high-risk breast cancer gene (BRCA1/2 (n=53), CDH1, PALB2, TP53 (n=5)), and 34/94 (36.2%) of patients tested positive for a PV in a gene characterized as moderate-risk at the time of disclosure (CHEK2, ATM, NBN). MRIs were recommended to 43/58 (74.1%) patients with a high-risk breast cancer gene PV, 20/34 (58.8%) patients with a moderate-risk gene PV, and 171/1,053 (16.2%) patients without a breast cancer risk gene PV. Multivariate logistic regression models revealed that patients with a high-risk gene PV were more likely to undergo MRI screening within 3 months of receiving genetic test results (OR=6.54 95% CI [3.09 - 14.43], $p < 0.001$), within one year (OR=1.34 95% CI [1.18 - 1.52], $p < 0.001$), two years (OR=1.43 95% CI [1.24 - 1.65], $p < 0.001$), and three years (OR=1.44 95% CI [1.25 - 1.66], $p < 0.001$) when compared to patients without a PV. Patients with a moderate-risk PV were also more likely to have undergone MRI within 3 months of receiving genetic test results (OR=2.89 95% CI [1.05 - 7.81], $p = 0.036$), within one year (OR=1.33 95% CI [1.10 - 1.62], $p = 0.004$), two years (OR=1.31 95% CI [1.09 - 1.59],

p=0.004), and three years (OR=1.44 95% CI [1.18 - 1.76], p< 0.001), compared to those without a PV (Table 1).

Conclusions: After three years of longitudinal follow up of 2000 patients in this multicenter prospective cohort study, patients with a PV in a breast cancer susceptibility gene were more likely to undergo guideline concordant breast MRI compared to patients without a PV. Carriers of high-risk breast cancer gene PVs were over six times as likely to have undergone MRI compared to patients without PVs within the first three months after genetic results disclosure and counseling. These results demonstrate the effectiveness of MGPT and genetic counseling in guiding patients with PVs in breast cancer susceptibility genes to the appropriate adoption of guideline-concordant screening.

Odds ratios of MRI screening in patients carrying PV in breast cancer risk genes. Odds in relation to patients who do not carry a PV

	Odds Ratio	95% Confidence Interval	p-value
High-risk gene PV			
3 months	6.54	3.09 - 14.43	<0.001
1 year	1.34	1.18 - 1.52	<0.001
2 years	1.43	1.24 - 1.65	<0.001
3 years	1.44	1.25 - 1.66	<0.001
Moderate-risk gene PV			
3 months	2.89	1.05 - 7.81	0.036
1 year	1.33	1.10 - 1.62	0.004
2 years	1.31	1.09 - 1.59	0.004
3 years	1.44	1.18 - 1.76	<0.001

High risk gene PV: BRCA1/2, CDH1, PALB2, TP53; Moderate Risk PV: CHEK2, ATM, NBN.

Percent of patients having undergone an MRI at the specified time points

	3 Month	12 Months	2 Year	3 Year
High-risk gene PV	59.6%	67.2%	81.3%	81.6%
Moderate- risk gene PV	44.0%	57.7%	67.7%	81.5%
No PV	28.7%	39.1%	49.0%	50.9%

High risk gene PV: BRCA1/2, CDH1, PALB2, TP53; Moderate Risk PV: CHEK2, ATM, NBN.

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P6-02-08

Identifying preferences that may motivate choice of ovarian cancer risk prevention strategies using a discrete choice experiment.

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Background: Women with a familial or hereditary risk for ovarian cancer are at a much greater risk of developing ovarian cancer compared with women in the general population. This high risk demands prevention strategies to reduce ovarian cancer incidence and mortality. Currently there is little information about how women with a hereditary risk for ovarian cancer make trade-offs when choosing among prevention strategies and their associated risks. In anticipation of the likelihood that when given more personalized risk estimates, patients may have different preferences based on their mutation specific cancer risk as well as demographic and clinical factors, it is critical that we have the necessary information to develop counseling models that are tailored to individual patients' preferences for cancer risk reduction and tolerance of associated risks. Methods: We performed a discrete choice experiment to investigate how women at higher risk of ovarian cancer weigh benefits (e.g. reduced risk of ovarian) versus costs (e.g. increased risk of heart disease) in choosing a treatment strategy. N=396 premenopausal women with a personal history of breast cancer or familial history suggestive of increased breast and/or ovarian cancer risk were surveyed from August, 2019, to January,

2022. Participants were asked to choose between two sets of attributes that specified type of surgery (risk-reducing salpingo-oophorectomy [RRSO], risk reducing salpingectomy [RRS] vs. non-surgical surveillance), age of menopause (natural versus immediate), quality of menopausal symptoms (mild, moderate, severe), and risk of ovarian cancer, heart disease, or osteoporosis. Risks of disease varied in discrete intervals. We fit a Bradley-Terry logistic regression to estimate preferences. The binary response was the randomly generated choice set selected versus the set not selected. Results: Women were more likely to choose sets with either surveillance (odds ratio [OR]= 1.28, 95% confidence interval [CI] 0.98, 1.67) or RRSO (OR= 1.39, 95% CI 1.07, 1.81) over RSS. In weighing trade-offs in the choice sets that included type of surgery, women had a stronger independent preference for reducing the risk of ovarian cancer (OR= 0.66 of choosing set per 10% increase in risk, 95% CI 0.62, 0.71) than in reducing the risk of osteoporosis (OR= 0.82 per 10% increase, 95% CI 0.75, 0.90) or heart disease (OR = 0.82 per 10% increase, 95% CI 0.76, 0.88). Women also had a strong preference for delaying the expected age of ovarian cancer (OR= 1.34 per 10-year increase in age, 95% CI 1.19, 1.51). Women had strong preferences for having a natural age of menopause (OR= 1.58 compared to immediate menopause post-treatment, 95% CI 1.27, 1.95), and better less severe symptoms (OR= 0.65 for each ordinal increase in the severity of symptoms, 95% CI 0.60, 0.70). Conclusions: Our results suggest that women may prefer either surveillance or the most extensive type of surgery (RRSO) over more limited surgery (RRS). In weighing trade-offs, reducing the risk of ovarian cancer seemed to be more important than reducing the risk of osteoporosis or heart disease. Still, having a natural age of menopause and reducing the severity of symptoms could motivate the choice of treatment. Our work will allow us to estimate thresholds of measured factors that may motivate women to choose a specific treatment strategy.

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P6-02-09

Racial/Ethnic Groups Have Different Rates of Pathogenic Variants in Common Cancer Genes

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Background:

Racial/ethnic disparities have been well-documented in access to cancer screening and treatment, as well as treatment outcomes. Less is known regarding the yield of genetic pathogenic variants (PVs) in non-white populations.

Methods:

Patient data was obtained from the Informed Genetics Annotated Patient Registry (iGAP), an IRB-approved multi-center longitudinal, observational study, in which 2148 patients self-declared race/ethnicity and underwent germline genetic testing at any lab. Analyses were limited to 24 cancer susceptibility genes (ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, NBN, PALB2, PTEN, STK11, TP53, APC, BMPR1A, CDK4, EPCAM, MLH1, MSH2, MSH6, MUTYH, PMS2, RAD51C, RAD51D, SMAD4), 21 of which have clinical management guidelines from the NCCN (excluding NBN, BARD1, CDK4).¹ Descriptive statistics were used to assess and compare data from these populations and germline genetic testing results.

Results:

The Registry included 2148 patients, 1662 (77.37%) with a personal history and 1536 (71.51%) with a family history of cancer. The patients were 74.39% White, 6.33% Hispanic, 5.59% African/Black, 5.03% Asian, 1.63% Other, 1.35% Ashkenazi, and 5.68% Unknown. The overall germline PV rate in the cohort was 0.1089 PVs/patient tested, with 234 PVs detected in 227 patients.

The PV rate among racial/ethnic groups were as follows: White 170/1598 (0.1064), Asian 8/108 (0.0741), Hispanic 27/136 (0.1985), African/Black 11/120 (0.0917), Ashkenazi 6/29 (0.2069). In patients self-reporting as Hispanic, the PV rate was similar to PV rate in those self-reporting as Ashkenazi, and significantly higher ($p=0.00027$) than PV rate in those of other self-reported race/ethnicity. Gene level PV rates are shown in Table 1.

Conclusions:

Those who reported being Hispanic had an increased overall PV rate. This could be due to the greater representation of Hispanics from New Mexico who may have Ashkenazi ethnicity. Further studies are needed to understand whether these differences are a result of disparate access to testing, true population differences, lack of data in non-White populations skewing variant classification or other factors.

Gene PV Rates by Racial/Ethnic Category

Table 1.

PV Genes	White		Hispanic		African/Black		Asian		Ashkenazi		Total (w/other and unknown)	
	N	PV Rate	N	PV Rate	N	PV Rate	N	PV Rate	N	PV Rate	N	PV Rate
CHEK2	55	0.0344	3	0.0221					2	0.0690	64	0.0298
BRCA2	30	0.0188	5	0.0368	4	0.0333	3	0.0278			44	0.0205
BRCA1	17	0.0106	10	0.0735	2	0.0167			1	0.0345	33	0.0154
ATM	21	0.0131	2	0.0147	1	0.0083	1	0.0093	1	0.0345	26	0.0121
PALB2	9	0.0056	2	0.0147							12	0.0056
PMS2	6	0.0038			1	0.0083	1	0.0093	1	0.0345	9	0.0042
NBN	8	0.0050	1	0.0074							9	0.0042
MSH6	4	0.0025	2	0.0147					1	0.0345	8	0.0037
RAD51D	3	0.0019	1	0.0074	1	0.0083	2	0.0185			7	0.0033
BARD1	5	0.0031			1	0.0083	1	0.0093			7	0.0033
RAD51C	4	0.0025	1	0.0074	1	0.0083					6	0.0028
BRIP1	4	0.0025									5	0.0023
TP53	2	0.0013									2	0.0009
PTEN	1	0.0006									1	0.0005
MSH2	1	0.0006									1	0.0005
N Patients in Cohort	1598		136		120		108		29		234	1.0000
PV Rate by RE	170	0.1064	27	0.1985	11	0.0917	8	0.0741	6	0.2069		

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12/9/2022

7:00 AM - 8:15 AM

P6-02-10

Prevalence of breast cancer predisposing variants in patients with breast carcinoma in situ

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Background. Carcinoma in situ (CIS) of the breast is a non-obligatory pre-malignant breast lesion and a highly suspected precursor of invasive cancer. Although the selection criteria for referral to genetic testing are well established for patients diagnosed with invasive breast cancer, these are not clear for patients diagnosed with CIS. Our goal is to assess the prevalence of predisposing pathogenic variants in key genes, as well as to describe factors in patients with CIS that might be associated with genetic predisposition. Methods. A total of 267 patients solely diagnosed with CIS (mean age 43.65 years, range 18-74) through years 2010-2022, were referred for genetic testing and were analyzed, following their informed consent,

implementing a 42-gene panel. Of these, 81.5%, 12.4% and 5.8% were ductal, lobular and mixed CIS, respectively. Patients having a synchronous invasive breast cancer diagnosis were not included in the study. Of patients with known grade, 52.28%, 28.9% and 18.8% were grade 3, 2 and 1, respectively. Strong family history for breast cancer (>2 close family relatives) was positive in 28% (75/267) of patients, while 67.8% of CIS were hormone receptor positive. Results. A total of 12.7% (34/267) of patients carried pathogenic variants in seven clinically actionable genes, i.e. CHEK2 (10), BRCA2 (9), BRCA1 (5), ATM (5), PALB2 (2), MSH6 (2) and TP53 (1). Mean age at diagnosis of carriers was 42.1 years (range 29-61 years, $p=0.26$), 60% of patients had a grade 3 CIS diagnosis (OR 1.1, 95% 0.589-2.1, $p=0.73$), 96% had a hormone positive diagnosis (OR 1.4, 95% 0.78-2.50, $p=0.24$), while 73.5% (25/34) reported as having at least two close family relatives with breast cancer (OR 2.9, 95% 1.6-5.1, $p=0.0001$). The vast majority of carriers had a ductal CIS (DCIS) diagnosis, i.e. 91.2% (31/34) although this did not reach statistical significance (OR 1.087, 95% 0.64-1.82, $p=0.72$), probably due to small numbers. Notably, carriers were more likely to have a diagnosis with comedo characteristics, although this parameter has not been monitored closely for the whole cohort. Conclusion. Herein, an important fraction of patients with breast CIS carried pathogenic variants in clinically actionable genes, with the most frequent being CHEK2, BRCA2, BRCA1 and ATM. Notably, the prevalence is comparable to that of patients with invasive breast cancer. Strong family history for breast cancer was strongly associated with the identification of predisposing variants. Other factors, such as high grade, hormone positivity, age at diagnosis and others might also be associated with predisposition to CIS, but larger, prospective, studies are needed to confirm these. This is one of the few studies evaluating the inherited predisposition associated with both high and moderate penetrant breast cancer genes, highlighting that individuals with CIS diagnosis and strong family history for breast cancer should be offered the option to genetic testing via multigene panel.

Disclosure(s):

Florentia Fostira, PhD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Terminated, May 31, 2022); GlaxoSmithKline: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, May 23, 2022); Takeda: Consulting Fees (e.g., advisory boards) (Ongoing)

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P6-02-11

Implementation of multigene panel testing in triple-negative breast cancer. The PERSONA-breast trial

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Kahler Ribeiro Fontana S1, Bonetti E2, Bernard L3, Calvello M4, Bonanni B4, Bonizzi G 5, Veronesi P1,6, Mazzearella L 2, Galimberti V1 Introduction Triple-negative breast cancer (TNBC) is frequently associated with germline genetic variants associated with cancer predisposition. Approximately 20% of TNBC carry a germline BRCA1 or BRCA2 mutation. Germline mutations in other genes involved in DNA repair, specifically Homologous Recombination (HRR), including ATM, BARD1, BRIP1, CHEK2, PALB2, RAD50, RAD51C, RAD51D may be associated with TNBC however remain imprecise in several populations as in

Italy. In recent years, there has been an increase in multigenic panel testing thanks to better technology and the fact that genetic testing is no longer done just for prevention but they have become relevant in the clinical setting and this is especially true for triple negative disease. At the European Institute of Oncology, we conducted a prospective clinical trial, the PERSONA Breast trial, aimed at providing a more comprehensive picture of the mutational landscape and cancer risk in patients with TNBC by multigene germline genetic testing. Methods PERSONA is a prospective observational trial conducted between June 2018 and January 2022 on 313 patients with a diagnosis of TNBC \leq 60 years and able to undergo surgery (primary or post-neoadjuvant). Peripheral blood DNA was sequenced with the Illumina TruSight Cancer panel (94 cancer predisposition genes). Genes were classified as germline actionable (n. 15) or non-actionable (n. 79) according to their associated relative risk of cancer. Genetic variants were classified according to the American College of Medical Genetics and Genomics (ACMG) guidelines and the databases of genetic variants (ClinVar, LOVD, BRCA-Exchange,). All enrolled patients were followed up six-monthly for 10 years from informed consent or to death or withdrawal of consent. Results We present preliminary germline results from a 94-gene panel testing performed on a cohort of 313 TNBC patients. The clinical data of these patients was considered for a descriptive analysis of the cohort. Data on outcome such as overall survival and disease-free survival were not yet available. Germline multigene testing detected 62 unique (i.e., n. 49 in actionable, n. 13 in non-actionable genes) pathogenic (C5) and likely pathogenic (C4) variants in 25.2% of TNBC patients (79/313). As expected, 53.2% (42/79) of TNBC patients were carriers of a C5/C4 in BRCA1. C4/C5 were identified also in other actionable genes: 13.9% (11/79) in BRCA2, 8.9% (7/79) in MUTYH, 3.8% (3/79) in PALB2, 2.5% (2/79) in MSH2, 1.3% (1/79) in PMS2, and 1.3% (1/79) in TP53. In addition, 12 TNBC patients had C4/C5 variants in non-actionable genes, and 4 were carriers of both C4/C5 variants in actionable and non-actionable genes. Multigene testing resulted in the identification of 655 (i.e., n.82 in actionable, n. 573 in non-actionable genes) variants of uncertain significance (C3 or VUS) in 89.8% (281/313) of patients. Of the 281 C3 carriers, 60 had other variants (C4 and/or C5), of an uncertain result (in whom C3 was the highest class of variant) only in 70.6% (221/313) of TNBC patients. In 13 patients (13/313; 4.1%) only benign (C1) or likely benign (C2) variants were identified. Regarding family history, 67% of BRCA1 carriers versus 30% of BRCA2 carriers were familial. Conclusion Germline multigene testing in TNBC can identify C4/C5 in actionable genes providing information for a more tailored management of TNBC. Our study showed that the rate of VUS remains high using multigene testing. Of note, VUS were mainly identified in non-actionable genes supporting the rationale of the use in the clinical setting of phenotype-specific multigene panels, including a minor, but more appropriate, number of genes.

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P6-02-12

Underutilization and disparities in germline genetic testing for breast cancer patients diagnosed in Chile

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Introduction 10% of Breast Cancer (BC) cases are thought to carry a germline pathogenic variant (PV) in a susceptibility gene. Most clinicians utilize the National Comprehensive Cancer Network (NCCN) guidelines criteria to both identify these patients and, in those who test positive, to provide adequate follow-up and/or surgery recommendations. In Chile, BC Guidelines, established in 2004, defined treatment strategies for invasive BC (iBC) which significantly reduced mortality. However, these guidelines do not define strategies for germline genetic testing nor contemplate coverage for those who needs them. Thus, we face many obstacles to genetic testing implementation such as out-of-pocket cost and lack of genetic counsellors. The aim of the study is to determine how many BC Chilean patients are at risk according to international guidelines, how many are being tested and what are their clinical characteristics. Methods Retrospective analysis of a prospective database of iBC patients treated in a public hospital (PH) and in an Academic Private Centre (AC) in Santiago, Chile from January 2012 to March 2022. All patients who had enough information (age, family history (FH), BC subtype) for NCCN Version 2.2022 categorization were included. Patients whose only indication for germline testing was the potential use of PARP-inhibitors were excluded. Clinical characteristics were extracted from clinical charts. Results 4,365 iBC patients met criteria. 51.1% were treated in PH and 49.9% in a AC. 2,260 patients (51.8%) fulfilled NCCN criteria for germline testing, distributed unevenly between PH (46.0%) vs. AC (56.9%, p=0.0001). Compared to PH, patients in AC were diagnosed at younger age (54 vs 56 years, p=0.0001) and were more likely to report FH (69.4% vs. 53.7%, p=0.0001). No difference between BC

subtypes was reported. Considering only those fulfilling criteria, germline genetic testing was performed in 326 patients (14.4%) with a significant difference according to UH vs AC (18.7% vs. 9.1%, $p=0.0001$). 58% of these tests were performed in the last 3 years. Multivariate logistic regression showed that being diagnosed before 46 (HR=5.3, $p=0.0001$); FH (HR=2.2, $p=0.0001$); localized vs. metastatic disease (HR=3.7, $p=0.001$); triple negative (TN) BC (HR=1.8, $p=0.0001$) and being treated in AC (HR=1.9, $p=0.0001$) were independently associated with germline genetic testing being performed in patients fulfilling NCCN criteria. 82 PV were documented, being the most frequent BRCA1/2 (18.1%) followed by PALB2 (1.8%) and ATM (1.2%). Being diagnosed with TNBC (HR=3.8, $p=0.0001$) and having a first-degree relative with cancer (HR=4.4, $p=0.0001$) were the only factors associated with carrying a pathogenic BRCA1/2 mutation. Conclusion In Chile, less than 20% of iBC patients who meet NCCN criteria for germline testing are being tested. In this sample of our Public Health System, where over 80% of the Chilean population is treated, fewer than 1 in 10 individuals fulfilling criteria have undergone testing. New evidence suggests that probably a wider span than suggested by NCCN of patients should be counselled and tested, deepening even further the underutilization of germline testing in Chile. Lack of knowledge and training in oncology providers and out-of-pocket costs might influence these results. National guidelines are urgently needed.

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P6-02-13

Expanding the reach of germline genetic testing: Use of web-based risk assessment to inform medical management amongst patients at breast and imaging centers

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Background Developing an effective approach to the identification of individuals at increased cancer risk is key to preventing and/or providing early diagnosis of cancer. However, outside of targeted genetics clinics, under identification of individuals with hereditary cancer risk is well recognized, due in part to ever evolving complexity of germline genetic testing criteria and lack of systematic framework to perform robust risk assessment on all patients. In contrast, breast and imaging centers are ideally positioned to maximize the impact of positive genetic test results due to immediate availability of surveillance and diagnostic tools. Here we present data from breast and imaging centers using a patient-facing digital platform offered universally to all patients before their scheduled appointment designed to collect personal and family health information and assess cancer risk and genetic testing eligibility based on current guidelines. Methods We conducted a retrospective observational study of patients in breast and imaging centers who used a web-based risk stratification tool before standard ambulatory appointments to assess their lifetime risk for breast cancer based on the Tyrer-Cuzick (version 8.0) risk algorithm and eligibility for National Comprehensive Cancer Network (NCCN®) genetic testing criteria at the time of assessment. Testing criteria included hereditary breast, ovarian, pancreatic, and prostate cancers, Lynch syndrome, and familial adenomatous polyposis (FAP). Data was pulled for patients seen from June 2020 through May 2022 at participating breast and imaging centers throughout the United States. Outcome measures included percentage of individuals who completed the risk-assessment, met testing criteria, pursued germline genetic testing, received a positive germline result, and/or had a Tyrer-Cuzick breast cancer risk $\geq 20\%$.

Results A total of 251,492 individuals completed assessments; 250,011 (99%) were females aged 18 years or older. Overall, at the time of assessment 80,814/251,492 (32.1%) met genetic testing criteria and 24.4% (19,694) of those meeting criteria opted to proceed with germline genetic testing. An additional 1,561 individuals who did not meet criteria pursued genetic testing. Of the 18,532 completed genetic tests, 1,507 (8.1%) had positive genetic test results. The majority of positive individuals (93%) met testing criteria. 40.7% (613/1,507) of positive results had an impact on breast cancer risk management options. In addition to individuals identified as high-risk through germline genetic testing evaluations, 13.1% (28,108/214,269) of individuals assessed using the Tyrer-Cuzick algorithm had $\geq 20\%$ lifetime risk of breast cancer and met the threshold for modified medical management. Conclusion In this study, the web-based assessment tool provided a standardized workflow that enabled individuals interested in receiving cancer risk assessment and germline testing an opportunity to do so. When offered to all patients, this digital platform can offer a scalable opportunity for breast and imaging centers to identify individuals eligible for modified medical management for breast cancer risk and other inherited cancer syndromes, which may ultimately improve the prevention and early treatment of individuals with cancer predisposition.

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P6-02-14

Contralateral breast cancer risk in patients with or without BRCA mutation

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Background: Patients who carry mutated BRCA1 or BRCA2 genes have a significantly increased risk of breast cancer and developing contralateral breast cancer (CBC). In this study, we aimed to investigate the acceptance rate of BRCA1/2 testing in Korean breast cancer patients and to determine the risk of CBC in Korean patients with BRCA 1/2 germline mutations. Methods: This study included 13,109 patients with first primary breast cancer who were treated at Seoul National University Hospital from January 2005 to December 2018. These patients were divided into high-risk for BRCA1/2 mutation group and low-risk group. High risk patients were defined as those who were eligible for BRCA testing per Korean National Health Insurance Service. The high-risk group was further classified into three groups; BRCA1/2 mutation carrier, BRCA 1/2 non carrier and BRCA/12 untested. Results: Among the 4,446 high-risk patients, 962 (21.7%) patients underwent BRCA1/2 testing. The testing rate varied among different indications (47.8% of patients with a family history, 23.3% of patients under 40 years of age, and 13.0% of patients with triple negative breast cancer). The risk of the CBC in BRCA mutation group was higher than other groups (p value < 0.001). The 10-year cumulative risk of CBC was 11.0% BRCA1 mutation carrier and 7.4% for BRCA2 mutation

carrier. In the BRCA1/2 non-carriers, the cumulative risk of CBC was 5.7%. Interestingly, the CBC risk for BRCA1/2 non-carriers significantly higher than BRCA1/2 untested group and the low-risk group ($p < 0.001$). When compared to the BRCA1/2 untested group, the relative risk for CBC was 6.7-fold increase for the BRCA1/2 mutation carrier group (95% CI = 3.65-12.22, $p < 0.001$), and 2.3-fold increase for the BRCA1/2 non-carriers group (95% CI = 1.44-3.83, $p < 0.001$). The relative risk for CBC in high-risk group also depended on subtype of breast cancer and family history. Hormone receptor negative breast cancer patients had a 1.5-fold (95% CI = 1.02-2.31, $p = 0.04$) increased risk of CBC and patients with one or more 1st degree relative with breast cancer had 2.4-fold increased risk (95% CI = 1.55-3.67, $p < 0.001$). Conclusion: About one out of five Korean breast cancer patients, who are eligible for the BRCA1/2 testing, undergo testing for BRCA1/2 germline mutations. We observed increased CBC risk not only for the BRCA1/2 mutation carriers but also for the BRCA1/2 non-carriers. At present, we are conducting multi-gene panel testing for the BRCA1/2 non-carriers to understand the mechanisms of the increased CBC risk.

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P6-02-15

Don't get lost in translation: Evidence-based Network for the Interpretation of Germline Mutant Alleles (ENIGMA) recommendations for reporting germline cancer susceptibility gene variants in 19 languages – breast cancer as a model

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Genetic testing for cancer susceptibility is a cornerstone of precision cancer prevention and care. Major communication hurdles remain for the differently specialized professionals involved in the identification, counselling, and clinical management of at-risk individuals. This may be ascribed to gaps in the genetic/genomic literacy of health care providers and to an ambiguous lexicon used for variant description. The Evidence-based Network for the Interpretation of Germline Mutant Alleles (ENIGMA) international consortium endorses controlled terminology and a framework for interpretation and reporting of germline variants in cancer susceptibility genes (PMID: 30962250). However, for most ENIGMA affiliates a language other than English is used for written and verbal communication of genetic test results, potentially confounding local application of the published framework. The ENIGMA Clinical Working Group thus launched a Vocabulary Translation Project (VTP) to translate the ENIGMA recommendations into the various languages spoken by the membership. The VTP involved 65 ENIGMA members from 22 countries organized into 19 language-specific teams, covering Catalan, Chinese, Czech, Danish, Dutch, Finnish, French, Galician, German, Greek, Italian, Japanese, Malay, Norwegian, Polish, Portuguese, Spanish (Castilian), Swedish, and Tagalog. Excerpts from the original publication were selected for translation based on a majority consensus and

included a glossary of terms and recommendations for interpreting and reporting germline sequence variants in (breast) cancer susceptibility genes. Using a two-step process, each team conducted the relevant translation followed by independent back-translation to English. The VTP proved useful to reappraise the reference text. It disclosed transnational issues, which prompted revision of the original source to emphasize that risk estimates and actionability were based on breast cancer as an exemplar. It also highlighted country-specific differences with regards to breast cancer risk assessment (e.g. different absolute/relative breast cancer risk cut points) and management. As a secondary outcome, via electronic survey of the participating teams we documented the perceived high value of the translation effort and its expected positive impact on more consistent clinical management of carrier individuals. The identified target audience encompasses medical geneticists, physicians of other specialties participating in multidisciplinary teams, genetic counselors, primary care physicians, as well as non-health care professionals, e.g. journalists and science communicators. The outreach program includes dissemination of the translations via local, regional, and especially national networks and their use for education and training purposes. Because French, Portuguese, and Spanish are widely used as official, co-official, or secondary languages, the reach of the VTP potentially extends to a greater number of countries and territories, mostly in Central and South America, Caribbean, and Africa. By moving a step forward towards terminological coherence across disciplines and borders, we will facilitate more precise delivery and clinical application of genetic test results for breast cancer predisposition. Our translated recommendations will improve interdisciplinary cross-talk and carriers' awareness of the risks and implications associated with their status, contributing to more informed decision-making. We used breast cancer as a blueprint. Application of the model to other cancer types will require calibration on the cancer-specific absolute and relative risks.

Disclosure(s):

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P6-02-16

Breast cancer prognosis of germline BRCA1/BRCA2 mutation carriers of young women: a retrospective hospital-based cohort

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Background Studies evaluating prognostic impact of germline BRCA1/2 mutations (gBRCAm) on breast cancer patients reported controversial results. The primary aim of this study was to investigate outcomes of young gBRCAm patients with very early onset of breast cancer (< 30 years) compared with noncarriers. Methods In this retrospective study, 149 patients 30 years aged or younger at early breast cancer diagnosis between 2005 and 2019 were included in Oscar Lambret Center. Outcomes were overall survival (OS) and disease-free survival (DFS), defined as time from first diagnosis to first recurrence, second cancer or death from any cause, at 2 years, 5 years, and 10 years. Key patient data, kaplan-meier plots and outcomes were described by BRCA mutation status. Hazard ratios (HR) were calculated using Cox proportional-hazards models. Results Twenty-eight (18.8%) patients were gBRCAm carriers. The median follow-up was 6.5 years (IQR 0.25-16.5). Twenty-three deaths, 41 recurrences and 2 second cancers were reported. OS was 89.3% [70.4–96.4] in gBRCAm patients vs 99.1% [95% CI 93.9–99.9] in non-carriers patients at 2 years; 85.0% [64.7–94.1] vs 92.3% [85.1–96.1] at 5 years and 75.3% [52.5–88.3] vs 80.2% [66.6–88.7] at 10 years. There was no difference in OS between groups in multivariable analysis (HR=1.63 [0.55–4.77], p=0.37). Similar results were noted when comparing disease-free survival (HR=1.42 [0.64–3.11], p=0.38). Conclusions In this cohort of 149 patients with very early onset breast cancer, outcomes of gBRCAm mutation carriers did not differ from non-carriers when adjusted for others prognostic factors.

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Florent HEGO, n/a: No financial relationships to disclose

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P6-02-17

A Real-World Study of BRCA1 and BRCA2 Germline Mutations among High Hereditary Risk Subjects and Patients with Breast and Ovarian Cancer in Lebanon

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Background: The prevalence of pathogenic BRCA mutations in high hereditary risk breast cancer patients (pts) in ethnic Lebanese Arab women was 5.6% in a study published in 2015 (El Saghir, et al. *The Oncologist*). In this study, we look at real world practice prevalence of BRCA mutations among pts with breast and/or ovarian cancer referred for testing because of positive family history (FH) and/or young age at the American University of Beirut Medical Center (AUBMC)..

Methods: The study was approved by the Institutional Review Board at AUBMC. We retrospectively collected clinical, radiological, pathological and genetic information on breast and ovarian cancer pts at a high hereditary risk for whom Sanger sequencing of all coding exons and immediately flanking intronic regions of BRCA1 and BRCA2 was performed between January 1, 2010 and Jan 1, 2019 at AUBMC. Between Jan 2019 and Aug 2020, Next Generation Sequencing (NGS) of 70 cancer-associated genes was referred to and done in Centogene labs (Germany). 346 subjects were included in the study; 235 pts with breast and/or ovarian cancer, and 101 subjects of young age or with a positive family history.

Results: 210 pts had breast cancer (209 females, 1 male); 81 were diagnosed at age ≤ 40 , 81 aged 41-50, and 48 aged >50 . 185 pts had BRCA sequencing and 25 had NGS panel testing. 31 pts had ovarian cancer; 28 had BRCA testing and 3 had NGS. 3 pts had ovarian and breast cancer; all had Sanger sequencing, 1 male pt with both breast and prostate cancers had BRCA testing. The 101 subjects who were tested in the setting of positive FH of cancers or a known deleterious mutation in first degree family members were either target tested for the known

familial mutation or had BRCA screening.

The incidence of BRCA1 and BRCA2 mutations in women with breast cancer was 8.5% (18/210 patients) and 19.3% (6/31 patients) in women with ovarian cancer. Of the 3 pts who had both breast and ovarian cancer, 1 had a BRCA1 mutation.

Almost all patients with hereditary breast cancer had a positive FH and the majority were < 40 years of age. 8 out of 13 BRCA1 pts had Triple Negative disease (61%). Of the 101 subjects with no history of cancer, 9 out of 30 with relatives who had BRCA1 mutation carried the same mutation, and 3 out of 15 with BRCA2 carried the mutation. The remaining 56 pts were tested because of positive FH; 3 out of 56 had a pathogenic mutation (1 BRCA1, 1 BRCA2 and 1 RAD51D). Of the 28 pts who had NGS panel sequencing, 1 patient had RAD51D, 1 had a PALB2 mutation, 1 had BARD1 and 1 had APC risk variant.

Conclusions: In this real-world practice study of patients and subjects referred for germline mutation testing. BRCA mutation rate in pts with breast cancer was 8.5% (18/210) and 19% in ovarian cancer (6/31). Young age (< 40 years) and a positive FH are the most useful criteria to select pts with breast cancer for mutation testing, especially in the setting of limited resources. This is the first study to report a 20% rate of BRCA pathogenic variants in patients with ovarian cancer in Lebanon and Arab countries; we highlight the need to refer all ovarian cancer pts for counseling and genetic testing. NGS is important to detect mutations other than BRCA1 and BRCA2 in our population where 50% of cases are below age 50.

Table 1. Incidence of BRCA1/2 mutations, age, and family history in pts with breast and ovarian cancer

Cancer	Gene	Deleterious Mutation (%)	Age at diagnosis	Positive FH
Breast Cancer	BRCA1	13/210 pts (6.2%)	≤40: 11/13	12/13
	BRCA2	5/210 (2.4%)	≤40: 3/5	5/5
Ovarian Cancer	BRCA1	4/31 (12.9%)	<50: 2 & >50: 2	4/4
	BRCA2	2/31 (6.4%)	<40: 1 & >50: 1	2/2
Breast and Ovarian Cancer	BRCA1	1 out of 3	45	1/1

Table 1. Incidence of BRCA1/2 mutations, age, and family history in pts with breast and ovarian cancer

Disclosure(s):

Nagi El Saghir, Professor: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pierre Fabre: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g.,

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P6-03-01

The MERIT Cohort: An MD Anderson Initiative to Integrate Blood and Imaging Biomarkers to Personalize Breast Cancer Risk

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Background: The MERIT cohort (Mammography, Early Detection, Risk Assessment, and Imaging Technologies, 2017-present) has enrolled women receiving annual screening mammograms (MG) at MD Anderson with a primary goal to integrate clinical data and imaging data with blood biomarker profiles to determine risk of developing breast and other cancers. Here we report interim results for breast cancers among post-menopausal women in the cohort categorized based on breast density and BMI and differences between participants who underwent MRI/MG screening vs standard annual MG screening.

Methods: The study annually collects comprehensive health measurements, questionnaire information, imaging data, and blood specimens. Plasma is processed and frozen within 4 hours of collection (draw-to-freezer, >500,000 aliquots to date) for biomarker research. Part of the cohort also has MRI screening every 6 months alternating with standard mammography (MRI/MG). BI-RADS breast density was determined by radiologist scoring using the baseline mammogram. Self-reported post-menopausal status (12 months without a menstrual period) was used to classify participants. When not available, those participants older than 50 years were classified as post-menopausal.

Results: 4,392 of the 6,222 eligible subjects from MERIT were post-menopausal and included in the analyses. The average follow up was 2.4 mammograms per participant. MRI/MG screening was used for 385 (8.8%) participants who were more likely to be younger (59.6 vs 62.1 years, $P < 0.01$), have lower BMI (27.9 vs 28.6, $P = 0.02$) and dense breasts (64% vs 50%, $P < 0.01$). The rates of breast cancer were overall higher for those screened by MRI/MG vs standard MG (13.9 vs 6.9 cases per 1,000 mammograms). A total of 79 breast cancers (7.6 cases per 1,000 mammograms) were diagnosed with the highest rate of breast cancers in high BMI participants with dense breasts (see table). A blood-based biomarker profile for risk of breast cancer with high BMI was developed using matched pre-diagnostic plasma by mass spectrometry metabolomic analyses.

Conclusions: The MERIT cohort has a higher-than-average rate of breast cancers, in part explained by a high-risk MRI/MG screening group. High BMI and dense breasts were generally associated with higher rates of breast cancer. The differences in the rates of breast cancer

incidence for the high BMI group between non dense and dense breasts is likely understated for the standard mammogram group because of the lower sensitivity of mammography in dense breasts. Interestingly, the rates of breast cancers in the low BMI/non dense breast group were almost equally high as the low BMI/dense breast group, likely a result of reduced sensitivity of mammography for dense breasts. For future work, we will integrate the blood biomarker profiles with the breast density and BMI information to develop a more personalized risk model.

MERIT Cohort Breast Cancers

Breast Density	Annual MG Screening			MRI/MG Screening			All Post-menopausal
	<25.0 BMI	≥25.0 BMI	All BMI	<25.0 BMI	≥25.0 BMI	All BMI	
Non dense (a,b)	10.8	4.8[‡]	6	16.4	7	8.6	6.2
DCIS	3.2	0.3	0.9	0	0	0	0.8
Invasive BC	7.5	4.5	5.1	16.4	7	8.6	5.4
Dense (c,d)	3.9*	11.7*[‡]	7.8	13.7	19.2	16.7	8.9
DCIS	2.1	3.8	3	6.8	13.7	10.7	3.9
Invasive BC	1.7	7.9	4.9	6.8	5.5	6.1	5
All	5.8	7.5	6.9[†]	14.2	13.8	13.9[†]	7.6

Rates of diagnosed breast cancers per 1,000 mammograms for post-menopausal women (N = 79 breast cancers)*[‡]P<0.01, [†]P<0.05, Fisher's exact test

Disclosure(s):

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P6-03-02

Social determinants, food deserts, and their combined contribution to breast cancer mortality

Presenting Author(s) and Co-Author(s):

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Recent studies have found that both food deserts (FD) and lower socio-economic status (SES) are individually associated with increased breast cancer mortality in the US. However, further work is needed to investigate their combined contribution to breast cancer mortality. Furthermore, valid inference for area-level disease mapping requires careful consideration of spatial clustering. In our study, we utilize data from the USDA Food Access Research Atlas and the American Community Survey. Breast cancer mortality data come from the National Center of Health Statistics 2014 report. We consider a latent class mixture model to determine deprivation categories which incorporate six SES proportion variables (no car, poverty, no HS graduation, crowded housing, unemployment, crowded housing), two FD (Low income and > 1 mile from supermarket and receiving snap benefits and > 1 mile from supermarket) variables. Our latent class model has three levels: Low, Moderate, and High, making up 36.6%, 45.6%, and 17.8% of US counties, respectively. We then incorporated these levels as a fixed effect in a Bayesian hierarchical spatial negative binomial model using R-INLA. In this model, we account for both spatially structured and unstructured effects. Counties classified as “High” on our deprivation categories were associated with a 50% increase in breast cancer mortality rates (95% CrI: [1.12, 2.02]). Also, the county proportion of women >65 was significantly associated with 1.42 times higher breast cancer mortality (95% CrI [1.37, 1.42]). Policies that allow for access in the face of deprivation may contribute to lower overall breast cancer mortality.

Disclosure(s):

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P6-03-03

Persistence and compliance of the French metastatic breast cancer population

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Keywords Metastatic breast cancer, Endocrine therapy, Targeted therapy, Oral chemotherapy, French population
Context Oral anti-cancer treatments have been shown to be effective when followed carefully. Tamoxifen, for example, reduces the risk of relapse by half within 10 years of the diagnosis [1]. However, these treatments are frequently poorly adhered to. To determine the categories of patients at risk and the appropriate moment to contact them, we developed predictive models trained on anonymised reimbursement data extracted from the French Health Insurance database. **Objective** The primary objective is to model a metastatic breast cancer patient's persistence and compliance to the treatment. We aim at detecting unwanted episodes (non persistence and non compliance) six months before they happen. The oncologist may then follow the patient more closely. **Methods** Patients data is extracted from the SNDS database, one of the largest structured databases of health data in the world. It contains reimbursement data of the French Health System, covering 98% of the French population (66 million persons). Useful data are, for example, hospitalisations, drug purchases or the patient's age and city of residence. From this database, patients were selected on the basis of a diagnosis of metastatic breast cancer (if hospital stay) or on the basis of specific treatments for metastatic breast cancer. Men and patients under 18 are excluded from the study. We consider that a patient has a non persistent event if she has no treatment stock for 2 months (during a phase of targeted therapy or oral chemotherapy) or 3 months (during a phase of endocrine therapy) and if no change in treatment, palliative care entry or death is observed. The

compliance is labelled through the MPR (Medical Possession Ratio): a patient is considered non-compliant if the MPR of her 3 nexts purchases is below 80%. The proposed models are trained to detect non-persistence and non-compliance events in the next 180 days. We created several groups of features describing the patient and her healthcare pathway. Results 250 000 patients were spotted with a breast cancer in the SNDS database. Amongst these, around 40 000 were spotted for a metastatic breast cancer between 2013 and 2018. 14% of the patients had at least one non persistence episode and 46% had at least one non compliance episode. For the persistence study, we used a logistic regression with a feature selection. This model has a Gini coefficient of 0.35. For the compliance study, we used a deep learning model based on a GRU model. This model has a Gini coefficient of 0.37. A multivariate analysis shows that the following features had a significative impact on both predicted risks (persistence and compliance) : age, previous compliance, type of oral treatment(s) currently followed (endocrine therapy, targeted therapy, or oral chemotherapy), number of different oral treatments followed in the past year. In both models, if the patient's age is between 50 and 70 years it does not correlate with an increased risk. On the other hand, the more they deviate from this interval, the more likely they are to be non-compliant. Conclusion Both studies have models with quite the same interpretation. Patients younger than 50 or older than 70 are more likely to be non-persistent and non-prevalent. The past compliance is highly correlated to the future events. The consumption of oral chemotherapy in comparison to oral endocrine and targeted therapy is linked to an increased risk in both studies. Bibliographie [1]: E. Ekinci, S. Nathoo, T. Korattiyil et al. (2018) Interventions to improve endocrine therapy adherence in breast cancer survivors: what is the evidence? J Cancer Surviv 12:348-356

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P6-03-04

Ipsilateral infusions are not associated with increased risk of breast cancer-related lymphedema in patients enrolled in a prospective screening program.

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BACKGROUND: Patients treated for breast cancer (BC) who are at risk of breast cancer-related lymphedema (BCRL) have been instructed for decades to avoid venipuncture, injections and infusions in the extremity ipsilateral to BC treatment. These instructions are given in theory to prevent BCRL development, despite lack of supporting data. Given fear of BCRL is high amongst the population at risk, it has been found that patients heed this advice regardless of level of BCRL risk. It has been previously found that there is no association between blood draws or injections in the ipsilateral arm and increases in arm volume in patients treated for BC and screened for BCRL. Despite these findings, risk of BCRL associated with the most invasive of BC treatments, infusions in the ipsilateral arm, has not been examined. As patients with BC

require ongoing invasive medical procedures, data would inform patient care and drive clinical practice guidelines during and after BC treatment. **PURPOSE:** The purpose of this study was to determine whether patients treated for breast cancer who receive one or more infusions in the arm ipsilateral to BC treatment are at higher risk of BCRL than those who do not receive ipsilateral infusions. **METHODS:** From 2005 to 2021, 2049 patients treated for BC were enrolled in a prospective BCRL screening trial and screened from preoperative baseline through last follow-up. Screening included objective arm volume measurements via perometry; relative volume change (RVC) increase $\geq 10\%$ from preoperative baseline >3 months postoperatively was used to define BCRL. Infusions data were collected directly from the electronic medical record and all postoperative infusions were included in data analysis. Patients were censored at cancer recurrence. Infusions data included route, laterality, date and substance infused. Demographic and clinical information were obtained through medical record review. Marginal structural models were used to estimate the hazard of BCRL attributable to any (vs. no) ipsilateral infusion. Time-varying inverse-probability weights were used to account for time-varying confounding by RVC and earlier adjuvant infusions, and adjusted for baseline confounding by baseline BMI, axillary lymph node dissection (ALND), regional lymph node radiation (RLNR), neoadjuvant chemotherapy, and number of neoadjuvant ipsilateral infusions. **RESULTS:** The eligible cohort included 2018 patients. 240 patients received at least one ipsilateral infusion; 651 did not receive ipsilateral infusions; 1,127 did not receive infusions. Patients who received ipsilateral infusions received a median of 2 (interquartile range (IQR) 1, 3) ipsilateral and 8 (IQR 4, 15) total infusions. 681 (34%) patients received adjuvant chemotherapy infusions; the most frequent adjuvant regimens received included ACT (314 patients, 16%); TC (162 patients; 8.0%); and ACTH ($\pm P$) (47 patients, 2.3%). Of those who received any ipsilateral infusions, 77% had chemotherapy drugs infused, compared to 84% of participants who did not have ipsilateral infusions. Fluids, antacids, and antihistamines were the most common non-chemotherapy infusions. Patients underwent BCRL screening over a median of 5 visits (IQR 3,8) with a median follow-up of 56 months (IQR 31, 90 months). There was no significant difference in BCRL risk between patients who received at least one ipsilateral infusion and those who did not receive ipsilateral infusions (HR, 0.85; $p=0.60$). **CONCLUSIONS:** Infusions in the at-risk arm were not associated with increased risk of BCRL in this cohort of 2018 patients at risk of and prospectively screened for BCRL.

Disclosure(s):

Cheryl L. Brunelle, PT, MS, CCS, CLT: PureTech Health: Consulting Fees (e.g., advisory boards) (Ongoing)

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Alphonse G. Taghian, MD PhD FASTRO: ImpediMed: A.G. Taghian was loaned equipment from ImpediMed for use in investigator-initiated clinical trials (Ongoing); PureTech Health: Consulting Fees (e.g., advisory boards) (Ongoing); VisionRT: Consulting Fees (e.g., advisory boards) (Terminated, November 1, 2019)

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P6-03-05

Clinico-pathological co-variates define a predictive model of breast cancer related lymphoedema (BCRL) in patients undergoing axillary surgery for breast cancer

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Clinico-pathological co-variates define a predictive model of breast cancer related lymphoedema (BCRL) in patients undergoing axillary surgery for breast cancer CC Tang^{1*}, J Timbres^{2*}, KWD Ramsey¹, A Mera², S Irshad², E Sawyer², AA Khan¹ ¹ Department of Plastic Surgery, The Royal Marsden Hospital, London, UK ² School of Cancer and Pharmaceutical Sciences, Faculty of Life Sciences and Medicine, Guy's Cancer Centre, King's College London, London, UK. *These authors contributed equally Introduction Breast cancer-related lymphoedema (BCRL) negatively impacts body image, limb function and quality-of-life during cancer survivorship and affects 20% of women undergoing axillary clearance (ALND).¹ Stratifying women undergoing axillary intervention into high- and low-risk groups for BCRL is important to identify those most likely to benefit from surgical interventions for lymphoedema prevention (eg LYMPHA) and mitigate BCRL risk in this subset of patients. In this study, we aimed to identify prognostic factors for lymphoedema incidence to develop a more accurate model of BCRL risk. Methods We performed a retrospective cohort study of breast cancer patients undergoing axillary surgery with (Ly+) and without (Ly-) subsequent lymphoedema. Controls were identified from the Breast Cancer Clinical Database, Guy's and St Thomas' Hospital NHS Foundation Trust (GSTT) and diagnosed between 2000-2016, while cases were

identified from the Lymphoedema Clinic at GSTT, diagnosed between 2000-2020. A multivariate logistic regression model was derived from univariate analyses using a stepwise, iterative process, confirmed with lasso regression, and evaluated within training and validation datasets to define a predictive risk score using methods described by Pavlou et al.² Results 2040 patients (Ly+=541, Ly-=1499) who underwent axillary surgery (ALND = 1171, SLNB = 755) (were included in our analysis with a median follow up of 7.2 years (Ly+) and 9.8 years (Ly-). The final predictive model of BCRL risk contained variables for: mastectomy, grade, T-stage, N-stage, ER status, chemotherapy and radiotherapy. Here, specifically radiotherapy including a supraclavicular fossa field was associated with developing lymphoedema. The Hosmer–Lemeshow goodness-of-fit test showed the model to be well calibrated, and evaluation of the risk score using ROC curves showed good discrimination (AUC: 0.795). Lymphoedema was not found to negatively affect overall (unadjusted HR: 1.19 (95% CI: 0.92-1.53); p=0.178 and adjusted HR: 0.53 (95% CI: 0.38-0.73); p< 0.001) or disease free (unadjusted HR: 2.03 (95% CI: 1.59-2.61); p< 0.001 and adjusted HR: 0.92 (95% CI: 0.68-1.23); p=0.57) survival. Conclusion Our study identified clinico-pathological factors such as mastectomy, grade, T-stage, N-stage, ER status, chemo- and radiotherapy (specifically radiotherapy including a supraclavicular fossa field) to be predictive of developing BCRL following axillary surgery. Our model requires further validation but may have utility in stratifying patients for whom surgical strategies for lymphoedema prevention could be deployed to mitigate BCRL risk. References 1. DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. *Lancet Oncol.* 2013 May;14(6):500-15. doi: 10.1016/S1470-2045(13)70076-7. Epub 2013 Mar 27. PMID: 23540561. 2. Pavlou M, Ambler G, Seaman S R, Guttman O, Elliott P, King M et al. How to develop a more accurate risk prediction model when there are few events *BMJ* 2015; 351 :h3868 doi:10.1136/bmj.h3868

Disclosure(s):

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P6-03-06

Determining prognostic factors and optimal surgical intervention for young patients with triple-negative breast cancer

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Background Triple-negative breast cancer (TNBC) is more frequently diagnosed in young patients, with an incidence of 26% of this population compared to 12% overall, and is characterized by high malignancy and poor prognosis. Limited data are available that contribute to a comprehensive summarization of the prognostic factors and the determination of surgical strategy that are associated with young patients with TNBC. We aimed to determine the optimal surgical approach (breast-conserving versus mastectomy) for patients aged < 40 years with TNBC and establish a prognostic model. Methods We performed a cohort study with a median follow-up of 31 months using the Surveillance, Epidemiology, and End Results (SEER) data of young patients < 40 years diagnosed with stage I–III TNBC between 2010 and 2016. A Cox proportional hazards model was used to investigate the effects of baseline characteristics on breast cancer-specific survival (BCSS) and overall survival (OS). To ensure that differences in outcomes were not based on baseline differences in demographic and clinical characteristics, we performed Kaplan–Meier analysis before and after propensity score matching (1:1). Subgroup analyses stratified by TNM stage as well as further propensity score matching analyses were performed. A nomogram was constructed from the multivariate logistic regression to incorporate all the prognostic factors to predict the BCSS rates of patients at 3 years and 5 years. Young patients < 40 years diagnosed with stage I–III TNBC between 2006 and 2016 in Shenzhen Second People's Hospital (SSPH) were enrolled as external validation. Results A total of 2,854 patients from SEER dataset and 250 from SSPH were included in this study. On multivariable analysis, unmarried status, lack of health insurance, advanced T stage, advanced N stage, invasive lobular carcinoma or mixed histologic type, were all significantly associated with poor BCSS and OS. Young patients with TNBC were more likely to undergo mastectomy than breast-conserving surgery. Notably, patients with T1N0M0 or T2-4N+M0 tumors who underwent breast-conserving surgery achieved longer BCSS and OS than those who underwent mastectomy; however, the type of surgery did not influence survival rates among patients with T1N+M0 or T2-4N0M0 tumors. The nomogram was constructed by the five variables and passed the calibration and validation steps (C-index: 0.774 for training cohort and 0.768 for validation cohort). The area under the receiver operating characteristic curves (AUCs) predicting the 3-year and 5-year BCSS rates were calculated (0.783 and 0.774 in training cohort; 0.786 and 0.772 in validating cohort). Conclusions A localized surgical approach may be a superior option for young patients with TNBC, especially those with T1N0M0 and T2-

4N+M0 tumors. Marital status, health insurance status, T stage, N stage, and histological type were independent prognostic factors, and a nomogram established based on these variables successfully predicted the 3- and 5-year survival probabilities among these patients.

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Yi-Zi Zheng, n/a: No financial relationships to disclose

Yan Liu, n/a: No financial relationships to disclose

Zhen-Han Deng, n/a: No financial relationships to disclose

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P6-03-07

Development of an at-home breast health assessment test, to increase compliance with screening mammography using proteins from tears.

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Anna E. Daily^{1,*}, Prashanth Ravishankar¹, Wanyi Wang³, Ryan Krone³, Steve Harms^{1,2}, and V Suzanne Klimberg^{1,4,5} ¹Namida Lab Inc, Fayetteville, Arkansas; ²The Breast Center-Medical Associates of Northwest Arkansas, Fayetteville, Arkansas; ³Elite Research LLC, Irving, Texas; ⁴Department of Surgery, University of Texas Medical Branch, Galveston, Texas; ⁵Breast Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, Texas. *anna@namidalab.com Background: There is a growing body of evidence to support tears as a non-traditional biological fluid in clinical laboratory testing. In addition to the simplicity of tear fluid processing, the ability to access key cancer biomarkers in high concentrations quickly and inexpensively make them an attractive biofluid source. Here we report our biomarker discovery study on tears to identify and validate candidate biomarkers for breast cancer and develop a model that is significantly associated with a positive breast cancer diagnosis. Methods: Participants were recruited from individuals having a yearly screening mammogram, biopsy, and/or recently diagnosed with breast cancer. Imaging results were obtained from clinical sites and samples were then classified as: control (normal imaging no biopsy) or diagnosed breast cancer pre-treatment (diagnosed by biopsy). Biomarker discovery was conducted using 102 individual tear samples collected using the Schirmer strip collection method. Liquid chromatography/tandem mass spectrometry (LC-MS/MS) was performed to identify protein biomarker candidates with altered expression levels in breast cancer patients. ELISA assay to confirm LC-MS/MS trends for biomarkers of interest was conducted using 171 tear samples. An additional round of validation utilizing 848 samples was performed which included protein concentrations determined by ELISA and collection of demographic and clinical covariates. The resulting concentration data, combined with the demographic and clinical covariates, was analyzed using logistic regression analysis to build a model for classification of samples as positive or negative. Results: A total of 301 proteins were identified by LC-MS/MS and narrowed to a list of 14 proteins (p-value < 0.05) with potential significance in breast cancer patients. Three biomarkers, S100A8 (p-value = 0.0069), S100A9 (p-value = 0.0048), and Galectin-3 binding protein (p-value = 0.01) with an increased expression in breast cancer patients were selected for validation using ELISA. Logistic regression analysis produced three models, which were then evaluated on breast cancer cases and controls at two diagnostic thresholds and resulted in sensitivity ranging from 52% - 90% and specificity from 31% - 79%.

Conclusions: Our results demonstrate clinical feasibility for tear proteins to detect breast cancer and includes the most extensive published data set of individually analyzed tear samples. This analysis suggests that models developed using tear fluid have clinical validity and could be used in further development of a biological assay. We envision positioning this assay as a tool for activation around breast health screening for low to average risk patients who may be screening avoidant or adverse to encourage participation in screening mammography.

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Anna Daily, PhD: Namida Lab, Inc: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

Prashanth Ravishankar, PhD: Namida Lab Inc: I am an employee of Namida Lab Inc and work as a Research and Development Scientist. (Ongoing), Salary (Ongoing)

Victoria S. Klimberg, MD, PhD, MSHCT, MAMSE, FACS: Namida Lab, Inc.: Consulting Fees (e.g., advisory boards) (Ongoing)

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P6-03-08

Trained Artificial Intelligence (AI) for Predicting Treatment Termination Based on Patient Observations in Advanced Breast Cancer

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Background: In various fields outside of medicine, AI-supported systems have been established that can predict an undesirable event. The purpose of such systems is to detect events earlier and, if necessary, to be able to prevent them. In medicine, it would be particularly interesting to be able to make such predictions based solely on patient observations. Methods: The usage from 323 patients with advanced breast cancer with a total of 78542 documentation days was used. In addition, the premature termination of use was defined as an undesirable event. The data was then processed and annotated. A deep-learning neural network (NN) classifier was trained on this dataset independently on all documented days to predict this target endpoint. The patient classifier score was computed by averaging over daily scores. Overall classifier accuracy and binary cross entropy loss were computed as performance indicators on training and test data sets (2:1 split). Results: After tuning the hyperparameters, the best-performing NN comprised three hidden layers, each with 88 neurons, using ReLU (linear ramp) activation, and an output layer using sigmoid activation. In the test collective, this model achieved a prediction accuracy of 87%. Discussion: The present application shows for the first time that treatment discontinuation can be predicted with a very high degree of accuracy using patient data alone. This opens up new possibilities in the early detection of possible therapy failures and can represent an essential auxiliary tool in medical care in the future.

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P6-04-02

Ki67 Assessment Protocol: Companion Diagnostic Biomarker for LUMINA Prospective Cohort Study

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Introduction: Luminal A breast cancer is associated with low proliferation, indolent disease biology and limited benefit from chemotherapy. The LUMINA prospective study recently demonstrated a very low 5 year local recurrence rate (2.3%) in women ≥ 55 years with grade I-II, T1N0 luminal A breast cancer (defined as ER $\geq 1\%$, PR $> 20\%$, HER2 negative and Ki67 index $\leq 13.25\%$) treated with breast conservation surgery and endocrine therapy without radiation, supporting the safe omission of radiation in this molecularly defined low risk group. Here, we report the protocol for multicentre Ki67 scoring, the embedded integral companion diagnostic employed in LUMINA. Methodology: Ki67 immunohistochemistry was performed on full-face sections at one of the 3 labs and scored by pathologists using an adaptation of the International Ki67 Working Group (IKWG) method. Prior to the start of the study, quality assurance and quality control programs were set up to standardize staining and scoring protocols. All pathologists completed the IKWG training and calibration exercise using a tissue microarray-based series of 18 breast cancers. Inter-laboratory variability was assessed annually during the study period on a set of 9 breast cancer cases with a range of Ki67 scores that purposely over-represented the 13.25% threshold. Stained slides were scanned and images annotated to demarcate invasive carcinoma. Next, 5 random, non-overlapping, 1 mm virtual cores were generated via software and 100 nuclei assessed per core using a keyboard-based counting aid. Ki67 index was derived as the percentage of all counted tumor nuclei that

are positively stained. For cases with high Ki67 heterogeneity, additional virtual cores were generated and scored and a 95% confidence interval (CI) of Ki67 index was estimated. The goal was to confidently assign a case as luminal A ($\leq 13.25\%$) or B ($> 13.5\%$). If the 95% CI crossed 13.25% a recount was performed by an additional pathologist. Results: Quality Assurance Programs: Mean Ki67 index across all cases, labs and years was 13% with high concordance across specimens and score ranges. Observed intra-class correlation coefficients (ICC) were ≥ 0.9 , showing near perfect agreement in quantitative Ki67 evaluation. About the 13.25% cutpoint, the observed Kappa statistics were ≥ 0.7 indicating excellent agreement for assignment of luminal A vs. B status. A sub-study was conducted to compare the method of randomly selected virtual fields with the IKWG 'global weighted score' method for visual assessment of full-face sections. For this purpose, the 9 quality control cases were reassessed by the same pathologist using the updated IKWG method. Results showed an ICC of 0.96 (0.95% CI: 0.91-0.98) indicating that the Ki67 score generated by the methodology employed in LUMINA trial is highly concordant with the IKWG scoring methodology validated for use on full face sections. Ki67 index summary statistics across LUMINA: Of the 724 eligible cases, 69% (n=500) were assigned as luminal A (median Ki67=7.5%; IQR 5.2-9.8%) and 31% (n=224) as luminal B (median Ki67=19%; IQR 17-23%). Median pathologist scoring time was 4 minutes / case; 45% of cases required scoring of > 5 virtual cores. Per protocol, 39% cases where the initial CI crossed 13.25% were rescored by additional pathologist for final luminal A consensus assignment. Conclusions: Ki67 is a practical biomarker for identifying molecularly defined low-risk luminal A cancers. Our structured quality assurance approach for the trial led to excellent reproducibility and concordance among decentralized labs, supporting applicability of a distributed, inexpensive methodology beyond clinical trial settings and in resource restricted environments.

Disclosure(s):

Torsten Nielson, MD, PhD, FRCPC: Bioclassifier LLC: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Veracyte: Royalty (Ongoing)

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Computational pathology based HER2 expression quantification in HER2-low breast cancer

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Background HER2 directed therapies for breast cancer (BC) rely on accurate estimation of HER2 expression by pathologist scoring of immunohistochemically (IHC) stained tissue according to ASCO/CAP guidelines. Emerging HER2-targeted antibody drug conjugates (ADCs) like trastuzumab deruxtecan (T-DXd), have demonstrated efficacy in the HER2-low (IHC 1+ or IHC 2+/ISH-) population (Modi, NEJM 2022). A deeper understanding of the spectrum of HER2 expression and its spatial distribution could provide insights about the mode of action of ADCs, including potential bystander activity. Computational pathology-based methods like Quantitative Continuous Scoring (QCS) can help here by objectively quantifying HER2 expression levels on a per cell basis from digitized HER2 IHC slides (Gustavson, SABCS 2020). We applied QCS to a cohort of HER2-negative (HER2-neg) patients (pts) from a retrospective study (NCT04807595) to quantify the prevalence of HER2 expression in this population and investigate the relationship with manual scoring. Methods To analyze the prevalence of HER2 expression in the HER2-neg population, we used available digital images (N=207 pts) from retrospectively rescored HER2 slides from tumors categorized as HER2-low or IHC 0 (IHC 0 or >0 < 1+). QCS algorithm was applied to perform an instance segmentation of each tumor cell into the membrane, cytoplasmic and nuclear sub-compartments. HER2 expression levels on the membrane were estimated from a Hue-Saturation-Density model (Van der Laak, JQCS 2000) in terms of optical density (OD). Descriptive statistics and spatial modelling were used to aggregate cell-level information to a slide level score using the membrane OD values and tumor cell locations. A novel Spatial Proximity Score (SPS) was used to mathematically model the proportion of tumor cells that could potentially be targeted either directly or via bystander activity of ADCs. The analysis is ongoing, complete results with additional patient data to be presented. Analytical validation of the QCS algorithm demonstrated high correlation between OD values as measured on the automatically detected membranes from QCS and those measured on consolidated manual membrane annotations (N=2157 cells) from three pathologists (R = 0.993). This is very similar to the correlation observed between individual pathologists (R = 0.995). Results In the analyzed cohort (N=207), median OD of HER2-low tumors was significantly higher compared to IHC 0 tumors (one-sided Wilcoxon p-value < 0.001). A significant increase of OD values was observed for increasing IHC categories from 0 through >0 < 1+ and 1+ to 2+/ISH- (one-sided Jonckheere-Terpstra p-value < 0.001). OD values within each IHC category showed considerable variability, particularly in IHC 1+ and IHC 2+. In 49% of pts (N=101), greater than 88% of tumor cells expressed HER2 at any intensity (OD \geq 10). Among the remaining 106 pts, the number of potentially ADC-susceptible cells (within 25 μ m radius of HER2 expressing cells) as estimated by SPS was at least double the amount estimated by single cell-based scores alone in 45 cases (42%) and increased by at least 50% in another 12 cases (11%). Conclusions Computational approaches such as QCS can help us to objectively characterize the spectrum and spatial distribution of HER2 expression. These mathematical models contribute to our understanding of potential mechanisms of action of ADCs. While this study confirmed a general association of QCS-based scores with manual IHC categories, we also saw considerable variation, as some IHC 1+ or 2+ samples had low OD. Building on these and other promising initial results (Gustavson et al, SABCS 2020), we will further explore clinical relevance of QCS-based scoring. Eventually, digital scoring may be able to define data-driven signatures to select HER2-low pts that might benefit from HER2 targeted therapies.

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12/9/2022

7:00 AM - 8:15 AM

P6-04-04

Clinical Relevance of PD-L1 and CD8 Expression in Triple Negative Breast Cancer

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Background: Immune checkpoint inhibitors such as PD-L1 are promising therapy targets in triple negative breast cancer (TNBC). In the present study, we examined the clinical relevance of PD-L1 and CD8 expression in TNBC patients treated with adjuvant chemotherapy. Methods: FFPE tumor material from 118 patients with early TNBC treated between 1999 and 2012 was included in our analysis. Immunohistochemical (IHC) expression of PD-L1 was determined by immune score using the diagnostic antibody SP142 (Ventana). CD8 IHC was performed using the SP57 antibody (Ventana). Follow-up data were available for all 118 patients with a median follow up time of 19.4 years. Biomarkers were examined as continuous or categorical variable (predefined cutoffs). Invasive disease-free survival (IDFS) and overall survival (OS) were analyzed using Cox regression models. Results: The median PD-L1 immune score was 1% and PD-L1 expression was classified as positive in 79/116 (68.1%, cutoff $\geq 1\%$) cases. Median CD8 expression was 10% and was scored as positive in 51/115 (44.3%, cutoff $> 10\%$) samples. Significant associations were observed between PD-L1 expression and tumor grade, Ki67, and CD8 expression. PD-L1-positive tumors were more frequently in the G3 group ($p=0.006$) and had higher Ki67 ($p < 0.001$) and higher CD8 expression ($p < 0.001$). PD-L1 but not CD8 expression was associated with IDFS or OS. Univariate Cox regression analyses showed that PD-L1-negative patients had a shorter IDFS (HR 0.52, 95%CI 0.30-0.89, $p=0.02$) and showed a trend towards shorter OS (HR 0.56, 95%CI 0.30-1.03, $p=0.06$). CD8 expression was neither associated with IDFS (HR 0.74, 95%CI 0.43-1.27, $p=0.27$) nor with OS (HR 0.87, 95%CI 0.48-

1.60, $p=0.66$). In multivariate analyses, PD-L1 expression was an independent prognostic factor for IDFS (HR 0.51, 95%CI 0.29-0.88, $p=0.016$) but not for OS (HR 0.53, 95%CI 0.28-1.01, $p=0.052$). Conclusions: Our results suggest that PD-L1 but not CD8 expression assessed by IHC predicted outcome in TNBC. Further analysis of larger, suitable patient cohorts is warranted to further assess the prognostic and predictive value of PD-L1 expression.

Disclosure(s):

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7:00 AM - 8:15 AM

P6-04-05

A fully automatic artificial intelligence system for accurate and reproducible HER2 IHC scoring in breast cancer

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Objective: Tumor HER2 expression is a key prognostic and treatment influencing factor in breast cancer. As with all immunohistochemistry (IHC) staining, visual interpretation of HER2 expression is subjective, which leads to intra- and inter-pathologist variability. Recent findings on the efficacy of HER2-targeted therapy on HER2-low patients raise the need for accurate and reproducible scoring. We developed a fully automated, artificial intelligence (AI) -based algorithm for HER2 scoring. The algorithm was based on ASCO/CAP 2018 guidelines and validated against rigorous ground truth (GT) established by multiple blinded expert pathologists. Methods: Algorithm development: We developed a solution that employs two steps: The first step consists of an ensemble of Deep Learning networks that process tissue regions and classify them as various tissue classes: Invasive cancer, Ductal Carcinoma In Situ (DCIS) and other morphologies. These networks were trained on slides that were automatically labeled by a separate AI system that analyzed the corresponding H&E slides and projected its findings to the HER2 IHC slides using a registration algorithm. To further enrich the training set, especially with rare and difficult cases, a team of 8 expert pathologists manually marked tissue areas and assigned them to one of the tissue classes. In total, the training set consisted of 6,400 manual annotations and 1,300 automatically-annotated slides, both collected from 9 laboratories and

scanned using 3 different scanners. The second step is an ensemble of Object Detection networks that process only the regions classified as invasive cancer, detect the tumor cells within them, and classify their staining pattern (e.g., Not stained, Moderate incomplete, etc.). Finally, the detected cells are counted, and the ASCO/CAP guidelines are applied to derive the slide-level HER2 score. Validation: The validation set was comprised of 453 HER2 slides stained using the VENTANA anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody as per manufacturer's instructions. HER2 slides included biopsies and excisions with different breast cancer diagnoses (e.g., Infiltrating Ductal Carcinoma (IDC), Infiltrating Lobular Carcinoma (ILC), rare invasive subtypes, with and without DCIS) from 3 different laboratories. Ground truth was established by the consensus scores of a panel of 3 pathologists, who scored HER2 according to the guidelines without additional clinical considerations, such as scoring borderline 1+/2+ cases as 2+ to have additional tests performed. Results: The algorithm showed very high performance for detecting invasive cancer in HER2 tissue sections, with AUC of 0.967 (measured on 4-fold Cross-Validation classifying invasive vs. other regional classes). The algorithm demonstrated an overall accuracy of 80.3% for the HER2 scores when compared to the GT. When using different cutoffs for binary classification the resulting performance was: for 0 vs 1+/2+/3+ Kappa was 0.800; 0/1+ vs 2+/3+ Kappa was 0.728 ; for 0/1+/2+ vs 3+ Kappa was 0.954. The Quadratic Kappa between the AI score and the GT was 0.898, which is considered almost perfect. The performance of the AI was similar across the different laboratories and diagnoses(e.g. IDC, ILC). Conclusion: This study reports the successful development and independent validation of a fully automatic AI-based solution for accurate HER2 scoring in breast cancer. AI solutions, such as the one reported here, could be used as decision-support tools for pathologists in routine clinical practice, enhancing the reproducibility and consistency of HER2 scoring, thus enabling optimal treatment pathways and better patient outcomes. Accurate and automatic IHC scoring solutions can also contribute to the development of new prognostic, predictive and companion diagnostic tools.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-04-07

Primary Diagnosis of Breast Biopsies supported by AI versus Microscope: Multi-Site Clinical Reader Study

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Objective This study aimed to clinically validate the use of an AI-based solution by pathologists for the primary diagnosis of breast core needle biopsies as compared with the gold standard practice (review on the microscope). **Methods** A two-arm prospective reader study comparing the performance of pathologists using an AI-based solution with pathologists using a microscope was performed at two sites (different staining and digital scanners). Both arms were compared to ground truth (GT) established by the consensus of two breast pathologists. Rates of major discrepancies between each arm and GT, as determined by an adjudicating pathologist, were compared. **Results** Eight pathologists participated in the study and reported on 385 cases (442 HES and 330 H&E slides), each case being reported twice, once in each study arm. Pathologists first reviewed only H&E/HES slides, if requested and available, they were provided with IHCs, while the AI results were on H&E/HES only. The major discrepancy rates of the microscope arm and of the AI arm against GT were 4.42% and 3.12%, respectively, demonstrating a 29.4% reduction in major discrepancies. Pathologists with AI demonstrated very high accuracy for the detection of invasive carcinoma with sensitivity and specificity of 100% for both, as well as for DCIS/ADH with sensitivity of 92.4% and specificity of 97.8%. **Conclusions** This multi-site reader study reports diagnostic accuracy improvements by pathologists performing diagnosis and reporting with the support of a first read AI solution for

breast biopsies. The AI solution performed accurately and generalized well for different staining platforms and different scanners. Thus, AI solutions could be used as significant aiding tools for pathologists in clinical decision-making in routine pathology practice, enhancing the quality and reproducibility of diagnosis.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-04-08

Machine learning-based characterization of the breast cancer tumor microenvironment for assessment of neoadjuvant-treatment response

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Background:

Neoadjuvant treatment of breast cancer has been shown to potentially reduce the extent and morbidity of subsequent surgery. Response to neoadjuvant therapy may also be prognostic; complete pathologic response (pCR) following neoadjuvant treatment is associated with improved long-term outcomes. pCR, defined as the absence of residual invasive cancer, is determined by evaluation of H&E-stained breast resections and regional lymph nodes following neoadjuvant treatment; however, pathologist assessment is subject to intra- and inter-reader variability. Here we report machine learning (ML)-based models to identify tissue regions and cell types in the tumor microenvironment (TME) of H&E-stained breast cancer specimens. Model predictions were used to derive tumor bed area, a key component of the residual cancer burden score (RCB) used to assess neoadjuvant-treatment pathological response.

Methods:

Convolutional neural network (CNN) models were trained using digitized H&E-stained whole slide images (WSIs) of 2700 neoadjuvant-treated breast cancer specimens (resections and biopsies) from 4 sources, and an additional 1100 breast cancer primary resections from TCGA. 229,901 pathologist annotations were used to train CNN models to segment tissue regions (cancer epithelium, stroma, diffuse inflammatory infiltrate, ductal carcinoma in situ, lymph nodes and necrosis) and cell types (cancer epithelial cells, fibroblasts, lymphocytes, macrophages, foamy macrophages and plasma cells) at single-pixel resolution. These tissue region segmentations were then used to derive tumor bed area using a convex hull algorithm. Each model was evaluated by board certified pathologists for performance. Model predictions of tumor bed area were evaluated in comparison to mean measurements from 3 pathologists for each of 22 held-out test slides. To further assess cell model performance, 5 pathologists exhaustively annotated 120 frames (300 x 300 pixels) on test samples from a dataset not used in model development (N=536; resections and biopsies) to produce consensus ground truth cell labels. Model predictions were compared with pathologist annotations in these frames using Pearson correlation, precision, recall, and F1 metrics. Only those classes with greater than 50 consensus cells identified were evaluated.

Results:

CNN predictions of tissue and cell classes within H&E breast cancer WSIs showed concordance with manual pathologist consensus labels. The weighted average Pearson correlation (across the relevant cell types) between the model and consensus was 0.75, comparable to the correlation of 0.81 between pathologists and consensus. Classification metrics for each cell class are reported in Table 1. Reduced performance of the model relative to the average pathologist performance may be due to heterogeneous slide characteristics and

infrequency of some cell types in the data. For prediction of tumor bed area, CNN model predictions showed moderate correlation with pathologist consensus (Pearson $r=0.65$, 95% CI: 0.38-0.81).

Conclusions:

CNN model classification of cell types and tissue regions across entire H&E breast cancer WSIs shows concordance with pathologist consensus. Model predictions of tumor bed area also show concordance with pathologist assessment and can be used to derive the RCB score. These models can be reproducibly applied to quantify diverse histological features in large datasets, potentially enabling improved standardization and efficiency of pathologist evaluation of the breast cancer TME and neoadjuvant response.

Classification Metrics for Individual Cell Classes

Cell Class	Precision (Model)	Precision (Pathologists)	Recall (Model)	Recall (Pathologists)	F1 (Model)	F1 (Pathologists)	Cell Count
Cancer Epithelial Cell	0.438	0.613	0.598	0.587	0.506	0.6	589
Fibroblast	0.446	0.485	0.644	0.35	0.527	0.407	463
Plasma Cell	0.303	0.656	0.759	0.496	0.433	0.566	79
Lymphocyte	0.707	0.721	0.848	0.553	0.771	0.626	1364

Disclosure(s):

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7:00 AM - 8:15 AM

P6-04-09

Variations in diagnostic practice of Ki67 scoring suggest standard guidelines needed for pathological assessment: survey results of global Ki67 testing methods

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BACKGROUND The cell proliferation biomarker Ki67 is expressed during every phase of the cell cycle and has long been used as a diagnostic tool for cancer prognosis, especially for hormone receptor positive breast cancer (HR+ BC). More recently, Ki67 has emerged as a companion diagnostic to select patients for the medicines targeting high risk HR+ BC. We report survey results of local Ki67 immunohistochemistry (IHC) testing practices across 99 pathology labs in 11 countries supporting clinical trial sites in 2020-2021 for the coopERA Breast Cancer clinical study in neoadjuvant HR+ BC (NCT04436744). **METHODS** The survey was disseminated to pathology labs across five continents to assess local Ki67 IHC staining, analysis, and scoring methodologies. Metrics included pre-analytical considerations (e.g. sample type and requirements) and analytical considerations (e.g. test validation status, antibody, scoring methods, reporting). **RESULTS** All pathology labs reported requiring formalin-fixed, paraffin-embedded (FFPE) tissue for local Ki67 testing with 89% using sections with thickness of 2-5 microns. For the Ki67 test, the majority (65%) reported using an in vitro diagnostic assay, 23% used a validated test, and 8% utilized a research-use-only assay. Ki67 antibody selection varied among the labs with 46% using the MIB-1 mouse monoclonal (Dako Agilent), followed by 33% using the 30-9 rabbit monoclonal (Ventana) and 12% reporting the SP6 rabbit monoclonal (Thermo Fisher). A majority (65%) reported using single pathologist visual assessment for scoring, and 17% reported using two or more pathologists. Use of automated digital image analysis (ADIA) was reported by 18% of labs, either alone or in combination with pathologist visual assessment. A significant portion (75%) reported using the International Ki67 in Breast Cancer Working Group (IKWG) recommendations, whereas 7%

reported using only digital image analysis (e.g. Ventana Virtuoso). A minority (7%) indicated neither and instead described variations of “eyeball” or “hot spot” visual estimates. Most labs (65%) reported counting at least 500 cells with 15% of these counting more than 1000 cells. Remaining labs (30%) counted less than 500 or no cells. Predominantly, 85% reported counting cells in at least 3 or more high power fields. Most labs (96%) report Ki67 scores as a percentage of positive nuclei and the remaining minority reported using other methods (e.g. ranges [$< 10\%$, $10\text{-}20\%$, etc.] or H-score [0-300]).

CONCLUSIONS The survey results suggest high global variability of local Ki67 testing practices with the highest variability observed in the test validation status, Ki67 clone, and scoring methods. Despite efforts by the IKWG to harmonize and increase the clinical validity of Ki67 as a biomarker, many labs indicating IKWG compliance had survey answers that were discordant with the specific guidelines set forth by the working group. Taking into account the totality of all answers provided by each respondent, only 51% of the surveyed labs fully conformed to the IKWG recommendations. Moreover, a small fraction conducts global estimations without specific cell counting or use “hot spot” scoring methods, despite the high variability and low reproducibility of these scores both intra- and inter-lab. This study demonstrates the benefits of using a central assay in clinical studies to reduce the variability of local Ki67 results in identifying high risk HR+ BC patients and suggests more work is needed to streamline the analytical practices of local Ki67 methodologies, which may directly impact clinical decisions such as the use of neoadjuvant therapies in HR+ BC.

Disclosure(s):

Heather M. Moore, PhD: Genentech, Inc.: Salary (Ongoing); Pfizer: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing); Roche: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

Wendy W. Lin, Ph.D.: Amgen: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing); Genentech: Salary (Terminated, June 11, 2021); Roche: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Terminated, June 11, 2021)

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12/9/2022

7:00 AM - 8:15 AM

P6-04-10

Recurrence Prediction in Ductal Carcinoma In Situ (DCIS) Patients from Tissue Microarrays (TMAs)

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Recurrence Prediction in Ductal Carcinoma In Situ (DCIS) Patients Using Generative Adversarial Network (GAN) Augmented Deep Learning Model Background: DCIS patients have an excellent overall survival rate and over-treatment is always a cause for concern due to potential side-effects. Standard clinicopathological factors (age, growth pattern, tumor size, margin status and grade) have been shown to have limited value in predicting recurrence and segregation of high and low risk patients. Early and accurate recurrence prediction would facilitate a more aggressive treatment policy for high-risk patients (mastectomy or adjuvant radiation therapy), and simultaneously reduce over-treatment of low-risk patients. In this work, we have developed a deep learning (DL) classification framework that predicts recurrence in DCIS patients from Tissue microarrays (TMAs) hematoxylin and eosin (H&E) images using a generative adversarial network (GAN) augmented deep learning (DL) classification model. A GAN is a class of DL models, in which two adversarial neural networks, generator and discriminator contest among each other to generate high quality images. During the adversarial training process, the generator learns to synthesize realistic images similar to those in the training set while the discriminator learns to distinguish between real and generated images. In recent years, high quality medical images have been generated by GAN models. To the best of our knowledge, this is the first time a GAN model has been used to generate H&E images to

train a DL classification model to predict recurrence in DCIS patients. Materials and methods: The cohort was comprised of 68 DCIS patients, aged between 35-89 years, lesion size of 5-90 mm, with a mix of low (15%), intermediate (35%) and 50% high grade cases. Patients were treated with mastectomy and/or a combination of lumpectomy, radiation and hormone therapy. TMAs were constructed from 2mm cores (1-3 cores per patient) in consultation with a breast pathologist to create hematoxylin and eosin (H&E) images for further analysis. The cohort was split into independent training (n=50 patients, 10 with recurrences at 5years) and validation groups (n=18 patients, 6 with recurrences at 5years). TMA (H&E) images were divided into smaller image patches of size 256x256 to train a GAN to generate image patches. A DL classification network (Resnet-Inception v2) was trained using TMA image patches and aggressive image patches generated by GAN to predict recurrence. The ability to generate synthetic image patches of aggressive lesions permitted training of a large DL classification network and predict recurrence in DCIS patients. Importantly, manual annotation was not necessary for the process. Results: The DL classification model trained with both TMA and GAN generated image patches predicted recurrence with an AUC of 0.87, sensitivity of 0.83 and specificity of 0.91 in the validation dataset. The DL classification model trained with image patches from TMAs only predicted recurrence with an AUC of 0.81. Conclusions: The use of a GAN model to generate H&E images circumvents the needs for a large cohort and accurate labor-intensive manual annotation of histopathological images, which is often required for training a large DL classification model. The use of GAN generated aggressive image patches during training significantly improves recurrence prediction accuracy of the DL classification model. Validation in independent larger cohorts is ongoing, and if successful, could provide a novel assay for risk prediction that does not waste precious tissue samples.

Disclosure(s):

Ghose Soumya, PhD: General Electric: Receipt of Intellectual Property Rights / Patent Holder (Ongoing), Salary (Ongoing)

Yesim Gokmen-Polar, PhD: Indiana/Emory University: Receipt of Intellectual Property Rights / Patent Holder (Ongoing)

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12/9/2022

7:00 AM - 8:15 AM

P6-04-11

Improved quantitative fibrosis indices reveal diverse survivals of triple negative breast cancer patients

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Background: The ability of cancer cells to metastasise influences the mortality rate of patients with cancer. Extracellular matrix (ECM) from stromal organization is associated with tumorigenesis and metastasis in breast cancer. It is proposed that morphological features of collagen, based on second harmonic generation (SHG) microscopy, within the tumour environment can be a quantitative image-based biomarker for to predict the survival rate of triple-negative breast cancer (TNBC) patients. To this, we have developed quantitative fibrosis indices by combining multiple collagen features in breast tumour to reveal the diverse survivals of TNBC patients.

Method: The patients (n = 216) in this study were diagnosed with TNBC in Singapore from 2003 to 2015. Disease-free survival (DFS) and overall survival (OS) were defined as time from the point of diagnosis to recurrence or to death/the date of the last follow-up, respectively. The constructed tissue microarrays (TMA) of breast tumours were scanned by the SHG microscope (Genesis, HistoIndex Pte. Ltd., Singapore). 33 collagen parameters were quantified from each sample. These collagen parameters were used to build disease free survival (DFS) index, overall survival (OS) index for prediction of early recurrence (DFS < 1 year) and early death (OS < 4 years), respectively. Kaplan-Meier survival analysis was further performed to assess long-term survival of TNBC patients with high and low risk as stratified by the indices, tumour grade and tumour size. The indices were validated using leave-one-out method.

Results: Both DFS-index and OS-index were created using 10 collagen parameters chosen by sequential selection methods. Due to insufficient follow-up time, 12 patients and 81 patients were excluded from the early recurrence analysis and early death analysis, respectively. The DFS-index could differentiate low-risk patients with DFS ≥ 1 year (n=179) and high-risk patients with DFS < 1 year (n=25) (training p < 0.001; validation p=0.157) with a cut-off value DFS-index=0.880. The OS-index could differentiate the low-risk patients with OS ≥ 4 years (n=101) and high-risk patients with OS < 4 years (n=34) (training p < 0.001; validation p=0.011) with a cut-off value OS-index=0.703. The log-rank test showed DFS-index (training p = 0.001; validation p=0.025) and OS-index (training p < 0.001; validation p=0.011) could be used for the prediction of disease-free survival and overall survival. Kaplan-Meier survival analysis revealed tumour size >20mm (DFS, p=0.605; OS, p=0.136) and tumour grade=3 (DFS, p=0.328; OS, p=0.768) had poor predictive value in this study.

Conclusion: Quantitative assessment of fibrosis in breast cancer correlates with long-term survival of TNBC patients. This study used DFS-index and OS-index combined complex morphological collagen features and obtained better prediction results than tumour size and tumour grade.

Table: The difference between low and high risk groups differentiated by developed indices, tumour size and tumour grade. Low-risk group has a longer DFS and OS months based on DFS-index and OS-index.

		Low-risk group		High-risk group		Log-rank test
		Patient number	DFS/OS months Mean (std)	Patient number	DFS/OS months Mean (std)	
DFS-index	Training	79	68.1(45.8)	125	52.5(43.4)	p=0.005
	Validation	78	64.6(47.0)	126	54.7(43.2)	p=0.049
OS-index	Training	79	94.3(40.0)	56	64.3(46.0)	P=0.001
	Validation	81	88.9(41.3)	54	71.4(48.4)	p=0.011
Tumour size	DFS	55	52.0(43.1)	159	56.7(46.0)	p=0.605
	OS	54	57.8(42.1)	159	62.2(46.1)	p=0.136
Tumour grade	DFS	38	51.3(42.5)	179	56.2(45.9)	p=0.328
	OS	38	55.7(43.9)	178	62.0(45.4)	p=0.768

Disclosure(s):

Yayun Ren, n/a: HistoIndex Pte Ltd, Singapore: Salary (Ongoing)

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12/9/2022

7:00 AM - 8:15 AM

P6-04-12

Differential diagnoses of breast biopsies by spatial parametric modeling of histological structures and explainable AI

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Background: Pathologists typically diagnose the breast tissue slides under a microscope by examining: (i) lumen and ductal morphology, (ii) nuclei size, shape, and spatial arrangement and their combinations, (iii) intraductal architecture, and (iv) textural properties. These features may be subtle and can overlap between diagnoses which contribute to inter- and intra-observer variability. We aim to mitigate this arbitrary nature of breast diagnoses with an exemplar-driven precision pathology pipeline based on spatial parametric modeling of histological structures.

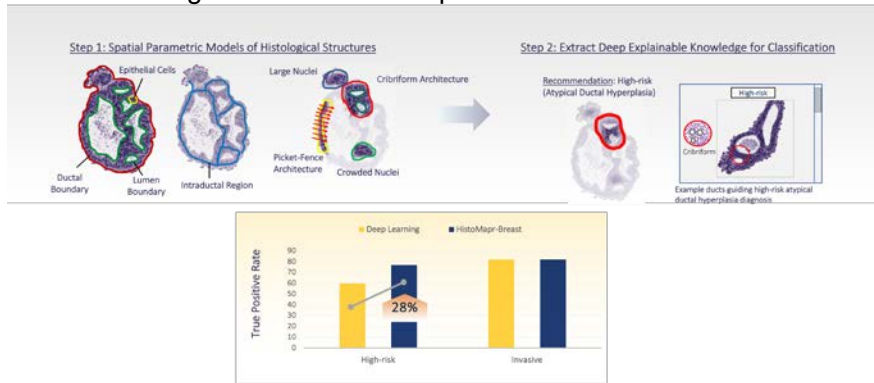
Methods: For our study, we consider a broad spectrum of breast biopsies including: (i) invasive breast cancer, (ii) three high-risk benign lesions: ductal carcinoma in-situ, atypical ductal hyperplasia (ADH), flat epithelial atypia (FEA), and (iii) three low-risk benign lesions: usual ductal hyperplasia, columnar cell change and Normal; where the risk is indicated by the relative chance of developing breast cancer. We build spatial parametric models for a dictionary of histological structures that pathologists frequently use (also documented in the standard reference book from WHO on the classification of tumors) in making complex diagnostic decisions. These models enable our precision pathology pipeline to simultaneously identify distinct exemplar images to account for inter-class heterogeneity, and learn the relative importance of lumen/ductal morphology (LD), intraductal structures including nuclei morphology and spatial arrangements (ID) and textural features (T) from automatically identified exemplar images in assigning diagnostic labels. In doing so, we assert that the assignment of relative importances to LD, ID, and T features is driven by similar looking ducts ('exemplars') which were previously encountered during pathology training or clinical practice.

Results: We evaluated the inferential power of our exemplar-driven precision pathology pipeline on two separate breast core biopsy image datasets, i) dataset containing 4539 regions of interest (ROIs) images extracted from 387 whole slide images (WSIs, 40x), and ii) dataset containing 1237 ROI images extracted from 93 WSIs (20x). Our precision pathology pipeline shows significant improvement (~20%) in the overall classification performance compared to state-of-the-art black box deep learning methods (e.g., graphical neural networks) on both datasets. In particular, while our performance in detecting invasive lesions is comparable to baseline methods, we show a significant improvement ($p < 0.01$) in detecting diagnostically important high-risk ADH and FEA ROIs compared to the baseline methods, where inter- and intra-observer variability is a problem.

Conclusions: A key highlight of our method is in its ability to provide pathologist friendly diagnostic explanations without largely compromising on the classification performance. The strategy outlined in this work can be generalized to other tissue histologies from other organs as defined in the WHO Classification of Tumors books. Further, our approach can facilitate a

communication platform between pathologists and computational scientists to interact and develop AI-driven algorithmic tools that can enhance patient care in a clinical setting. Our framework provides pathologist-friendly explanations paving the way for better, transparent, and trustworthy diagnostic tools.

Differential diagnoses of breast biopsies



The precision pathology pipeline optimizes the identification of a broad spectrum of breast biopsies (invasive, DCIS, benign), including difficult borderline cases (e.g., ADH, FEA, etc.). It provides pathologist-friendly explanations integrated into a clinical workflow for better, transparent, and trustworthy diagnostic aid. This approach addresses the limitations of standard black-box AI in building trust with pathologists.

Disclosure(s):

Akif Burak Tosun, PhD: SplIntellx, Inc.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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7:00 AM - 8:15 AM

P6-04-13

Centralized adequacy assessment of ductal carcinoma in situ samples for the COMET study (AFT-25)

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Introduction COMET (Comparing an Operation to Monitoring, with or without Endocrine Therapy) is a phase III clinical trial randomizing patients diagnosed with low-intermediate grade DCIS to either active monitoring or surgery. The study has a planned accrual goal of 1200 patients and is enrolling until 12/31/22. The protocol requires agreement between two pathologists (who do not need to be at the same institution) that a case fulfills COMET eligibility criteria. If there is disagreement, a third pathology review is required. As per protocol, tissue blocks or unstained slides of biopsies containing DCIS from enrolled patients are sent to a designated central location. While central pathology review is not a pre-requisite of the study, a retrospective review of received materials was performed to determine adequacy for correlative molecular and spatial profiling studies. Methods Sites submit either a tissue block or twenty (20) sequentially numbered, unstained, serial five-micron tissue sections from a diagnostic biopsy of DCIS to the Alliance Foundation Trials (AFT) central biorepository, a CAP-accredited biobank. All submitted biospecimens are de-identified (coded) and investigators are blinded to arm assignment and primary study outcomes. To evaluate the adequacy of specimens for subsequent correlative science studies, one unstained slide from each submitted slide set was stained with routine hematoxylin and eosin by the biobank, scanned at 40X magnification with an Aperio scanner, and provided to one of two expert breast pathologists for adequacy review. Slides were rated as "DCIS present", "DCIS absent", or "possible DCIS." To conserve tissue, submitted tissue blocks are held in abeyance pending future correlative science planning. Results As of May 2022, tissue has been submitted from 789 of 856 eligible patients enrolled in the trial, demonstrating a very high level (92%) of case submission compliance. Despite the limiting size of such lesions and general clinical center hesitancy to release blocks for clinical trial research, tissue blocks were received from 376 of 789 (48%) of cases. Among 359 cases involving slide-only submissions that have been retrospectively reviewed to date, 294 were definite DCIS (82%), 25 (7%) were classified as possible DCIS, and 40 cases (11%) were classified as no DCIS present in the section reviewed. In no case was high grade DCIS or invasive breast cancer observed. Of the cases considered possible DCIS, atypical cells were present, but the lesions were too small or incomplete to confirm DCIS. The small percentage of cases that lacked DCIS or definite DCIS could be attributed to the receipt of a different block or subsequent (deeper) section from the same block used for the initial diagnosis. These cases were previously known to the submitting institutions. Conclusion Interim analysis at 71% accrual demonstrates both the feasibility of obtaining diagnostic biopsy material of limited size and the adequacy of these samples for subsequent correlative science studies that aim to improve pathology diagnostics and patient management.

Disclosure(s):

Rachel Factor, MD: OncLive (MJH Healthcare Holdings, LLC, Cranbury, NJ 08512): I participated in a one time round table discussion on 12/15/2021 that involved an honorarium for OncLive (Terminated, December 15, 2021)

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P6-04-14

Comparison of next-generation sequencing and real-time PCR for PIK3CA testing in hormone receptor-positive/HER2-negative breast cancer on metastatic and matched primary tumor samples

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Introduction: Based on the SOLAR-1 study, the PI3K α -specific inhibitor alpelisib has been approved in combination with fulvestrant for postmenopausal women, and men, with HR+/HER2-, PIK3CA-mutated, advanced or metastatic breast cancer (BC). Despite PIK3CA mutations occurring in ~40% of HR+/HER2- BC, PIK3CA molecular testing is a new task to be carried out in clinical practice. Adopting the most appropriate testing strategy (RT-PCR vs. NGS) on the most appropriate biological sample is of capital significance in oncologic pathology. Here, we sought to assess the concordance rate for PIK3CA molecular analysis between different technical platforms in both metastatic and matched primary tumors. Methods: From our Institutional registry, n=16 HR+/HER2- metastatic BC, which were found to harbor PIK3CA mutations via next-generation sequencing (NGS) assays [custom panel and OncoPrint Comprehensive Assay (OCA) v3 (Thermo Fisher Scientific, Waltham, MA, USA)], were selected. In half of the cases (n=8), matched primary tumors were available and were subjected to PIK3CA testing with NGS. The analytical performance between NGS and a semi-closed RT-PCR (EasyPGX®, Diatech Pharmacogenetics, Italy) was assessed in 13/16 (81.3%) metastatic samples for which archival slides and blocks and/or residual extracted DNA were available, and all the primary tumors. Results: Overall, upfront testing of PIK3CA mutational status with NGS detected genetic alterations in exons 7, 9, and 20. A concordance rate of 100.0% was observed between primary and metastatic tumors. On the other hand, the analysis of primary tumors (n=8) and 13/16 (81.3%) metastatic samples with RT-PCR revealed a concordance of 42.9%. Analytical performance comparison showed that the two technologies were concordant in 7/13 metastatic cases (53.8%). In two of the discordant cases (15.4%), RT-PCR did not identify the PIK3CA mutations due to their absence from its reference range. Interestingly, visual inspection of the RT-PCR raw data increased the concordance to 76.9%. In primary tumors, consensus between the two testing methods was observed in 5 (62.5%) cases. Discussion: The concordance rate analysis shows that upfront PIK3CA molecular testing with NGS appears to be more efficacious compared with RT-PCR. Our data suggest that primary tissues reflect the PIK3CA mutational status when tested with NGS. RT-PCR is simpler with a shorter turnaround time, and less expensive than NGS approaches, however, trained personnel are required for accurate results interpretation. In addition, the limited reference range of this testing method should be taken into account for potential false negative results. Conclusion: In terms of PIK3CA molecular testing, NGS should be the preferred method in comparison with RT-PCR. Primary tumors represent a valid biospecimen to be used for this analysis in the absence of the metastatic sample.

Disclosure(s):

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7:00 AM - 8:15 AM

P6-04-15

AI-based prediction of tertiary lymphoid structures and lymphocyte immune infiltration in breast carcinomas

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Introduction Tertiary lymphoid structures (TLSs) and tumor-infiltrating lymphocytes (TILs) in breast carcinomas are prognostic for survival and predictive of certain therapy responses. The presence of TLSs and TILs are identified by manual pathological examination; however, this method often lacks reproducibility, limiting its use in routine clinical practice. Here, we demonstrate that morphological evaluation of whole slide images (WSIs) using an artificial intelligence (AI)-based analytic workflow comprised of convolutional neural network (CNN)

deep learning models that accurately and reproducibly characterizes TILs, measured as the lymphocyte immune-infiltrated area (LIIA), and TLSs in the tumor microenvironment (TME) of breast carcinomas. **Methods** We collected a cohort of 445 TCGA breast cancer H&E WSIs, including clinical and sequencing data, and divided this cohort into luminal invasive lobular carcinoma (ILC) (n = 192), HER2-enriched (n = 110), and basal-like (n = 143) molecular subtypes. After 55 samples were excluded due to artifacts or incomplete clinical annotation, a total of 390 samples were analyzed. A combination of CNN-based deep learning models was used to detect and classify the tumor area, TLSs present in the TME, TLS density (number of TLS per mm² of tumor), and lymphocyte-rich regions. The LIIA was calculated as the area of the stromal and TIL components of the TME. Validation was performed by manually annotating 10 random WSIs from the dataset. Spatial model predictions of the tumor and TLSs were combined to identify TLS locations. Each model's predictions were verified by univariate (Kaplan-Meier) and multivariate (Cox regression) survival analyses, and the log-rank test was used to calculate overall survival. Additionally, the relationship between TLSs and LIAs with CD274 expression (PD-L1) and a high tumor mutational burden (TMB > 10) was analyzed. Statistical analyses included Spearman's rank correlation and Mann-Whitney tests. **Results** TLS were detected in 53% (n = 207) of the samples, with a mean density of 26.02 TLS/mm² (Q3 = 5.53 TLS/mm²). TLS density was higher in basal-like subtype samples compared to luminal and HER2-enriched subtypes. While LIIA and TMB-high samples exhibited a significant relationship (p = 0.00001), no significant association was found between TME and TLS quantities or density. PD-L1 gene expression exhibited weak to moderate correlations with predicted LIIA in basal-like (r = 0.38, p = 0.00001) and HER2-enriched subtypes (r = 0.38, p = 0.0001). The luminal subtype had no significant correlation between PD-L1 expression and predicted LIIA. As a result, LIIA and TLS were characterized as positive prognostic factors for the basal-like subtype. After adjusting for age, stage, and grade, the LIIA and TLS density were found to be significant independent positive prognostic overall survival factors for the basal-like subtype (LIIA HR: 0.02, p = 0.003; TLS-high group HR: 0.09, p = 0.002). For the HER2-enriched subtype, TLS density was also a significant predictor (HR: 0.05, p = 0.035), while LIIA was not a statistically significant prognostic factor (HR: 0.0002, p = 0.08). Associations were not observed between the TLSs and LIIA between the ILC subtypes and survival outcomes. The same result was observed for univariate analyses. **Conclusion** The developed analytic pipeline accurately identified the presence of LIIA and TLS on H&E slides, demonstrating the potential of CNN for automated characterization of the breast cancer TME. AI-based TLS and LIIA quantification can be a robust tool for pathology processes, offering additional information to help in clinical decision-making. This approach can be used to detect features of immune morphology biomarkers in other cancer types.

Disclosure(s):

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7:00 AM - 8:15 AM

P6-04-16

ART: Automated Region segmentation of Tumor on HER2-stained breast cancer tissue

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Background Computational pathology-based methods, eg, Quantitative Continuous Scoring (QCS) [Gustavson, SABCS 2020], are built to provide objective and quantitative methods to

assess HER2 expression in breast cancer (BC). For accurate HER2 quantification, it is important to exclude non-invasive epithelium from analysis since HER2 overexpression could be more frequent in ductal carcinoma in situ (DCIS) and pleomorphic lobular carcinoma in situ (PLCIS) than in invasive BC [Lari, J Cancer 2011]. Generally, computational pathology-based approaches require experts to delineate the invasive BC regions of interest for analysis and exclude all benign/non-invasive epithelium. Developing a tool that delineates the invasive BC regions automatically without human intervention to avoid subjectivity of manual annotation by pathologists is ideal. We developed a novel, deep-learning-based system, called DualScaleNet, to perform Automated Region segmentation of Tumor (ART) by automatically identifying the invasive BC regions and excluding benign/non-invasive epithelium on HER2-stained digitized images. Identification and diagnosis of these regions, especially the in situ tumors are a challenge as they can mimic benign and invasive lesions causing wrong HER2 evaluation. Additional stains (eg, p63 for myoepithelial cells or laminin for basement membrane) are often required for diagnosis [Pinder, Mod Pathol 2010] but were not available for this study. Methods DualScaleNet works simultaneously on HER2-stained immunohistochemistry (IHC) image patches at 2 different resolutions. The target branch uses a higher resolution RGB image (0.5 $\mu\text{m}/\text{pixel}$) to learn accurate local details; the context branch uses a lower resolution image (4.0 $\mu\text{m}/\text{pixel}$) to incorporate more context in visual learning. The algorithm generates 4 output image layers representing probabilities of 4 classes: invasive tumor, ductal/lobular carcinoma in situ, benign epithelium, and other tissue. The final segmentation result is generated by assigning each image pixel the class with the largest probability value. The algorithm was trained using ground truth (GT) annotations generated by 5 pathologists using 6157 square field of views (FOVs), 200-500 μm in size. These FOVs were collected from 850 whole slide images (WSI), spanning 9 commercial BC sample cohorts stained with different HER2 assays and scanned by several versions of the Aperio AT2 scanner. The samples included a mixture of biopsies and resections and covered different BC histologies and HER2 staining intensities. To evaluate the reproducibility of tumor area detection by human pathologists, an interpathologist comparison in detection of invasive tumor regions was performed using 225 FOVs annotated by multiple pathologists. Results Analysis generated an average Dice/F1 Score of 81.6% among different pathologists for invasive cancer. On the same sample set (independent of the ART training set), the invasive cancer detection by the ART algorithm was on par with human pathologists, achieving a similar average Dice/F1 score of 80.7%. Conclusions Novel deep learning-based ART algorithm provides accurate segmentation of invasive cancer on HER2-stained IHC images. The performance was verified against the GT annotations provided by multiple pathologists. Since the algorithm is trained using annotations from multiple pathologists, it is not possible to generate higher accuracy with computational pathology than is achievable between independent pathologists. Importantly, the same WSI read by the ART will consistently output the exact same tumor region identification result thus removing the inherent human subjectivity and variability, while improving the turnaround time for analysis. This development serves as the necessary foundation upon which a computational pathology-based diagnostic can be built.

Disclosure(s):

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7:00 AM - 8:15 AM

P6-04-17

High Intra- and Inter-block concordance of HER2 immunohistochemistry (IHC) scores across breast cancer samples and impact of decalcification procedures

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Background & Objective Trastuzumab deruxtecan is effective in HER2-positive (IHC3+ or ISH-positive) and HER2-low (IHC1+; IHC2+/ISH-negative) breast cancer. We assessed consistency of HER2-positive and HER2-low categorization by IHC across and between breast cancer samples with a range of HER2 expression. The impact of decalcification procedures on HER2 IHC staining was also assessed to determine whether HER2 expression is likely to be compromised in decalcified samples from metastatic bone disease. Methods Three non-consecutive tumor sections (approximately 100 µm apart) from 50 commercially obtained breast cancer resections (2 blocks/resection) and 20 biopsies (sections ~40 µm apart) representing a range of HER2 IHC expression, and with known ISH status, were stained using the VENTANA anti-HER2/neu 4B5 IHC assay, scored per ASCO-CAP (2018) guidelines and intra-block/inter-block concordance reported for HER2-positive and HER2-low categorization. To investigate the impact of decalcification, four resection samples were formalin-fixed, divided into four pieces, of which three were pre-treated with either 10% formic acid, Decal STAT or Richard Allan ScientificTM Decalcifying Solution before processing and staining with the 4B5 IHC assay. Results A single pathologist reviewed all samples. Intra-block agreement for HER2-low (proportion of blocks in which 3 of 3 sections had identical status) was 89.5% for biopsies (17/19) and 80.6% for resection samples (n=79/98). Inter-block agreement (proportion of resections in which two independent blocks had the same majority status for HER2-low) was 91.7%. Intra and inter-block agreement for HER2-positive was >90%. Exposure to Decal STAT or Richard Allan ScientificTM Decalcifying Solution caused a significant reduction in HER2 IHC1+ and IHC2+ staining in breast cancer samples. 10% formic acid had no apparent impact on HER2 IHC staining in all four samples tested. Conclusion There was high HER2-positive and HER2-low agreement within breast cancer biopsies and resection blocks and highly consistent HER2-positive and HER2-low categorization between different blocks from tumor resections. Our results suggest HER2 staining heterogeneity does not impact determination of HER2-positive and HER2-low status in the majority of cases. Accurate

assessment of HER2 IHC1+ and IHC2+ status was observed to be compromised by Decal STAT and Richard Allan decalcification solutions. Decalcification of bone metastasis samples for HER2-positive and HER2-low status determination may be possible using formic acid, but this would require further validation.

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7:00 AM - 8:15 AM

P6-04-18

Rapid diagnosis of breast biopsies with open-top light-sheet microscopy

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Intro: Detection of breast cancer is achieved through a diagnostic work-up that involves specialized breast imaging, image-guided biopsy, and pathological assessment. Pathology results typically require ~ 3 business days before a diagnosis is rendered, creating avoidable anxiety in women presenting with a breast abnormality. We describe a solution to deliver a rapid preliminary diagnosis within 30 minutes of biopsy. This rapid preliminary diagnosis has the potential to reduce anxiety, streamline patient care workflows, and reduce healthcare costs. Methods: Fresh 14 gauge breast biopsies in normal saline were received directly from the breast imaging clinic and immediately stained using the nuclear marker SYBR Gold (Invitrogen) and pan-protein marker Atto 655 NHS Ester (Sigma) prepared in dimethyl sulfoxide, washed, and cleared for imaging at a refractive index of 1.46 using 2,2'-Thiodiethanol (Sigma). The full process requires approximately 14 minutes for staining and clearing. After staining, we placed the biopsy in a custom-built specimen holder and imaged a 100-micron cross section along the full length of the biopsy using our custom open-top light-sheet microscope. Images were subsequently converted computationally to a standard hematoxylin and eosin (H&E) color format using Fiji and Aivia (Leica) software and were ready for evaluation by a pathologist on the same day they were collected. Results: Using the protocol above, we demonstrated the ability to stain, clear, image, and visualize needle core biopsies within 30 minutes of receiving the tissue sample. Processing the data and converting to the H&E color palette required

additional time, often requiring 60-90 minutes, surpassing the overall 30 minute turnaround time goal. The images contained identifiable stroma, epithelial cells, immune cells, and duct structures to a depth of 100 microns. Discussion: We describe a method to obtain a microscopic image for preliminary diagnosis within 30 minutes of receipt of tissue. The quality of the images produced by the method shows promise for preliminary diagnosis. Additional optimization is needed in sample preparation and data processing to meet the 30 minute turnaround time requirement. This optimization can be achieved by parallelization of the data processing on a cluster or cloud to reduce the time by an order of magnitude, which is currently under investigation by our team. The imaging and data processing will also be accelerated by multi-resolution imaging, which will decrease the time of imaging and dataset size for processing. A diagnostic study, comparing the preliminary light-sheet-based diagnosis to the final formalin fixed paraffin embedded (FFPE) pathology, is underway.

Disclosure(s):

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Engaging pathologists in a social peer-to-peer learning collaborative to discuss the emergence of HER2-low breast cancer

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Introduction: Recent advances in research have shown clinical effectiveness when targeting the lower range of HER2 expression (ie, HER2-low) in patients with metastatic breast cancer. American Society for Clinical Pathology worked in collaboration with Q Synthesis to develop a peer-to-peer learning collaborative to proactively prepare pathologists for HER2-low and to discuss the clinical implications around this emerging classification. This CME project was supported by an educational grant from AstraZeneca Pharmaceuticals LP and Daiichi Sankyo Inc. Methods: ASCP launched a peer-to-peer (P2P) learning collaborative (HER2 Breast Trailblazers) where small groups of pathologists met to discuss some of the practical implications associated with HER2-low. 38 pathologists from a mix of academic and community settings participated in this CME program. For foundational knowledge, learners completed online modules covering scientific updates on HER2-low. Through small-group, case-based discussions, learners reviewed operational challenges and opportunities to prepare for HER2-low. They applied this knowledge to lead projects at their own institutions focusing on the anticipated changes around HER2-low. ASCP also launched a series of peer-led Twitter Chats that were designed to reach a broad audience and foster open dialogue about the emerging science of HER2-low breast cancer. This approach engaged Twitter users who were eager to share and disseminate the education to their colleagues. Twitter Chats provided peer-to-peer feedback regarding ways to navigate obstacles, barriers, and other challenges affecting HER2 testing in breast cancer. Results: The learners identified the following challenges and opportunities: Defining HER2-low: Several learners had heard misconceptions around the definition of HER2-low. Recent studies have defined HER2-low as IHC 1+ or IHC 2+ with ISH-negative. Interobserver concordance with IHC 0 vs 1+: Several learners discussed the challenges around interpreting IHC 0 vs 1+. They felt that some pathologists may need guided feedback to improve their diagnostic skills. Use of IHC vs. ISH: Several learners only performed ISH for HER2 testing on all breast cancer samples. If HER2-low emerges as a third category, they would need to return to IHC. Implications for non-metastatic breast cancer: Recent HER2-low studies have focused on patients with metastatic breast cancer. If HER2-low emerges as a third category, it is unclear whether this designation will also be used in patients who have early-stage breast cancer. Leadership: As pathologists prepare for HER2-low, they have opportunities to lead projects to assess and improve IHC interobserver concordance, coach others on IHC interpretation, increase operational efficiency, strength communication skills, and build up the team by proactively anticipating challenges around HER2-low. Conclusions: HER2-low breast cancer appears to be emerging as a new classification and pathologists need to be prepared to ensure accurate testing and interpretation. Through a peer-to-peer learning collaborative, pathologists identified ways to proactively prepare and demonstrate leadership so

that cancer centers and laboratories may be ready to embrace a new paradigm of HER2 classification in breast cancer. A series of public Twitter Chats broadened this discussion and increased awareness among pathologists.

12/9/2022

7:00 AM - 8:15 AM

P6-05-01

Employment status patterns in a cohort of young women with breast cancer in Mexico

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Background: Breast cancer diagnosis and treatment carries a disruption in multiple aspects in the life of women. For young women affected by this condition, the evidence of employment status and its change is limited. This study aims to document the first change in employment that may be experienced by young women with breast cancer and determine which factors could influence such patterns. Methods: Mexican women from the Joven & Fuerte prospective multicenter cohort, aged ≤ 40 , diagnosed with stage I-III breast cancer between 2015-2021 with at least 6 months of follow-up were included. Participants with a documented recurrence, missing employment status information, diagnosis of a new primary breast cancer or a second type of cancer were excluded from the analysis. Patients completed surveys at baseline, 6 months, and yearly for up to 5 years to assess sociodemographic characteristics, employment status, medical and treatment data. Women were categorized on a scale of employment status

as follows: full-time > part-time > student > medical leave > unemployed. Subsequently, an increase or reduction in employment status was considered whenever a participant moved up or down a category, respectively. Only the first employment status change was analyzed. The Kaplan-Meier failure estimate was employed to calculate the increase or decrease in employment status at 1 year and 2 years post-diagnosis. Competing risk regression models were undertaken to explore variables associated with a decrease in employment status. Results: A total of 142 women with a median age at diagnosis of 36.5 years (IQR 33-39) and median follow-up of 17 months were included in the analysis. Baseline employment status for these patients was: employed - full time (27%), employed - part time (14%), student (1%), medical leave (4%) and unemployed (54%). At 12 months, 18.5% of participants had a reduction in their work activities (95% CI 12.8 - 26.4%) and this proportion further increased to 25.8% at 24 months (95% CI 18.7 - 34.8%). In contrast, 11.8% (95% CI 7.3 - 19.0%) and 23.2% (95% CI 15.9 - 33.2%) of participants exhibited an increase in their work activity at 12 and 24 months, respectively. The most common patterns in first employment status change were from unemployed to employed - full time (19%), employed - full time to employed - part time (13%) and employed - full time to unemployed (13%). Age, education, monthly income, number of people who contribute to the household, number of children, being financially responsible for another person, mastectomy, chemotherapy, radiotherapy and endocrine treatment were not associated with an increase or reduction in work activity. Postmenopausal status at 1 year postdiagnosis was associated with a higher hazard for experiencing a reduction in work activity (SHR=3.05, 95% CI 1.38 - 6.72, p=0.006). Conclusion: The results from the present study appear to be in line with those of a European cohort. Further studies are needed to identify other potential factors that influence employment status trajectories. The development of interventions that tackle actionable characteristics of young patients with breast cancer at risk of employment disruption is imperative.

Disclosure(s):

Cynthia Villarreal-Garza, n/a: AstraZeneca: Contracted Research (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Myriad Genetics: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

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P6-05-02

PRESENCE OF BRCA MUTATIONS AND PRE-CHEMOTHERAPY SERUM ANTI-MULLERIAN HORMONE LEVELS PREDICT RISK OF AMENORRHEA IN WOMEN WITH BREAST CANCER

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OBJECTIVE: The likelihood of post-chemotherapy (ChT) amenorrhea is still empirically determined. Our aim was to determine the predictors of amenorrhea risk post- ChT in women with breast cancer(ca). As acute amenorrhea (< 12mo post-ChT) can be temporary, we used amenorrhea status 12 and 18 months post-ChT as the primary endpoint.

MATERIALS AND METHODS: 102 women aged 18-44, with regular cycles and stage I-III breast ca were prospectively and longitudinally followed for their menstrual pattern changes at 6, 12, and 18mo after the completion of adjuvant ChT with an Anthracycline-Cyclophosphamide-based (AC) or Cyclophosphamide-Methotrexate +5-Fluorouracil regimen on an IRB-approved protocol. Prior ChT, ovarian surgery, pelvic RT, family history of POI, and infertility diagnosis were the exclusion criteria. AMH was measured pre- and immediately post-ChT. Amenorrhea was defined as no bleeding for 4 consecutive cycles. Preand/or post-ChT AMH levels, age and BMI at the onset of ChT, BMI, tamoxifen use, regimen type (AC-based vs. not), and BRCA mutation (m) status (positive vs. not) were evaluated for the prediction of

amenorrhea risk.

RESULTS: In multivariable-adjusted logistic regression models, age ($p=0.03$) and AMH ($p=0.03$) were significant predictors of amenorrhea at 12mo, and BRCAm status ($p=0.03$) at 18 mo; these models yielded areas under the ROC curve of 0.77 and 0.76, respectively. An undetectable AMH post-ChT was best predictive of amenorrhea with shorter follow-up, but not at 18mo. In longitudinal analysis (with data at 0, 6, 12, and 18 months) estimating 'time-trends', a baseline AMH < 2.0 ng/ml (optimal cut-off from ROC curve) and BRCAm status were associated with the risk of amenorrhea. The baseline AMH ≥ 2.0 group showed attenuated time-trend vs. the AMH < 2.0 ng/ml group (ratio of ORs=0.91, 95% CI=0.86-0.97, $p=0.002$), while the BRCA-positive group showed a steeper time-trend in the odds ratio (OR) of amenorrhea, compared to the non-positive group (ratio of ORs=1.12, 95% CI=1.04-1.20, $p=0.003$) (Table 1). Sensitivity analyses demonstrated the robustness of these findings, for example, yielding an 8-10% increased risk of amenorrhea for BRCAm carriers, with p-values of 0.008- 0.04.

CONCLUSIONS: Age, pre-and post-ChT AMH levels, and BRCAm status are potential predictors of amenorrhea at 12 and 18mo post-ChT. These predictors may help better guide fertility preservation decision-making in women with breast ca. The higher likelihood of amenorrhea in women with BRCAm suggests that they may be more prone to lose their ovarian function post-ChT and should be accordingly counseled.

Table 1. Longitudinal analysis at 0, 6, 12 and 18 months for the difference in amenorrhea trend between groups dichotomized by baseline factors

Difference in time trend between 2 groups (per 1 month)	Multivariable-adjusted model Ratio of Odds Ratios (95% CI), p-value
Reference group+	0.98 (0.89, 1.08), p=0.65
AMH at baseline: > vs. ≤2.0*	0.91 (0.86, 0.97), p=0.002
Age: > vs. ≤40	1.05 (0.99, 1.11), p=0.14
BMI: > vs. ≤25	1.05 (0.99, 1.11), p=0.09
Tamoxifen vs. not	1.05 (0.96, 1.14), p=0.31
CMF vs. AC-based regimen	1.02 (0.95, 1.11), p=0.57
BRCA positive vs. not	1.12 (1.04, 1.20), p=0.003

+Time trend (i.e., odds ratio for month) for reference group of AMH≤2.0, Age≤40, BMI≤25, no tamoxifen, AC-based and not BRCA-positive.

*Cut-off was suggested from ROC curve in Figure S1.

Ratio of odds ratio=1 indicates null value, i.e., no difference in time-trend between 2 groups, measured by odds ratio (of 1 month increase and outcome) in each group separately.

Longitudinal data were fit via a Generalized Estimating Equation (GEE). Sensitivity analyses (e.g., based on Generalized Linear Mixed effects model (GLMM)) are presented in Table S3.

Disclosure(s):

Shari B. Goldfarb, MD: Ms. Medicine LLC: Consulting Fees (e.g., advisory boards) (Ongoing); Nanology: Consulting Fees (e.g., advisory boards) (Ongoing); Paxman Cooling LTD: grant recipient (Ongoing); Revision Skincare: Consulting Fees (e.g., advisory boards) (Ongoing); Sermonix Pharmaceuticals LLC: Consulting Fees (e.g., advisory boards) (Ongoing); Spectrum Pharmaceuticals: Consulting Fees (e.g., advisory boards) (Ongoing); Sprout Pharmaceuticals: Grant Recipient (Ongoing)

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7:00 AM - 8:15 AM

P6-05-03

Post-Mastectomy Implant Complications in a Hispanic Breast Cancer Patient Population

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Introduction: Breast cancer is the most common cancer diagnosed in women in the United States with primary treatment consisting of a combination of surgery, systemic therapy, and radiation. Breast reconstruction has been shown to improve quality of life in women and utilization is increasing with time. There is a large amount of evidence demonstrating the complications of radiation therapy on implant-based breast reconstruction including but not limited to, capsular contracture, infection, and reoperation. However, the majority of these studies have examined populations consisting primarily of non-Hispanic white patients with breast cancer. In general, hispanic populations are not well represented in research studies or Phase II/III clinical trials. Therefore, the goal of this study was to analyze the impact of radiation therapy on post mastectomy implant-based breast reconstruction complications in self-identified Hispanic patients.

Methods: We retrospectively reviewed patients who underwent mastectomy with implant reconstruction between January 1, 2017 and December 1, 2019. The inclusion criteria included female patients 18 years or older who self-reported as Hispanic or Latino. Exclusion criterias included patients who did not undergo mastectomy, did not undergo tissue-expander or implant reconstruction, or did not self identify as Hispanic descent. Outcomes infection needing antibiotics, capsular contracture Baker grade II-IV, and implant loss. Statistical analysis was performed using Chi-squared analysis.

Results: A total of 258 patients of Hispanic or Latino women were included in the study. This included 343 total number of breasts, with 228 breasts that underwent mastectomy with

reconstruction due to breast cancer and 115 breasts that underwent prophylactic mastectomy with reconstruction. The median age at time of initial mastectomy was 49 years (range 19-86). 46 total breasts received adjuvant postoperative radiation and 296 breasts did not receive radiation. Median radiation dose to the chest wall was 50 Gy (range 42.56 - 60) in 2Gy (range 1.8 - 2.66) fractions. All patients who received postoperative radiation had at least 1 complication. The rate of complications and comparison between radiated breast compared to non-radiated breasts is demonstrated in table 1.

Conclusion: The goal of this study was to analyze the impact of radiation therapy complications on post-mastectomy implant-based breast reconstruction surgeries in patients of Hispanic descent. We demonstrate that the rate of capsular contracture is significantly higher after radiation therapy and the rate of overall complication after radiation therapy is higher (even though non statistically significant) compared with patients who do not undergo radiation. While these results are comparable to similar studies done in non-Hispanic groups, this is the first study to our knowledge that has looked at post-mastectomy complications focusing specifically on a Hispanic population. Mastectomy and subsequent implant reconstruction, radiation, and complications can have negative psychological effects on patients and can manifest differently with varying cultural backgrounds. It is imperative to understand the complications associated with race to better allow practitioners to cater treatment and support for a diverse patient population with breast cancer.

Table 1: Complications

Table 1: Complications

	With Radiation	No Radiation	p-value
Infection needing antibiotics	6/46 (13%)	23/296 (7.8)	0.467
Capsular contracture Baker II-IV	11/46 (23.9%)	31/296 (10.5)	<0.001
Implant loss	14/46 (30.4%)	43/296 (14.5%)	0.081

Disclosure(s):

Brianna Conte, n/a: No financial relationships to disclose
Caroline Shermoen, n/a: No financial relationships to disclose
Danielle Cerbon, MD: No financial relationships to disclose
Susan Kesmodel, MD, FACS: No financial relationships to disclose
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P6-05-04

Patterns in palliative care use and their impact on survival in the elderly metastatic breast cancer (MBC) population: a National Cancer Database (NCDB) Analysis

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Background: About 6% of patients diagnosed with breast cancer (BC) will have metastatic disease at time of diagnosis. In this case, treatment is palliative and focused on systemic therapies. Both American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) recommend early integration of palliative care (PC) for patients with metastatic disease to improve symptom management and quality of life while potentially decreasing mortality. However, the frequency by which elderly patients with metastatic breast cancer (MBC) receive PC is unknown. This is especially relevant as improvements in health care have allowed for longer life expectancy and an increase in America's aged population. The goal of this study was to use the NCDB to describe national patterns in PC use in elderly patients over 75 years of age with MBC and evaluate differences in overall survival (OS).

Methods: Women with a diagnosis of BC at age ≥ 75 years and with metastases at time of initial diagnosis from 2010 to 2019 were identified from the NCDB. Patients were stratified into age subgroups of 75-79, 80-84, and ≥ 85 years. Chi-square tests were used to compare categorical variables. Kaplan Meier curves were used to determine OS distributions for patients by age and receipt of PC. Log-rank tests and multivariable cox proportional hazards modeling was performed to assess the difference in OS between patients who received and did not receive PC.

Results: Of 17,325 eligible women included in the final analysis, 39.4% were 75-79, 30.1% 80-84, and 30.4% ≥ 85 years of age. Overall, 20.5% of patients utilized PC. The table below describes the baseline characteristics of patients who received PC versus those who did not. Rates of PC utilization varied among the age subgroups, with the lowest utilization in the ≥ 85 years of age group, $p < 0.0001$. Performance status as measured by Charlson-Deyo Score did not impact rates of PC use, $p = 0.3196$. Use of PC varied across races with higher use in Non-Hispanic White patients and lower in Hispanic and Non-Hispanic Black subgroups, $p < 0.0001$. In the overall population, the use of PC increased from 17.9% in 2010 to 23.2% in 2019, $p = 0.0003$. This was primarily driven by the statistically significant increase in the 75-79 age group (18.4% to 26.8%, $p = 0.0003$). Although there were numeric increases in PC use from 2010 to 2019 in the 80-84 (20.9% to 24%, $p = 0.2899$) and ≥ 85 (13.9% to 17.9%, $p = 0.1082$) age groups, these differences were not statistically significant. Palliative care receipt did not

impact overall survival. Three-year OS rates were 27.8% (CI: 26.1-29.5) and 27.8% (CI: 27.0-28.7), for patients who received PC compared to those who did not, respectively, p=0.512.

Conclusions: Over the last decade, we observed an increase in PC utilization in patients \geq 75 years with MBC. However, significant increases were only seen in the 75-79 age group. Palliative care use was lower among patients \geq 85 years compared to those 75-79 or 80-84 years of age. Performance status did not influence receipt of PC. There were no differences in OS between elderly patients who received PC versus those who did not. Future follow up analyses will be needed to determine the impact of PC on OS in this population. Clinicians should be encouraged to integrate PC into the treatment of elderly patients with MBC, particularly those \geq 85 years, as this can improve symptoms and quality of life.

Table 1. Patient Baseline Characteristics by Palliative Care Receipt

Variable	Total N=17,325 (%)	No Palliative Care N=13,765 (79.5%)	Received Palliative Care N=3,560 (20.5%)	P-Value
Age				<0.0001
75-79yos	6,834 (39.4)	5,376 (39.1)	1,458 (41.0)	
80-84yos	5,218 (30.1)	4,079 (29.6)	1,139 (32.0)	
85+yos	5,273 (30.4)	4,310 (31.3)	963 (27.1)	
Race/Ethnicity				<0.0001
Hispanic	632 (3.6)	544 (4.0)	88 (2.5)	
Non-Hispanic Black	2,048 (11.8)	1,652 (12.0)	396 (11.1)	
Non-Hispanic White	13,596 (78.5)	10,716 (77.8)	2,880 (80.9)	
Other	387 (2.2)	317 (2.3)	70 (2.0)	
Unknown	662 (3.8)	536 (3.9)	126 (3.5)	
Charlson-Deyo Score				0.3196
0	12,271 (70.8)	9,779 (71.0)	2,492 (70.0)	
1	3,127 (18.0)	2,486 (18.1)	641 (18.0)	
2	1,141 (6.6)	889 (6.5)	252 (7.1)	
\geq 3	786 (4.5)	611 (4.4)	175 (4.9)	

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Rima Patel, MD: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-05-05

Patient-reported outcomes, perceptions, and knowledge about recurrence in women with high-risk hormone receptor-positive (HR+) breast cancer (BC)

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Background: Over half of HR+ BC recurrences occur >5 years (y) from diagnosis (dx). While the risk of late recurrence is constant and extends for at least 20y, little is known about

concerns, perceptions, knowledge, and interest in risk reduction in longer-term HR+ BC survivors.

Methods: From 1/2021-1/2022, we prospectively identified patients (pts) at Dana-Farber Cancer Institute with a history of stage II/III, HR+/HER2- BC, ≥ 5 y from dx, without recurrence. Pts were invited to participate in a study investigating circulating tumor DNA and risk of recurrence as well as a separate, 1-time survey that assessed physical/mental health (PROMIS), dx/treatment concerns (Brief Illness Perception Questionnaire), risk perceptions, knowledge, and interest in risk reduction. "Overestimation" was defined as estimating $\geq 20\%$ risk based on the response to the question: "If 100 women with HR+ BC are treated according to recommended guidelines, about how many will have BC come back in the 5-10y following completion of active treatment." Descriptive statistics included medians and proportions. Logistic regression identified factors associated with overestimation of 5-10y metastatic recurrence risk.

Results: Among 166 women (of 209 sent surveys, 79%), median age at dx was 51 (range 21-76), 4% were Hispanic and/or Black; 19% did not have a college degree. Approximately 30% had stage III disease, most received chemotherapy (72%) and radiation (81%) and over half (57%) a mastectomy. Median time from dx was 10 y (range: 5-23). Almost all (97%) reported prior (44%) or current hormonal therapy (14% tamoxifen, 39% AI). Median PROMIS anxiety (53; range: 37-73), physical (51, range: 32-68), and mental (51, range: 25-68) scores were similar to population norms (score of 50). On a 0 (not at all)-10 (extremely) scale, the median rating for concern about dx/treatment was 5; for emotional impact of dx/treatment, the median rating was 9. Regarding risk perceptions, participants estimated that on average, a median of 15 and 10 women (of 100 women) would develop a loco-regional or distant recurrence, respectively, in the 5-10y interval; 43% and 40% estimated the risk of loco-regional and distant recurrence as $\geq 20\%$, respectively, for this interval. Pts without a college degree were more likely to overestimate 5-10y distant recurrence risk (multivariable OR: 3.66, 95% CI: 1.56, 8.59); age, chemotherapy receipt, surgery type, stage, and grade were not associated with overestimation. When asked, on average, which women have a higher chance of BC returning after 5y, 17% correctly responded HR+; 42% responded triple negative and 41% responded the risk was the same for both. While $>1/3$ responded they believed alcohol in moderation may decrease the risk of BC coming back, most also responded that having a healthy weight, eating ≥ 5 fruits/vegetables a day, and exercise may decrease this risk, with over half reporting engagement in these behaviors (Table).

Conclusion: While most longer-term stage II/III HR+ BC survivors report mental and physical health commensurate to population norms, inaccurate knowledge and perceptions about recurrence are common. Strategies to effectively communicate risk (e.g., pictograms, decision/conversation aids) and risk reduction information can promote an accurate understanding of risk in the setting of longer-term HR+ BC survivorship, potentially mitigating emotional concerns which are prevalent ≥ 5 y post-dx. The association between lower educational attainment underscores the importance of attention to literacy and numeracy when developing interventions to improve risk communication.

Table. Perceived impact of health behaviors on recurrence risk

Belief that behavior affects recurrence:	Healthy weight (%)	≥5 fruits/vegetables/day (%)	≥ 30 min moderate-vigorous exercise ≥5 days (%)	Alcohol in moderation (%)
May increase chance	9	1	1	35
Makes no difference	7	6	4	17
May decrease chance	82	89	91	37
Don't know	2	4	3	11
Engaged in behavior because it decreases recurrence				
Yes	59	59	55	-
No	12	15	12	-
No but I want to	29	26	33	-

Disclosure(s):

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7:00 AM - 8:15 AM

P6-05-06

Patient-reported anxiety and fatigue in women enrolled in the RxPONDER trial (SWOG S1007) by menopausal status

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Introduction: Anxiety and fatigue have been reported by women undergoing cytotoxic and endocrine treatment (tx) for breast cancer and can have lasting effects on quality of life (QoL). The differential effects of menopausal (meno) status, tx allocation and duration of symptoms are not well established.

Methods: Participants (pts) with hormone receptor positive, HER2 negative breast cancer with 1-3 positive lymph nodes and an Oncotype DX recurrence score of 0-25 enrolled in the RxPONDER trial were randomly assigned to endocrine therapy (ET) alone vs chemotherapy followed by ET (CET). A subset of English speaking pts in the US at the start of the trial were invited to complete health-related QoL (HRQoL) questionnaires shortly after randomization (baseline; BL) and 6, 12, and 36 months after BL until accrual goal reached. BL surveys were completed in clinic; cognitive function results presented separately. Standardized T scores (mean 50; SD 10) were computed for anxiety (PROMIS Emotional Distress – Anxiety Short Form 7a) and fatigue (PROMIS Fatigue Short Form 7a). Higher T scores indicate more anxiety or fatigue. The primary endpoint of this exploratory analysis was to compare mean anxiety and fatigue T score by tx arm by meno status. Separately by meno status, a GEE model was fit to

the three follow-up timepoints adjusting for BL to estimate the difference between tx arms and whether there was a time trend over the three follow-up measures.

Results: The accrual exceeded the goal of 500 pts with 74% of pts participating voluntarily until the QOL invitation was removed from the protocol (12/1/12). A total of 139 pre and 432 postmenopausal pts completed the anxiety questionnaire at BL. There was no difference in anxiety between tx arms [Table 1]. Mean anxiety score difference between CET and ET over time in the premenopausal cohort was -0.63 (p=0.63) and in the postmenopausal cohort was 0.59 (p=0.45). Although anxiety scores decreased over the three follow-up times, the change was not statistically significant.

A total of 139 pre and 429 postmenopausal pts completed the fatigue questionnaire at BL. Fatigue mean T scores in both the pre and postmenopausal cohorts were higher over time in the CET vs ET arm [Table 2]. Fatigue scores were 2.85 points higher for CET vs. ET over time in the premenopausal cohort (p=0.02) and 1.82 points higher in the postmenopausal cohort (p=0.007). Fatigue scores decreased over time for premenopausal (p=0.01), but not for postmenopausal (p=0.62) pts.

Dropoff occurred over time with 79%, 76%, 60% of pts at BL participating at 6, 12, and 36 months. Endocrine treatment adherence data are not yet available at each timepoint.

Conclusions: CET had a clinically significant negative effect on mean fatigue scores compared to ET alone in both pre and postmenopausal pts over time. Scores improved over time but did not return to BL. Pts had lower mean anxiety scores during tx compared to BL, but differences in scores between CET and ET groups out to 3 years did not significantly differ. Future therapeutic studies must continue to include HRQoL assessments to broaden our understanding of the full impact of chemotherapy and for the development of preventative and therapeutic strategies to manage these toxicities.

Table 1. Comparisons of mean Anxiety score by treatment arm and menopausal status

Menopausal status	Assigned Arm	Timepoint				CET vs. ET Difference
		Randomization	6 mos	12 mos	36 mos	
Pre	CET	57.05	50.83	51.62	51.36	-0.63 (p=0.63)
	ET	54.97	50.92	49.68	50.33	
Post	CET	56.09	50.99	51.40	51.33	0.59 (p=0.45)
	ET	54.54	50.50	48.86	49.20	

Table 2. Comparisons of mean Fatigue score by treatment arm and menopausal status

Menopausal status	Arm	Timepoint				CET vs. ET Difference
		Randomization	6 mos	12 mos	36 mos	
Pre	CET	48.11	52.46	51.64	49.99	2.85 (p= 0.02)
	ET	49.58	50.20	49.87	47.29	
Post	CET	49.99	53.75	52.84	52.80	1.82 (p=0.007)
	ET	50.29	51.68	50.88	51.01	

Disclosure(s):

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7:00 AM - 8:15 AM

P6-05-07

Oncologic outcomes of pregnancy after surgical treatment of breast cancer 35 years old or under

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Purpose: Recent advances in the treatment of breast cancer has led to the improvement of breast cancer patient's survival. With prolonged survival of these patients, pregnancy became an important issue, especially in those of young cancer patients aged 35 or under. Increased hormone levels during pregnancy, however, raises concerns of elevating the risk of cancer recurrence. The aim of this study was to validate the notion of increased risk associated with pregnancy after breast cancer treatment in young patients. Methods: From January 2009 to December 2020, newly diagnosed breast cancer patients of 35 years old or under who underwent curative surgery in Korea University Guro Hospital were enrolled in this study. Patients were categorized into 3 groups: nulliparous, pregnancy prior to treatment of breast cancer, and patients with pregnancy after breast cancer treatment. Their overall survival and disease-free survival were evaluated. Results: A total of 126 patients was enrolled in this study. Seventeen patients (13.4%) conceived and successfully delivered. The mean age of enrolled patients was 32.0 years old (± 3.1), and the mean follow up period after surgery was 56.8 months (± 34.2). There was no significant difference in overall survival ($p=0.490$) and disease-free survival ($p=0.740$) among different groups. Among 22 patients with re-diagnosis of breast cancer, 2 of them (9%) had breast cancer on their contralateral breast. Conclusion: In young patients, pregnancy after treatment for breast cancer did not affect their overall survival or disease-free survival as compared to nullipara or previously delivered groups. Therefore, pregnancy counseling should not be prevented in young breast cancer patients of 35 years old or under.

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P6-05-08

Distress Screening for Family Caregivers of Metastatic Breast Cancer Patients

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Metastatic breast cancer (MBC) is an incurable disease that affects over 168,000 women in the US. Family caregivers play a critical role in patients' adjustment to MBC by providing practical and emotional support. However, the extensive involvement of caregivers in patient care places them at increased risk for clinically significant psychological distress symptoms. In fact, research has shown that distress is as prominent for caregivers as it is for patients and that it can adversely affect caregiver support to the patient. Distress screening with appropriate triage and follow-up for psychosocial concerns is recognized by the Institute of Medicine (IOM) and National Comprehensive Cancer Network (NCCN) as critical for ensuring high-quality comprehensive cancer care. However, clinical tools to assist with recognizing caregiver distress are sparse, creating a practical barrier for caregivers to obtain needed psychosocial support. The NCCN Distress Thermometer (DT) is a validated single-item self-report measure that was developed to screen for cancer patient distress. It is often used with the NCCN 42-item Problem List (PL) which identifies sources of distress to help guide providers in making appropriate referrals. Although the DT has been validated for use with caregivers, most adult oncology practices have yet to establish protocols for identifying caregivers with high distress levels. Part of the problem is that many PL items ask about physical and other concerns that are related to either having or undergoing treatment for cancer. Developing a caregiver-focused PL could thus not only improve clinical uptake of distress screening for cancer caregivers, but also enable greater integration of family-centered support services as part of routine cancer care. With these goals in mind, this mixed-methods study sought to inform development of a PL to address the unique concerns of cancer caregivers. Methods: Caregivers of MBC patients completed a short survey containing sociodemographic questions and the NCCN DT. They also participated in semi-structured interviews about their role in symptom management, psychosocial impacts of cancer, and unmet needs. Interviews were audio-recorded and transcribed. The five NCCN problem domains (i.e., physical, emotional, family, practical, and religious/spiritual concerns) that have been identified as sources of distress were used to guide thematic analysis. Results: Nineteen caregivers (63.2% female; 47.4% racial/ethnic minorities) participated. Most were middle aged (M = 54.4, SD = 16.4) and either spouses (42.1%) or adult children (31.6%). Surveys revealed that caregivers had moderate distress levels (M=4.4 out of 10, SD=3.1); 53% exceeded the DT cut-off of 5, warranting further psychological evaluation. In the interviews, caregivers reported an average of 7.7 concerns (Range = 0 to 17 concerns). The most common issues were worry (63.2%), coping with the patient's emotions (57.9%), providing emotional support to the patient (52.6%) and assisting with activities of daily living (47.9%). Caregivers also expressed problems coordinating care with other family members, feelings of guilt, and unmet needs for information. Caregivers reporting more concerns reported significantly ($p < .05$) higher levels of psychological distress. Conclusion: Many of the concerns raised by MBC caregivers did not align with the NCCN PL, suggesting that development of a

caregiver-specific PL is warranted. Additional study is needed to determine whether such a PL could help to efficiently route caregivers to information and resources matching their needs and ultimately help to alleviate their distress.

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Cardiovascular Risk Evaluation for Breast Cancer Survivors: A Pilot Study

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Cardiovascular Risk Evaluation for Breast Cancer Survivors: A Pilot Study

Introduction

Breast cancer (BC) is the most common cancer in women in the United States (US). With advances in screening and treatment, there are increasing numbers of BC survivors. Preexisting or emerging cardiovascular (CV) risk factors and some cancer therapies put BC survivors at risk for long-term CV disease (CVD). ASCO clinical practice guidelines for prevention and monitoring of cardiac dysfunction recommend treatment of CV risk factors in cancer survivors, however, the application of these guidelines in clinical practice presents several challenges. In this pilot study, we describe the feasibility of performing CVD risk assessment in a cohort of BC survivors in a single institution in an urban area that serves mostly Black/African American (AA) populations.

Methods

We identified patients with early-stage BC treated between 2015 and 2022. Patients underwent CVD risk assessment including vital signs, hemoglobin A1c, lipid panel, transthoracic echocardiogram (TTE), 6-minute walk test (6MWT), troponin T, and B-type natriuretic peptide

(NT-ProBNP). The primary objective of the study was to describe the feasibility of performing a CVD risk assessment.

Results

Out of 69 eligible patients who were approached for the study, 50 were enrolled and completed the CVD risk assessment (72%). Among 19 patients who did not enroll or complete the risk assessment, time constraints to complete the work up was the predominant factor. The median age was 60.5 years (SD = 13.65; range 34-86), 76% self-identified as Black/AA, 14% as White, and 95% as Non-Hispanic. Half of the patients had hormone-receptor-positive BC, 34% human epidermal growth factor receptor 2 (HER2) positive disease (and received HER2-targeted therapies), and 28% triple-negative breast cancer (TNBC). In terms of treatment, 34% received anthracycline-containing regimens. CVD risk assessment results are shown in Table 1. Twenty-four (48%) of the patients had metabolic syndrome defined as the presence of 3 out of 5 CV risk factors (waist circumference, hypertension, low HDL, high triglycerides, insulin resistance). Although all patients had an ejection fraction (EF) above 55%, 7 patients (14%) had an abnormal global longitudinal strain (GLS). The median number of meters in the 6MWT was 369 (SD 94.46, range 67-531); 74% of patients walked a shorter distance than predicted by age and body mass index, indicating significant physical impairment. All patients had a troponin T value below the 99th percentile. The most frequent modifiable CVD-risk factors included obesity and hypertension.

Conclusion

Performing a low-cost CVD risk assessment in a population of mostly Black/AA BC survivors was feasible in this pilot study. We identified a high prevalence of CVD risk factors, with 48% of patients meeting metabolic syndrome criteria and the majority of patients demonstrated a very high level of functional impairment measured by 6MWT. Our findings underscore the importance of survivorship care focused on CVD risk in BC survivors. Limitations include the small sample size, single-institution study, and lack of CV and BC-related outcomes. The higher incidence of TNBC could be explained by a selection bias of patients receiving cytotoxic chemotherapy and the higher incidence of TNBC in the Black/AA population. Future research will focus on implementing this assessment in the survivorship clinic and establishing interventions to decrease CVD risk in cancer survivors.

Table 1: Clinical Measurements & Outcomes (n=50)	
Outcome or characteristic	%
Pre-existing conditions	
Hypertension	48
Hyperlipidemia	18
Diabetes	16
Current or previous smoking	38
BMI	
≤ 18.5 (underweight)	2
18.6-25 (normal weight)	16
25.1-29.9 (overweight)	26
≥ 30 (obese)	46
Blood Pressure	
≤ 130 and/or ≤ 80 mmHg	40
>130 and/or >80 mmHg	60
LDL (mg/dL)	
≤110	54
111-129	18
≥ 130	28
HDL (mg/dL)	
>45	84
40-45	10
<40	6
Triglycerides (mg/dL)	
<74	36
75-99	20
>100	44
Hemoglobin A1c (mg/dL)	
Normal (<5.7)	46
Prediabetes (5.8-6.5)	34
Diabetes (>6.5)	16
Cardiac Biomarkers	
Abnormal NT-proBNP (>125 pg/mL)	12 (range 133-523)
Echocardiogram	
Global longitudinal strain <-18 %	23 (range -14.4- -17.9)

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P6-05-10

An international survey on invasive lobular breast cancer (ILC) reveals gaps in knowledge and top priority research areas

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Background:

There is growing awareness of the unique etiology, biology, clinical presentation and progression of Invasive lobular breast cancer (ILC), but additional research is needed to assure translation of findings into management and treatment guidelines. We performed a survey to: 1) analyze the landscape of the current understanding of ILC, and 2) identify consensus research questions on ILC.

Methods:

The IRB-approved survey was developed with input from representatives of three major stakeholder groups - breast cancer clinicians/researchers, laboratory-based researchers, and advocates/patients. We fielded the survey from March to May 2022 using targeted email and via social media.

Results:

1,774 participants answered at least one question and 1,310 finished the survey. Participants are from 66 countries from all continents (except Antarctica). Respondents self-identified as clinicians (mostly medical oncologists and surgeons) (N=413), researchers (N=376), and breast cancer patients (1,121), with some belonging to more than one category. 26% of the patients who participated in the survey belong to advocate groups.

Only 46% of clinicians reported being confident in describing the differences between ILC and no special type (NST) (invasive ductal) breast cancer. Knowledge of histology was seen as important (73%), affecting their treatment decisions (51%), and refined treatment guidelines

would be valuable for patients with ILC in the future (76%). 85% of clinicians have never powered a clinical trial to allow subset analysis for histological subtypes, but the majority would consider it. 88% would participate in a consortium to conduct clinical trials on ILC. The top two most important research questions were: 1) determining mechanisms of endocrine resistance, and, 2) identifying novel therapeutic targets, repurposing existing drugs and progressing them to clinical trials.

Of the researchers, 48% reported being confident in describing differences between ILC and NST. They reported that ILCs are inadequately presented in large genomic data sets (52%), and that ILC models are insufficient (42%). Only 13% of respondents have inadequate access to tissue or blood from patients with ILC. The top two most important research questions identified by the laboratory researchers overlapped with those identified by the clinicians, i.e. understanding of endocrine resistance and identifying novel drugs that can be tested in clinical trials.

The majority of patients (52%) thought that their health care providers did not explain unique features of ILC, and that in general communication was limited. When asked about top research question, they chose: 1) Improvement of ILC screening/early detection, and, 2) Identifying new and specific imaging tools for ILC.

When comparing top priority topics across six research domains, there was a high degree of consistency, especially among clinicians and researcher, but less so when compared with the breast cancer patients (Table 1).

Conclusion:

In summary, we have gathered timely and representative information from an international community of clinicians, researchers, and patients/advocates that we expect will lay the foundation for a community-informed collaborative research agenda, with the goal of improving the management and personalizing treatment for patients with ILC.

TABLE 1: Ratings by all three stakeholder groups of the most critical and impactful ILC research topics. Top box scores between stakeholder groups were compared using chi-square analysis.

	Most Critical and Impactful			
	Research Questions			
	Clinicians	Lab Researchers	Patients/ Advocates	p-value
Epidemiology and Risk Reduction				
Therapy, Treatment Resistance and Disease Progression	43	50	60	<.0001
Identifying strategies to improve ILC screening/early detection	68	73	89	<.0001
Impact of obesity and lifestyle factors on risk of developing ILC and risk of relapse	38	38	50	0.0006
Diagnosis (Imaging and Pathology)				
Examining use of E-cadherin/p120 expression	52	55	74	<.0001
Improving diagnosis and understanding of mixed IDC/ILC	50	56	65	0.0002
Understanding the use of artificial intelligence	41	37	60	<.0001
Role of genomic predictors for ILC prognosis and prediction of therapeutic response	75	78	76	0.6822
Identifying strategies to improve ILC screening/early detection	73	73	90	<.0001
Therapy, Treatment Resistance and Disease Progression				
Identifying mechanisms of metastases	71	75	88	<.0001
Determining mechanisms of endocrine resistance in ILC	81	80	84	0.242
Identification of novel therapeutic targets and/or repurposing existing drugs for ILC	78	81	84	0.1775
Determining utility of immunotherapy in ILC	65	60	79	<.0001
Understanding value of liquid biopsies in patients with ILC	52	56	73	<.0001
Characterizing chemotherapy in ILC, and understanding differences to IDC	74	67	77	0.0034
Determining mechanisms of dormancy and risk for late relapse	70	73	87	<.0001
Developing and testing lifestyle interventions	34	32	48	<.0001
Imaging				
Optimizing current breast cancer screening modalities	62	60	83	<.0001
Identifying new and specific imaging tools for ILC	65	68	92	<.0001
Studying the importance of breast density	44	42	76	<.0001
Determining the utility of MRI	65	58	80	<.0001
Local therapy of the Primary Tumor				
Determining how to reduce the high positive margin rates in ILC	66	60	76	<.0001
Characterizing further whether breast conservation/radiation is as safe as mastectomy	52	50	63	0.0003
Determining whether radiotherapy can replace axillary surgery in ILC	57	52	61	0.039
Characterizing difference in post-mastectomy radiation between ER+ IDC and ER+ ILC	50	42	61	<.0001
Basic/translational research question				
Determining cell of origin for ILC	39	43	73	<.0001
Development of a centralized ILC data and tissue registry	56	70	77	<.0001
Developing and characterizing ILC models	47	70	71	<.0001
Characterizing differences in the tumor microenvironment between ILC and IDC	54	71	72	0.0001
Understanding of LCIS as a precursor ILC	43	46	60	<.0001
Characterizing subtypes of ILC (pleomorphic, mixed etc)	47	51	63	0.0001
Understanding of the unique etiology of ILC	46	49	66	<.0001
* Green: Highest rating within domain by stakeholder group				
* Red: Highest 2 ratings by group across all domains				

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P6-05-11

Active surveillance versus conventional treatment in low-risk DCIS; women's preferences in the LORD trial

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Background: Ductal carcinoma in situ (DCIS) is a potential precursor to breast cancer. Its incidence has increased multifold with the introduction of breast cancer screening and makes for 20% of all malignant breast lesions in women. DCIS has the potential to progress into invasive breast cancer. However, the majority of DCIS lesions are indolent and will never progress during the patient's lifetime. Consequently, there is a growing concern of

overdiagnosis and overtreatment for women with DCIS. The LORD trial is a non-randomized, patient preference trial comparing active surveillance to conventional treatment (i.e., breast conserving surgery with or without radiotherapy or mastectomy). The primary outcome of this trial is the percentage of women without an occurrence of ipsilateral invasive breast cancer after 10 years of follow up. Within the patient preference design, women are free to opt for either treatment arm. In addition to active surveillance of the DCIS, quality of life (QOL) of women included in the LORD trial is also actively monitored. The aims of this study were to: a) describe the distribution of participants within the treatment arms, b) identify women's motives to opt for their preferred treatment arm, and c) assess factors associated with a preference for either treatment arm. Methods: Data from the baseline patient QOL questionnaire was collected. This questionnaire was completed after the women's diagnosis and first consultation with their physician. Descriptive statistics were used to assess the distribution in both treatment arms. Thematic analyses were used to describe self-reported reasons for treatment selection derived from the open-ended question about treatment preference. Multivariable logistic regression analyses were used to assess associations between the patient characteristics and their preferred treatment arm. Results: In total 384 women completed the baseline questionnaire, of which 376 entered their final treatment decision. Of these women, 287 (76%) opted for active surveillance and 89 (24%) for conventional treatment. Most frequently cited reason for opting for active surveillance was that treatment was not yet necessary (55%). Also, patients' reasons for preferring active surveillance alluded to a high level of trust in the active surveillance plan (24%) and that disease progression could be picked up and treated in a timely manner (14%). Furthermore, 11% of patients cited the advice of their healthcare professional as a reason for opting for active surveillance and 8% cited reasons relating to altruism. Most reported reasons for opting for the conventional treatment arm were avoiding unnecessary risks (26%), avoiding cancer worry (18%), the notion that what doesn't belong, should be removed from the body (18%) and a need for closure (13%). In multivariable logistic regression analyses, high level of education (OR 2.17; 95%CI 1.09-4.38) and higher knowledge score (OR 1.8; 95%CI 1.07-3.02) were associated with a preference for conventional treatment. Furthermore, women opting for active surveillance more often reported the decision to be a shared decision between them and their healthcare professional (OR 2.30; 95%CI 1.18-4.47) compared to women who chose conventional treatment, who more often reported decision-making to be patient-driven. Age and tolerance of uncertainty were not significantly associated with treatment preference. Conclusion: The LORD trial is the first to actively offer women with low-risk DCIS a choice between conventional treatment and active surveillance. Within this trial, most women opt for active surveillance, even though clinical guidelines still recommend treatment for all women with DCIS. Women with low-risk DCIS report high levels of trust in their physicians and the safety of active surveillance. Their preferences also highlight the necessity to proof that de-escalating treatment of low-risk DCIS is safe.

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Understanding Patient Perspectives on Window of Opportunity Clinical Trial Participation in Breast Cancer

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Background: Window of opportunity (WOO) clinical trials take advantage of the waiting period between a patient's cancer diagnosis and standard treatment (usually surgery) to evaluate novel cancer therapies and their biologic effects in vivo. These types of trials are being increasingly harnessed in the clinical setting for the safe and rapid evaluation of novel therapeutic strategies in treatment naive patients, thereby expediting drug development. Distinct from neoadjuvant trials, no therapeutic benefit is envisaged and the patient's standard treatments are not intentionally delayed. The purpose of this study was to understand the

patient motivations and perspectives for participating in WOO trials. Methods: This study was conducted at an academic cancer center where two breast cancer WOO trials were ongoing (NCT04781725 and NCT04676516). Eligible patients with newly diagnosed operable invasive breast cancers participating in either of these WOO trials were recruited to this separate study. Patients were provided with a questionnaire that surveyed their motivation and perspectives for participation or lack of participation in the WOO trial Results: From April 2021- May 2022, the study recruited 89 patients with age ranging from of 40-78 yrs with tumors ranging from 1.5-4.3 cm. Surgical wait times ranged from 2-8 weeks. Of the 83 patients that participated in a WOO trial, the most common reasons for participation included (a) the potential to benefit other patients in the future (90%) (b) trust in their treating doctor (88%), (c) desire to contribute to scientific research (62%) and (d) a belief that they may benefit from the therapy (39%). For these patients, 49% reported that the possibility of a repeat biopsy would not deter them from trial participation; whereas 11% said that it definitely would. Of the 6 patients that chose not to participate in a WOO trial the most common reasons included (a) travel or transportation issues (50%) and (b) lack of belief of potential benefit to them (33%). For these patients, when asked whether the participation of a cancer patient in the design of the WOO trial would change their mind, all reported that it would not make a difference. Conclusion: WOO trials are becoming increasingly common in oncology research. Understanding patient perspectives for WOO trial participation is useful to inform trial design and communication approaches in future WOO trial efforts.

Disclosure(s):

Vanessa Lopez Ozuna, MD PhD: No financial relationships to disclose

Gregory R. Pond, PhD PStat: Astra-Zeneca: Consulting Fees (e.g., advisory boards) (Terminated, March 1, 2021); Merck: Consulting Fees (e.g., advisory boards) (Terminated, July 1, 2021); Profound Medical: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing); Takeda: Consulting Fees (e.g., advisory boards) (Ongoing)

John MS Bartlett, PhD: Agendia: Contracted Research (Terminated, December 31, 2020); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); BioNTech AG: Consulting Fees (e.g., advisory boards) (Terminated, December 31, 2020); Biotheranostics, Inc.: Consulting Fees (e.g., advisory boards) (Terminated, December 31, 2020), Contracted Research (Terminated, December 31, 2020), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, December 31, 2020), Travel expenses (Terminated, December 31, 2020); Breast Cancer Society of Canada: Travel expenses (Terminated, December 31, 2020); Cerca Biotech: Consulting Fees (e.g., advisory boards) (Ongoing); Exact Sciences: Contracted Research (Ongoing); Genoptix: Contracted Research (Terminated, December 31, 2020); Herbert Smith French Solicitors: Consulting Fees (e.g., advisory boards) (Terminated, December 31, 2020); Insight Genetics, Inc.: Consulting Fees (e.g., advisory boards) (Terminated, December 31, 2020); NanoString Technologies, Inc.: Contracted Research (Terminated, December 31, 2020), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, December 31, 2020), Travel expenses (Terminated, December 31, 2020); OncoCyte Corporation: Consulting Fees (e.g., advisory boards) (Ongoing); Oncology Education: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, December 31, 2020); oncoXchange/MedcomXchange Communications Inc: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Ontario Institute for Cancer Research: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Terminated, December 31, 2020); Rna Diagnostics Inc.: Consulting Fees (e.g., advisory

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7:00 AM - 8:15 AM

P6-05-13

The Psychological Impacts of COVID-19 on Breast Cancer Patients in China

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Background:

Approximately 30% to 50% of breast cancer patients experienced mental distress prior to the advent of COVID. The delayed access to cancer treatment due to the outbreak of COVID -19 pandemic posed a unique challenge to breast cancer patients and caused a significant level of mental distress among them. In the current research, we examined the psychological impacts of COVID on breast cancer patients in China using Symptom Checklist-90-R (SCL-90-R).

Method:

Participants were breast cancer patients at the outpatient clinic of Xijing hospital. The study was conducted virtually, and the questionnaires were distributed via Wenjuanxing, the Chinese alternative of Qualtrics. The researchers were healthcare workers affiliated with Xijing hospital, and the survey was sent to a breast cancer patient support group which included 1399 cancer patients and 6 healthcare workers. The initial sample consisted of 199 participants who signed an informed consent form to participate in the study. The inclusion criteria were as follows: 1) diagnosed with breast cancer, 2) aged 18 years or above, and 3) had no history of cognitive impairment or previous diagnosis of psychiatric disorders. The validated Mandarin version of the SCL-90-R (Wang, 1984) was then given to the participants to evaluate their psychological status. Categorical variables were summarized as numbers and percentages; continuous variables were described as mean (M) ± standard deviation (SD). Data were analyzed using IBM SPSS Statistics Version 26.

Results:

Participants (N = 195) filled out the SCL-90 questionnaire in February, 2020. All participants were female breast cancer patients treated at Xijing hospital, among which 16.41% , 36.41%, 19.49%, and 28.21% had respectively received treatment for less than a year, 1-3 years, 3-5 years, and 5 years or more. 64.62% of the patients were at stage I; 0.77% were at stage II and III; 4.62% were at stage IV according to TNM classification. The molecular type of participants

is as follows: 47.2% of ER+ HER2-, 31.8% of HER2+, and 21.0% of Triple negative. Participants whose treatments continued to be delayed, on average, reported an elevated general psychopathology score ($M = 1.48$, $SD = 0.47$) compared to participants whose treatments were resumed ($M = 1.30$, $SD = 0.34$), and the difference was statistically significant, $t(193) = 2.96$, $p = .003$, $d = 0.44$, 95%CI [0.06, 0.30]. The one-way ANOVA revealed a marginally significant effect of length of treatment delay on general psychopathology score, $F(4, 190) = 2.09$, $p = .08$, $\eta^2 = .04$. Follow-up multiple comparison analysis showed that participants who had their treatment delayed for 3 weeks to 1 month ($M = 1.70$, $SD = 0.70$) reported significantly higher general psychopathology scores than participants whose delay in treatment was less than 1 week ($M = 1.34$, $SD = 0.40$), $p = .05$. General health status ($p < .001$) and current treatment status ($p = .02$) are the only two variables that were statistically associated with general psychopathology score. Poorer perceived health status and current delay in treatment were associated with higher general psychopathology score. Additionally, younger age was associated with higher interpersonal sensitivity ($p = .01$) and hostility ($p = .006$).

Conclusions:

We found that breast cancer patients at an advanced stage were more likely to experience psychological symptoms with longer treatment delay, and whose treatments continued to be delayed reported elevated psychological symptoms than individuals whose treatment were resumed, regardless of treatment type. Additionally, a treatment delay of more than three weeks might have exacerbated breast cancer patients' psychological symptoms, whereas a short-term delay of less than three weeks was less likely to have a significant effect on one's mental well-being.

Table1: Demographic Characteristics and Health Status of The Participants

	Number of Patients	Percentage of Patients
Marital Status		
Married	177	90.8
Single, widowed, or separated	18	9.2
Education		
Middle school or below	109	55.9
High school or above	86	44.1
Occupation		
Unemployed or self-employed	44	22.6
Employed for wage	80	41.0
Retired	71	36.4
Age		
≤ 45	55	28.2
46-55	95	48.7
56-65	32	16.4
> 65	13	6.7
General Health Status		
Excellent	31	15.9
Great	105	53.8
Fair	51	26.2
Poor	8	4.1
Length of Treatment		
Less than a year	32	16.4
1-3 years	71	36.4
3-5 years	38	19.5
5 years or more	54	27.7
Length of Delay		
Less than a week	82	42.1
1-3 weeks	27	13.8
2-3 weeks	13	6.7
3 weeks to 1 month	14	7.2
More than 1 month	59	30.3
Breast Cancer Stage		
Stage I	126	64.6
Stage II and III	60	30.7
Stage IV	9	4.7
Molecular Type		
ER+ HER2-	92	47.2
HER2+	62	31.8
Triple negative	41	21.0

Table2A: Multiple Regression analysis for SCL-90 dimensions

SCL-90 dimension	General Index		Somatization		Obsessive-Compulsive		Interpersonal Sensitivity		Depression	
	β	SE	β	SE	β	SE	β	SE	β	SE
Age	-0.13	0.04	0.03	0.54	-0.12	0.54	-0.19**	0.43	-0.16	0.64
Education	-0.05	0.07	-0.09	1.01	-0.04	1.02	-0.03	0.80	-0.05	1.19
Occupation	-0.05	0.02	-0.03	0.31	-0.04	0.31	-0.02	0.25	-0.10	0.37
General Health	0.34***	0.04	0.35***	0.64	0.27***	0.64	0.29***	0.51	0.36***	0.75
Breast Cancer Stage	-0.01	0.05	-0.10	0.80	-0.04	0.80	0.02	0.63	-0.004	0.94
COVID effect on City	-0.05	0.06	-0.004	0.89	-0.11	0.90	0.03	0.71	-0.001	1.05
Current Treatment Status	-0.17*	0.06	-0.19***	0.94	-0.14	0.94	-0.15*	0.74	-0.16*	0.10
Length of Delay	-0.004	0.02	0.03	0.27	-0.007	0.27	-0.03	0.21	-0.01	0.31

* $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$

Table 2B: Multiple Regression analysis for SCL-90 dimensions

SCL-90 dimension	Anxiety		Hostility		Phobic Anxiety		Paranoid ideation		Psychoticism	
	β	SE	β	SE	β	SE	β	SE	β	SE
Age	-0.02	0.23	-0.21**	0.29	-0.07	0.32	-0.08	0.24	-0.14	0.36
Education	-0.06	0.38	-0.03	0.55	-0.04	0.60	-0.02	0.45	-0.002	0.56
Occupation	0.08	0.12	-0.07	0.17	-0.04	0.19	-0.02	0.14	-0.07	0.21
General Health	0.06	0.24	0.21**	0.35	0.22**	0.38	0.19*	0.28	0.26***	0.43
Breast Cancer Stage	0.03	0.30	-0.02	0.43	-0.02	0.47	-0.01	0.35	-0.008	0.53
COVID effect on City	-0.04	0.33	-0.05	0.48	-0.07	0.53	-0.10	0.40	-0.08	0.59
Current Treatment Status	-0.02	0.35	-0.12	0.51	-0.11	0.56	-0.12	0.42	-0.19**	0.62
Length of Delay	0.06	0.10	0.004	0.14	-0.03	0.16	-0.004	0.12	-0.01	0.18

Disclosure(s):

Yijia Wang, n/a: No financial relationships to disclose

Yuqing Yang, MD: No financial relationships to disclose

Changjiao Yan, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P6-05-14

The association of sleep quality with anxiety, depression and social support in breast cancer patients with chemotherapy

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Background:Chemotherapy has side effects on breast cancer patients, and sleep disturbance is one of the common psychological symptoms. Purpose: This study aimed to examine the incidence of sleep disorders and investigate the relationship between anxiety and depression, hope, social support and sleep disorders in breast cancer patients with chemotherapy in China.Results:Total 350 patients were administered questionnaires, and 329 patients completed the questionnaires. The recovery rate was 94%. The majority of participants reported clinically significant sleep disturbance prior to chemotherapy (67.8%), during chemotherapy (71.8%), and after chemotherapy (72.2%). Pearson correlation analysis showed that the higher the direct support, emotional support, social interaction support, informational support and total social support score, the lower the total PSQI score of breast cancer patients ($r = -0.212, -0.292, -0.236, -0.271, \text{ and } -0.195$ $p < 0.01$, respectively). Multifactorial model analysis showed that direct support, anxiety and age were the three main factors that affected sleep quality in breast cancer patients. Conclusions:social support may provide a powerful tool to reduce anxiety and improve sleep quality in breast cancer patients with chemotherapy.

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7:00 AM - 8:15 AM

P6-05-15

Standard of Care for HR+/HER2- Breast Cancer: Integrating The “Yale Model Shared Decision-Making Multidisciplinary Team Solution” into the Practice Setting

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Background: Breast cancer patients are faced with treatment choices that can involve complex preference-sensitive decisions. The National Quality Forum initiated a “Call to Action” to integrate shared decision-making (SDM) processes into practice where clinicians and patients work together to make healthcare decisions that align with what matters most to patients. Projects In Knowledge, @Point of Care, Dartmouth and Yale collaborated to develop a pilot educational initiative to address and improve patient-centered care and SDM processes in the institutional cancer care setting.

Methods: Training materials co-developed for the Yale Breast Cancer multidisciplinary team

(N=11: oncologists, nurses/NPs, pharmacist) address SDM, CDK4/6 Inhibitor treatment of metastatic HR+ HER2- breast cancer, and clinician-patient role play methods implementing SDM in treatment discussions/decisions with patients. Reinforcement training, based on interim interview and case role play assessments, was customized to meet specific needs of the team. Qualitative semi-structured interviews and simulation case role play observational methods, using a two-rater system, were used to assess improved SDM performance. Baseline pre-intervention interviews and case role play assessments were compared to interim post-intervention and end of pilot (EOP) post-reinforcement training intervention interviews and case role play assessments (using a Likert scale 0-4 rating score: 0=0%; 1=25%, 2=50%; 3=75%; 4=100%). Following the training and assessments, a focus group of team members provided insights into the performance of the group, assessed the acceptability, feasibility, and repeatability of the program, and informed future education.

Results: Semi-structured interview findings revealed that clinicians learned about nuances of CDK 4/6 inhibitors, crystallized their understanding of SDM through reinforcement training (customized in real time), and felt they were better able to implement SDM as a result of their case role play assessments. Training empowered the Yale Breast Cancer team to show pre- to post-education improvement in SDM case role play scenarios, ranging from 16% to 39%. Areas of greatest improvement: 1) determining decision style preference (+36%); 2) determining patients' risk/burden tolerance (+32%); 3) determining patients' activation, engagement, and self-efficacy (+34%), 4) determining trade-off decisions with patients (+39%), and 5) determining patients' readiness to make a decision (+32%). Future research should explore how best to integrate SDM into the real world time restricted clinical practice.

Conclusions: Educational training improved SDM skills for the multidisciplinary Yale Breast Cancer team, which can lead to improved clinician-patient decision-making and patient-centric care. The training process also facilitated team building and encouraged ongoing participation in SDM.

Overall Yale Breast Cancer SDM Pilot Case Study Role-Play Assessments

Overall Yale Breast Cancer SDM Pilot Case Study Role-Play Assessments (Data reflect findings for 11 participants who completed their case role play)			
Domain	Baseline: Percentage of SDM Domains Addressed (N=11)	End of Pilot: Percentage of SDM Domains Addressed (N=11)	Improvement Baseline vs EOP % Change
Reasonable Options	59%	75%	16%*
Decision Style Preference	28%	65%	36%**
Knowledge	47%	71%	24%**
Risk/Burden Tolerance	31%	63%	32%**
Activation, Engagement, Self-Efficacy	15%	48%	34%**
Trade-Off Decisions	32%	71%	39%**
Readiness	46%	78%	32%**

*P<0.05, ** P<0.005

(Data reflect findings for 11 participants who completed their case role play)

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-05-16

Social isolation induces gut dysbiosis, mitochondrial metabolic dysfunction, and infiltration of tumor immunosuppressive cells: do they explain enhanced mammary tumorigenesis?

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Inadequate social contacts and loneliness, often referred to as social isolation (SI), are associated with increased mortality from many diseases, including breast cancer. Up to 41% of breast cancer patients have been identified as feeling socially isolated. Moreover, socially isolated breast cancer survivors have a 43% higher risk of recurrence than socially integrated survivors. To prevent increased mortality, biological mechanisms which mediate the effects of SI on cancer need to be identified. One unexplored, but possible mechanism is through the gut microbiota. Through bidirectional interactions, the gut is affected by stress and the gut microbiota in turn can modulate stress response, host immunity and metabolism. Here we tested the hypothesis that SI induces gut dysbiosis. In our study, repeated in four separate experiments, adult female mice were divided into two groups – those kept group housed (GH, 4 mice per cage) and those housed singly in SI for 4 weeks. Several differences in the gut microbial family, genus and species levels were seen, but the differences were mostly unique to each of the four experiment. Beta-diversity was increased in three of the four studies in SI mice. Since beta-diversity is increased by aging, SI may accelerate the aging process. At the genus level, SI significantly suppressed the abundance of Akkermansia in all four studies and increased Acetatifactor in three studies. These two bacterial changes are expected to disrupt mitochondrial oxidative phosphorylation (OXPHOS), most likely by suppressing the short-chain fatty acid production. Further, low Akkermansia and high Acetatifactor are expected to increase inflammation. In a separate study, we discovered that SI impaired OXPHOS and activated inflammatory pathways in the mammary gland. We also have assessed immune cells in the spleen. SI increased the frequency of pro-inflammatory CD4+RORy+ cells, and the immunosuppressive Treg (CD4+Foxp3+) and PMN-MDSCs cells. In addition, SI increased PD1 expression in Foxp3+ cells, suggesting that anti-PD1 therapy might adversely affect socially isolated breast cancer patients by invigorating Treg cells. We are currently studying if the changes in the gut microbiota in SI mice are causally linked to their impaired mitochondrial metabolism, immunosuppression and increased mammary cancer mortality. We also plan to investigate if dietary modifications can reverse gut dysbiosis in SI mice and prevent their increased mortality from mammary cancer.

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P6-05-17

Recruitment challenges in a UK surgical de-escalation study: preliminary qualitative research findings from the SMALL trial

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Background SMALL (ISRCTN 12240119) is a novel UK phase III multicentre randomised trial comparing vacuum-assisted excision (VAE) to surgery for small screen-detected breast cancers with biologically favourable characteristics. Acceptance by the clinical community and recruitment to SMALL was anticipated to be challenging as it involves randomisation, surgical de-escalation and minimally-invasive percutaneous treatment (VAE). A QuinteT Recruitment Intervention (QRI) has therefore been integrated throughout SMALL's recruitment period, with the aim of optimising recruitment and informed consent. Methods The QRI in SMALL has involved the analysis of: a) screening log data b) written views from recruiters on the two treatments and their advantages/disadvantages c) in-depth semi-structured interviews with members of the Trial Management Group (TMG) and clinician-recruiters and d) audio-recordings of recruitment discussions with potentially eligible patients. Recruitment challenges were identified and addressed through the provision of written recruitment tips documents, and group and individual feedback sessions with recruiters. Results There was widespread support for the concept of the SMALL trial within the clinical community. Recruiters recognised the pioneering role of SMALL as the only current surgical de-escalation randomised trial in screen-detected breast cancer. Key recruitment challenges revolved around i) healthcare professionals (HCPs) who met patients early in the pathway providing information indicating that they were being referred for surgery (without mentioning SMALL or VAE), ii) concerns around the balance of de-escalation/escalation of different treatment modalities (e.g. some clinicians may prefer to de-escalate radiotherapy in preference to surgery in low-risk patients), iii) challenges in articulating equipoise in a surgical de-escalation trial, iv) patient preferences (primarily for surgery) and recruiter discomfort in exploring/addressing such preferences and v) fewer eligible patients than anticipated. QRI actions to overcome these issues included developing a tips document for HCPs meeting patients early in the pathway, highlighting the need to refrain from making treatment recommendations. A more generic tips document was also developed emphasising the importance of the early introduction of the study, provision of balanced information about both treatments, encouraging recruiters to engage with patients' concerns and preferences, and adequate explanation of randomisation. Group and individual feedback sessions focussed on two key areas – articulating equipoise through balanced information provision, and considering optimal ways to explore patient preferences where they are expressed. Despite the many set-up and recruitment challenges that arose from opening at the start of the pandemic, SMALL has recruited 142 patients to date from 23 sites, with an approached to randomised patient ratio of ~50%. Conclusion SMALL is a novel surgical de-escalation study in breast cancer, which will provide critical evidence to support reductions in treatment of good prognosis disease. Using a range of qualitative methodology, the QRI has identified both broad support for the study within the clinical community, but has also identified barriers to recruitment at both clinician and patient level. These challenges have been addressed employing a range of methods, and the recruitment level and approach/randomised ratio shows the overall acceptability of this study to patients. Further work will involve interviews with patients, with a focus on their views on de-escalation, and further recruiter feedback sessions. Taken together, this data will help inform the development and design of future de-

escalation and treatment optimisation studies in breast cancer. SMALL is funded by the UK NIHR HTA programme, award 17/42/32

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-05-18

Reasons for Delay in Indian Women Presenting with Primary Stage III or IV Breast Cancer: An Observational Study

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Background: Developing countries like India share higher burden of deaths due to breast cancer, despite having lower incidence than the west. Greater proportion of patients presenting with advanced stages of cancer is one of the reasons for this disparity. Since the factors leading to such delay have not been well studied in Indian patients, we decided to perform this study. Methodology: This was an observational study conducted from Jan 2021 to July 2022. Purposive Non-Random sampling was used and patients who had stage 3 or 4 breast cancer and were between 18-80 years of age were recruited. Interview was done on a one-to-one basis in a secluded area. Descriptive statistics were used, and chi-square was used to study the association of socio-demographic and clinical variables with the delay status of the breast cancer. Results: A total of 75 participants were enrolled in the study with mean age of 52.5 years and SD of 12.5 years. Out of these, 74 had lump as their first symptom. Only 14 of these 74 presented early i.e., within 3 months of onset of symptoms. Rest 60 participants presented late (more than 3 months after onset of symptoms). Between these two groups, difference in incidences of pregnancy associated lumps (0% in < 3 months vs 13.1% in \geq 3 months, $p=0.002$), patients being afraid of treatment related complications (0% in < 3 months vs 6.6% in \geq 3 months, $p=0.039$) and their inability to decide because of lack of knowledge (0% in < 3 months vs 6.6% in \geq 3 months, $p=0.039$) were statistically significant. To our surprise, the thought that the lump was harmless and painless, embarrassment, limited access to healthcare and distance from the nearest healthcare facility, financial limitations, educational status, socio-economic status, family history of breast cancer, fear of mutilating surgeries and use of traditional medicine or spiritual care didn't have significant effect on whether the patients presented within or after 3 months of onset of symptoms. On the question of COVID pandemic related delay, only 16% of all patients cited this as an additional reason for delay and this was again, not different between the patients who presented within or after 3 months of onset of symptoms. Conclusions: Health promotion in terms of proper evaluation of pregnancy related lumps and awareness about the management options of breast cancer may help patients to present earlier to healthcare facilities and may help in improving breast cancer related outcomes in developing countries like India.

Disclosure(s):

SIDDHANT KHARE, MBBS, MS, MRCS: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-05-19

Racial Disparities in the Quality of Life and Vaccination of Breast Cancer Survivors during COVID-19: A Longitudinal Study

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Background: Older adults with pre-existing health conditions such as cancer are at higher risks of COVID-related morbidity and mortality. Moreover, the pandemic has triggered new sources of anxiety and stress impairing their quality of life (QoL), such as fear of infection, financial challenges, and social isolation. The goal of this study is to evaluate the changes in QoL of breast cancer patients and survivors during the pandemic and assess whether racial/ethnic minority patients were disproportionately affected. As the COVID-19 vaccines become available, another goal of the study is to examine the vaccination rate and symptoms after vaccination among patients of different racial/ethnic groups.

Methods: Two waves of surveys were sent out to the breast cancer patients registered in the Chicago Multiethnic Epidemiologic Breast Cancer Cohort (ChiMEC) via RedCap in the summers of 2020 and 2021 with response rates of > 48%. To measure anxiety and stress, we calculated an overall score (ranging from 0-44) using 11 questions on a 5-point Likert scale, with lower score representing better QoL. The questions were adopted from existing item banks, and the items showed good internal consistency (Cronbach's $\alpha = 0.84$). The second survey also contained questions on vaccination status, concerns, and symptoms after

vaccination.

Results: In the first wave of survey in 2020, no significant racial differences were found in the anxiety/stress scores among the 1300 breast cancer patients. In the second wave of survey in 2021, 1348 patients responded, with 66% of them also respondents of the previous survey. Compared to 2020, the average anxiety/stress score in 2021 decreased from 13.2 to 12.2 for White patients, while increased from 12.8 to 13.6 for Black patients. Mixed effects models showed that the scores worsened significantly for Black patients while improved significantly for White patients. Compared to Whites, Black patients were significantly less confident to find medical help and keep up with work/home responsibilities, while significantly more likely to feel isolated and overwhelmed, and more frequently worried about being sick and going to hospitals. The racial differences in the anxiety/stress scores became insignificant after adjusting for annual household income in multivariate linear mixed effect models. In terms of Covid-19 vaccination, 92.2% of the respondents got vaccinated, with no significant racial/ethnic difference. However, there were more Black patients who had not decided yet or did not respond to this question (Table). The major concerns for patients were the long-term and short-term side effects of the vaccines. In terms of symptoms after vaccination, the most reported symptoms were pain at injection site (62.0%), tiredness (50.2%) and muscle or body aches (30.8%).

Conclusions: Through a longitudinal study, we found that although the anxiety/stress scores of our patients remained moderate, White patients were having improved QoL while Black patients were doing worse. A third wave of survey is planned in the summer of 2022 to further examine this trend. In our study, the vaccination rates were very high among all racial/ethnic groups and the symptoms after vaccination were similar to the ones demonstrated in the general population. We hope that this information can proactively address some patients' concerns about getting vaccinated.

Table. Summary of the Second Wave of Survey by Racial/Ethnic Groups

Table. Summary of the Second Wave of Survey by Racial/Ethnic Groups

	Whites (n= 942)	Blacks (n= 304)	Others ^a (n=102)	p-value ^b
QoL score, mean (sd)	12.2 (5.9)	13.6 (7.0)	14.2 (5.9)	<0.001
Age at diagnosis, mean (sd)	53.9 (11.3)	54.8 (12.8)	47.8 (10.6)	0.26
Years since diagnosis, mean (sd)	7.5 (5.2)	7.9 (5.1)	6.0 (4.4)	0.34
Vaccination status				0.002
Yes	851 (90.3%)	261 (85.9%)	94 (92.2%)	
Not yet, but planned	5 (0.5%)	8 (2.6%)	1 (1.0%)	
Not decided yet	30 (3.2%)	16 (5.3%)	1 (1.0%)	
No, not planned	32 (3.4%)	6 (2.0%)	3 (2.9%)	
Did not respond	24 (2.5%)	13 (4.3%)	3 (2.9%)	
Concerns for not getting vaccinated ^c				
Long-term side effects	47 (75.8%)	16 (72.7%)	4 (100%)	0.88
Short-term side effects	25 (40.3%)	7 (31.8%)	1 (25.0%)	0.84
Do not trust government/ CDC	24 (38.7%)	6 (27.3%)	2 (50.0%)	0.67
Doubt the vaccine's effectiveness	18 (29.0%)	8 (36.4%)	1 (25.0%)	0.48
Do not know if it's suitable	14 (22.6%)	5 (22.7%)	0	0.80
Already had COVID so not needed	8 (12.9%)	2 (9.1%)	1 (25.0%)	1.00
Do not feel affected	6 (9.7%)	0	0	-
Not convenient to get	2 (3.2%)	0	0	-
Others	13 (21.0%)	6 (27.3%)	0	0.43
Symptoms after vaccination ^d				
Pain at injection site	538 (63.2%)	141 (54.0%)	69 (73.4%)	0.008
Tiredness	455 (53.5%)	95 (36.4%)	56 (59.6%)	<0.001
Muscle or body aches	268 (31.5%)	64 (24.5%)	40 (42.6%)	0.031
Headache	223 (26.2%)	47 (18.0%)	29 (30.9%)	0.007
Chills	181 (21.3%)	26 (10.0%)	21 (22.3%)	<0.001
Fever	121 (14.2%)	18 (6.9%)	19 (20.2%)	0.002
Redness at injection site	105 (12.3%)	25 (9.6%)	9 (9.6%)	0.22
Swelling at injection site	85 (10.0%)	27 (10.3%)	8 (8.5%)	0.87
Nausea	48 (5.6%)	11 (4.2%)	3 (3.2%)	0.37
Itching at injection site	37 (4.3%)	21 (8.0%)	2 (2.1%)	0.019
Vomiting	5 (0.6%)	3 (1.1%)	0	0.41
Allergic reactions	5 (0.6%)	1 (0.4%)	0	1.00
Others	46 (5.4%)	12 (4.6%)	8 (8.5%)	0.61

^a Other patients include 59 Asians, 40 Hispanics, 1 Native American and 2 unknown

^b p-values for the comparison between Black and White patients were estimated using t-tests for continuous variables and χ^2 tests and Fisher's exact tests for categorical variables

^c Patients who did not plan to get vaccinated or who had not decided yet can select multiple answers for their concerns, so the number (%) of patients selecting each option were shown

^d Patients who got vaccinated can report multiples symptoms, so the number (%) of patients selecting each option were shown

Disclosure(s):

Fangyuan Zhao, MA: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-05-20

Quitxt Mobile Cessation Service for Cancer Patients: Development and Implementation Process

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Background: Physicians have unparalleled access to smokers. It is estimated that over 70% of smokers visit a physician every year, which provides a powerful opportunity to promote tobacco cessation by asking about smoking behaviors and providing cessation advice and counseling to tobacco users at every visit. In general, smokers consider a physician's advice to quit an important motivator to make a quit attempt. We adapted our Quitxt program to the patient population attending the Mays Cancer Center at UT Health San Antonio. Every patient is screened for tobacco use; if the patient is a tobacco user, healthcare providers (HCPs) advise them to quit, offer nicotine replacement therapy if needed, and recommend enrollment in the Quitxt program. Purpose: We present the development process and implementation of Quitxt, our evidence-based, bilingual mobile cessation service tailored to the patient population of the Mays Cancer Center (MCC). Methods: Tobacco screening was integrated into EPIC, and the Quitxt program was added to the BestPractice Advisories Banner. All patients are screened for tobacco use. If a tobacco-using patient is identified, the BestPractice Advisories Banner will appear, prompting HCPs to counsel patients to quit and encourage them to enroll in Quitxt. Selecting referral to Quitxt will activate our Patient Navigator (PNs) follow-up. PNs contact patients and provide support, positive reinforcement, and encouragement. They continue with monthly follow-ups for the duration of the program. The EPIC system also places instructions on how to enroll in Quitxt in the patients' after-visit summary. The Quitxt library of messages was adapted to the patient population of the MCC. We also developed a news-style video for HCPs with peer modeling on how to approach patients and enroll them in Quitxt. Results: The program will be launched at the MCC on August 1st, 2022. We will present the development and implementation process and preliminary results related to patient enrollment characteristics, stages of change, smoking abstinence, and patient navigation support. Conclusion: This project will greatly increase the accessibility and utilization of a bilingual evidence-based smoking cessation service among primary care and cancer patients. Quitxt will also serve as a model that can be easily adapted and replicated by any organization or network interested in serving their patients with an evidence-based cessation program. Quitxt represents an affordable approach to reach tobacco-using patients, produce a public health impact, reduce health service costs, and reduce tobacco-related diseases and mortality.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-05-21

Quality of Life and Perspectives of Older Adults with Early & Locally Advanced Breast Cancers Undergoing Pre-operative Therapy

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Background: Breast cancer (BC) is the commonest diagnosed cancer in Singaporean women. Increasingly, non-metastatic BC are treated aggressively with neoadjuvant therapy (NAT). Early identification and addressing supportive care needs of NAT treated patients is important for effective cancer care whilst maintaining optimal physical, psychological and social function. This project aims to explore the longitudinal trends of quality of life (QOL) of BC patients enrolled in a NAT program. Methods: This was a prospective cohort study of females aged ≥ 21 diagnosed with non-metastatic BC, referred to the NAT program at the SingHealth network of acute hospitals. The Functional Assessment of Cancer Therapy-Breast (FACT-B) was used as a health related QOL measure prior to NAT, within 2 months post definitive breast surgery and at 1-year post diagnosis. In older adults (OA) ≥ 65 years, the Attitude scale, Now vs Later as well as Health Outcome tool were also performed at baseline. Here we report pre-NAT baseline FACT-B and questionnaire results of OA patients recruited into the NAT program between Jun 2020 and Jun 2021. Results: Pre-NAT median FACT-B scores was 117 (IQR 102-126) for the entire cohort (n=119) and 116 (IQR 104-126) for OA (n=22). OA had significantly lower median Social Wellbeing score at baseline compared to patients < 65 years (p=0.01), while Physical, Emotional, and Functional Wellbeing were not significantly different. More than 50% of OA favoured QOL over quantity of life on the Attitude Scale. 68% of patients would rather have

QOL now than 1 year later with half expecting their QOL to reduce by 50% in this time period. When the time scale was extended to 5 years, 64% would rather have QOL 5-years from now instead of QOL now with close to 80% expecting their QOL to be lower in 5 years than presently. Of the 4 outcomes, maintaining independence scored the highest, followed by keeping alive, then reducing / eliminating pain and other symptoms. Conclusion: Our study suggests that OA with BC report similar QOL to younger patients at baseline prior to NAT. Majority of OA patients favoured QOL over quantity of life, and viewed the ability to maintain independence as more important than survival prolongation representing their unique attitude towards cancer treatment and outcomes.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-05-22

Multilevel, Multicomponent Intervention to Improve Informed Decision-Making about Clinical Trial Participation among Cancer Patients

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Background: Knowledge gained through cancer clinical trials (CTs) has been proven critical to preventing, diagnosing and treating the disease, and providing the evidence base for clinical

practice. Major advances in cancer treatment, which are essential for improving patients' outcomes, come from investigations of new therapeutic agents in CTs. Despite the large number of available studies and improvements in public awareness about CTs, participation of underrepresented minorities in clinical research has been persistently low, with only 2 to 5% of Latinos and African Americans participating in cancer treatment trials. Barriers to participation are multilevel, complex, and multifactorial, including study design, healthcare system barriers, and patient- and medical team-related factors. Structural inequities, social determinants of health, distrust of government, patient-doctor communication, cultural and language barriers, and lower levels of health literacy have all been cited as common barriers for Latino and African American populations. Purpose: To improve informed decision-making about cancer CT participation among cancer patients and community members through a bilingual multilevel, multi-communication approach, including 1) a randomized controlled educational trial (clinic-based settings), and 2) a community education module (community-based settings). We will assess the impact of the intervention on awareness, attitudes, self-efficacy, and intentions to consider CTs as an appropriate treatment option for cancer and improve CT participation rates. Methods: The clinical setting includes a 2-group, parallel, randomized study with 400 patients from the Mays Cancer Center. The intervention group receives 1) a bilingual educational video on CTs, 2) a low literacy booklet, 3) support from a patient navigator (PN), and 4) an invitation to join our Salud America! network providing online/social media CT information. The control group receives a general fact sheet on CTs. All healthcare providers involved in clinical research will participate in Webinars to raise awareness of implicit bias and the importance of inclusive research. The community-setting intervention features a prospective single-group pre/post design, where participants (400) act as their own controls. They will receive an educational session on CTs provided by a community health educator + a low literacy booklet. Results: Focus groups guided the development of the video script, booklet, and educational materials. The short video features real cancer patients sharing their experience with CTs and how they overcame common barriers. Patient recruitment starts in August 2022. Preliminary results will be presented. Conclusions: Multilevel interventions involving culturally tailored decision aids (i.e., online video, low literacy booklet) in combination with care coordination by a PN can effectively address common barriers influencing patient decision-making regarding CTs, raise awareness, and increase positive attitudes and CT participation among specific groups with low participation in clinical research. Keywords: health equity, clinical trials, Latinos, underrepresented groups

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-05-23

Lifestyle interventions and complementary care use among oncology patients: a survey in a large teaching hospital population

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Introduction After a cancer diagnosis and treatment patients often experience chronic symptoms such as fatigue, mental problems, decreased quality of life, sexual problems, hot flashes, nausea and postoperative pain. The unmet needs of patients managing these symptoms, improve the demand for Integrative Medicine (IM), which is lifestyle and evidence based complementary care. The prevalence of IM use varies in the Netherlands, according to published data. **Aim** The first aim of the study was to evaluate the prevalence and associates of the use of IM by patients after a cancer diagnosis. The second aim was to gain insight into the need for guidance of cancer patients in a large Dutch teaching hospital. **Methods** A cross-sectional design with data collected through a structured, self-reporting questionnaire. This was created by combining a validated questionnaire to evaluate IM use in the Netherlands and a questionnaire on IM use developed by The Dutch Breast Cancer Association. Cancer patients diagnosed with breast cancer, colon cancer, prostate cancer or testicular cancer were invited to fill out the questionnaire. They were all and treated in the period of 2018-2019. Patients were included one to three years after completing treatment. Descriptive statistics and logistic regression analysis were used to analyze the results. **Results** 1850 patients received the questionnaire and 1028 patients responded to the survey (56%). 29.4% used complementary care such as self-care products (8.3%), physician-assisted self-care (9%) or self-help techniques (10.5%). 40.3% made one or more lifestyle changes during or after cancer treatment regarding food (33.8%), exercise (56.1%), relaxation (40.9%), social factors (35.6%), life purpose (23.7%) and sleep (37.8%). Associates of complementary care use were breast cancer, gender (women) and age. The information about IM was mostly obtained by patients through the hospital or internet. Patients reported a preferred way to receive information by treating physician (53.9%), specialized nurse (59.2%), primary care physician (25.1%) or hospital brochure (26.3%). 82.3% of the patients, including patients who did not use IM at all, placed great value on receiving reliable information from their doctors or nurses about IM. **Conclusion** Up to two thirds of the oncology patients are using a form of IM. Internet is one of the most important information source. For safety reasons and to meet the demand of most oncology patients for reliable information, it's important to provide all oncology patients with evidence-based information regarding lifestyle and evidence based complementary care. The majority of patients place great value on receiving this information from their doctor or nurse.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-05-24

Implementing System Solutions for Survivorship Care Plans

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Background: A survivorship care plan (SCP) is a detailed cancer care summary and future care plan that is generally given to a patient upon completion of adjuvant treatment for a cancer diagnosis. The initial goals of SCPs were to educate patients and other health care professionals about the treatments received, make them aware about potential long-term effects of therapy, and emphasize recommendations for future cancer screening and care (1). Due to numerous barriers—scheduling, staffing, and lack of awareness—SCPs are not delivered to all eligible patients. To address this unmet need our multidisciplinary breast clinic (MDBC) established an Advanced Practice Professional (APP) Survivorship Clinic. With the acute impact of the COVID-19 pandemic, survivorship referrals decreased. We, therefore, developed and implemented system solutions to address SCP access. Methods: System solutions include partnering with the Cancer Registry to provide the list of patients potentially in need of survivorship visits, partnering with pharmacy to confirm patient eligibility, creating specifically designated telemedicine survivorship visits in our electronic scheduling system, prospectively scheduling persons identified, engagement of APPs across the MDBC, and establishing a single coordinating point. Numbers of SCPs delivered are tracked monthly and patient satisfaction is assessed through data collected Press Ganey surveys. Results: This presentation will share our process interventions and outcomes as they mature. Our early data demonstrate the efficacy of the workflow and appear promising. Conclusion: We anticipate that system-based solutions will provide more patients with SCPs and demonstrate patient satisfaction. Blaes AH, Adamson PC, Foxhall L, Bhatia S. Survivorship Care Plans and the Commission on Cancer Standards: The Increasing Need for Better Strategies to Improve the Outcome for Survivors of Cancer. *JCO Oncol Pract*. 2020 Aug;16(8):447-450. doi: 10.1200/JOP.19.00801. Epub 2020 Apr 8. Erratum in: *JCO Oncol Pract*. 2020 Nov;16(11):774. PMID: 32267803. Gache, K., Leleu, H., Nitenberg, G. et al. Main barriers to effective implementation of stroke care pathways in France: a qualitative study. *BMC Health Serv Res* 14, 95 (2014). <https://doi.org/10.1186/1472-6963-14-95>

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-05-25

HT Helper: A Mobile App to Promote Hormone Therapy Adherence among Breast Cancer Patients

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Background: Adjuvant hormonal therapy (HT) is highly effective and appropriate for nearly all women with hormone receptor-positive tumors, making such treatment the most widely prescribed therapy for patients with this type of breast cancer. Despite its proven benefits in

reducing cancer recurrence and improving survival, HT adherence is suboptimal (less than 80%). About 33% of patients do not take their medication as prescribed and are at increased risk of disease recurrence and lower survival. Smartphone ownership has increased substantially over the past decade, providing an extraordinary opportunity for innovation in the delivery of tailored interventions to improve patients' adherence to hormonal therapy. Purpose: We present preliminary results of a pilot study to test the feasibility of an intervention consisting of a theory-based, bilingual, culturally tailored, and interactive mobile app + patient navigation to empower patients' self-monitoring and management by facilitating patient education, self-efficacy, early identification and reporting of side effects, delivery of self-care advice, and timely feedback through direct communication between the patient and the oncology team. Methods: This is a 2-group parallel, randomized control trial recruiting patients (120) receiving hormone therapy treatment and attending the breast clinic at the Mays Cancer Center (MCC). The intervention group receives two components: 1) the HT Helper phone app; and 2) assistance from a patient navigator who will provide educational, psychosocial support and reinforcement, address common barriers, and facilitate the interaction with the medical team as needed. The control group receives the usual care and information provided by the MCC's breast clinic to patients undergoing HT. The app and navigation support are based on Social Cognitive Theory and principles of motivational interviewing. Patients are assessed at baseline, three and six months. The primary outcome is HT adherence. Additional variables of interest include self-efficacy, social support, depression, side effects, anxiety, and quality of life. We also assess app usability and satisfaction. Results: We have recruited 108 patients, 56 in the intervention group and 52 in the control group. The mean age is 57.5 years, 58.3% are Latinas, 41.7% have less than high school education, 54.2% have a family income of less than \$50,000/year and 52.8% have Medicare/Medicaid. In addition to descriptive data, we will present results of the 3-month and 6-month follow-ups. Conclusion: The anticipated outcome of this innovative, multi-communication study is a scalable, evidence-based, and easily adaptable intervention with potentially broad use to patients using oral anticancer agents. The intervention has the potential to improve breast cancer outcomes by reducing recurrence, improving quality of life and survival, and reducing healthcare costs. The ultimate goal of this innovative, multi-communication intervention is to improve overall survival and life expectancy, enhance quality of life, and decrease healthcare costs.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-05-27

FEASIBILITY, SAFETY AND EFFICACY OF A COMBINED SUPERVISED PHYSICAL EXERCISE AND NUTRITIONAL PROGRAM IN A SELECTED POPULATION OF LUMINAL METASTATIC BREAST CANCER PATIENTS: ONCARE-01 PILOT STUDY

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Background: Supervised exercise programs (SEP) have demonstrated an improvement in quality of life (QoL), cardiovascular health, treatment tolerance and disease outcomes in early breast cancer patients. In metastatic breast cancer (MBC), previous data suggest SEP are safe but no impact on QoL and a low adherence to programs were shown. These studies included a heterogenous population in terms of type of treatments received, numbers of previous lines or comorbidities. From our perspective, MBC profile that could benefit most from SEP needs to be explored. Thus, we conducted a pilot study to assess adherence, safety and impact on QoL of a combined SEP and nutritional program (NP) in a selected population of MBC of patients treated with cyclin-dependent kinase 4/6 inhibitors (iCDK 4/6). **Methods:** This is a prospective, single center, single arm pilot study. SEP consisted in a 12-week intervention with twice a week in-person resistance exercise session. Patients also completed weekly aerobic exercise goals in self-managed sessions monitored with activity trackers. SEP was conducted by registered Physical Activity and Sports Science instructors that followed American College of Sports Medicine guidelines. In addition, participants had an initial nutritional assessment and personalized counselling by a qualified nutritionist. Adherence to treatment, biological variables and QoL assessments (FACIT-Fatigue and QLQ-C30 questionnaires) were collected at baseline (B) and week-12 (w12). Primary endpoint was global adherence ($\geq 70\%$ of attended sessions relative to scheduled sessions). Secondary endpoints included safety, changes in biological variables and QoL. Paired samples t-tests (Wilcoxon) were used to assess biological changes and QoL. **Results:** Patients (n=26) were recruited from October 2020 to November 2021. Median age was 47,5 years (45-55); 84,6% of patients were ECOG 0. 42,3% of patients were receiving Abemaciclib; 34,6% Ribociclib and 23,1% Palbociclib in first (73,1%) or second (26,9%) line treatment. Patients had bone (69,2%); visceral metastasis (57,7%) or both (30,8%). 2 patients did not start the intervention and additional 7 patients discontinued the program prematurely, the majority of them due to COVID-related concerns. Considering all patients who at least attended one session, global adherence was 66% (39-77,5%) and 45,8% of patients achieved an adherence of $\geq 70\%$. Patients reported an improvement in QoL [B global QLQ-C30 66,6 (50-75), w12 75 (66,6-83,3); p 0,0121] and fatigue [B FACIT-Fatigue 37 (30-44), w12 42 (38-48); p 0,0017]. Sit-to-stand repetitions in 30-second period also improved [(B 15 (12-17), 19 (15-23); p 0,0002]. Same benefits were seen in patients with adherence $\geq 70\%$. No statistically significant changes were seen in body fat or muscular composition and handgrip scores. Importantly, no safety issues related to study intervention were reported. **Conclusions:** Even though the study was conducted during COVID-19 pandemic, global adherence was 66%. For the first time in MBC, SEP and NP combined program demonstrated to be safe and improved QoL in patients with first or second line MBC treated with iCDK4/6. Further research is needed to identify strategies that improve QoL in MBC.

Disclosure(s):

Alfonso Cortés, MD: Astra Zeneca: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Clovis Oncology: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Daiichi Sankyo: Travel Grant (Ongoing); GSK: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g.,

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Cristina Saavedra, MD: Lilly: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, July 14, 2022); Novartis: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, April 21, 2022); Pfizer: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, May 6, 2022)

Noelia Martínez-Jáñez, MD PhD: ASTRA ZENECA: Consulting Fees (e.g., advisory boards) (Terminated, July 15, 2022); DAICHI: Consulting Fees (e.g., advisory boards) (Ongoing); GILEAD: Consulting Fees (e.g., advisory boards) (Terminated, July 15, 2022); LILLY: Consulting Fees (e.g., advisory boards) (Ongoing); NOVARTIS: Consulting Fees (e.g., advisory boards) (Ongoing); PFISER: Consulting Fees (e.g., advisory boards) (Ongoing); ROCHE: Consulting Fees (e.g., advisory boards) (Ongoing)

María Fernández-Abad, MD: Daiichi Sankyo: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Eisai: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Novartis: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Roche Farma: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Seagen: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

12/9/2022

7:00 AM - 8:15 AM

P6-05-29

Experience of Financial Toxicity and Distress Among Individuals Diagnosed with Triple Negative Breast Cancer: Findings from the Cancer Experience Registry

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Background: Financial toxicity associated with cancer and its treatment can negatively impact treatment adherence and quality of life. Individuals with triple negative breast cancer (TNBC) may be at increased risk for financial toxicity due to the aggressive nature of the disease and high rate of recurrence. The objective of this study was to characterize financial experiences of TNBC survivors, their descriptions of communication with providers concerning treatment costs, and correlations between financial toxicity and psychosocial distress. Methods: From July 2017 to August 2021, 94 individuals with TNBC took part in Cancer Support Community's Cancer Experience Registry® (CER). Participants completed items related to financial distress, including Comprehensive Score for Financial Toxicity (COST), an 11-item (0=Not at all, 4=Very much) measure of financial well-being (range 0-44; lower scores indicate worse financial well-being), dichotomous (yes or no) items assessing patient-provider communication, and Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29 v2.0). Bivariate relations were assessed using Pearson's correlation. Results: Participants were 81% non-Hispanic White, 6% Black, and 6% Hispanic. Mean age was 52 years (SD=11.3); 14 (15%) reported household income <\$40K. Median time since diagnosis was 2 years; 15% (n=14) reported metastatic breast cancer and 36% were currently receiving treatment. Concerning out-of-pocket cancer-related costs, 56% of our sample reported spending >\$250 per month; 32%

>\$500; 13% >\$1000. To reduce costs, 23% sometimes, often, or always postponed seeking psychological support, 19% delayed follow-up on recommendations, 6% postponed doctor's appointments, and 5% skipped medication. The mean COST score was 23.0 (SD=12.3), indicating mild financial distress overall. Less than half of the sample (46%) indicated no financial toxicity (scores >25), 29% mild financial toxicity (scores 14-25), 22% moderate (score 1-13), and 3% severe (score of 0). The frequency of individual COST items showed 61% reported (somewhat, quite a bit, or very much) worry about future financial problems due to treatment costs; 14% were unable to meet monthly expenses; 49% reported concern about keeping their job or income; 47% reported frustration that they could not work or contribute as usual. COST scores were inversely correlated to PROMIS anxiety ($r=-.45$, $p<.001$), depression ($r=-.44$, $p<.001$), and sleep disturbance subscales ($r=-.48$, $p<.001$), such that lower financial well-being related to more symptomology. COST scores were positively associated with the social function subscale ($r=.46$, $p<.001$), so that better financial well-being related to higher social functioning. Regarding patient-provider communication, 70% reported their health care team did not discuss costs, 62% did not discuss impact of TNBC and treatment on work, and 59% did not discuss financial concerns. One-third (34%) wished they received more financial advice and assistance. Conclusion: In this sample of TNBC patients, average levels of financial toxicity were in the mild range. However, many reported moderate to severe toxicity (25%). Greater financial toxicity related to increased symptoms of anxiety, depression, sleep disturbance, and worse social functioning. Despite this, results indicate there is little patient-provider discussion about financial burden, with more than half of our sample reporting their health care team did not discuss costs, impact on work, or financial distress. One-third of participants indicated desire for more financial advice and assistance highlighting an opportunity to better serve TNBC patients, who may be at an increased risk of financial toxicity.

Disclosure(s):

Kara Doughtie, MA: No financial relationships to disclose

Erica E. Fortune, PhD: AbbVie: Contracted Research (Ongoing); Amgen Oncology: Contracted Research (Ongoing); Astellas Pharma: Contracted Research (Ongoing); AstraZeneca: Contracted Research (Ongoing); Bristol Myers Squibb: Contracted Research (Ongoing); Genentech: Contracted Research (Ongoing); Gilead Sciences: Contracted Research (Ongoing); Lilly Oncology: Contracted Research (Ongoing); Merck & Co., Inc.: Contracted Research (Ongoing); Sumimoto Dainippon Pharma Co: Contracted Research (Ongoing); Takeda Oncology: Contracted Research (Ongoing)

Heather Badt, MBA, LSS: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-05-30

Effects of a 12-Week Exercise Program on Breast Cancer Survivors' Quality of Life

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Background:

Previous studies have demonstrated that breast cancer survivors commonly experience a decrease in quality of life including an increased risk of depression, insomnia, cancer-related fatigue, and negative body image. Several studies have shown that exercise interventions, such as yoga, Pilates, water aerobics, and strengthening exercises, can improve survivors' quality of life. We implemented a 12-week exercise program in breast cancer survivors and evaluated body composition and quality of life changes. Here we discuss our findings evaluating 5 quality of life questionnaires.

Methods:

We evaluated 22 participants who completed a baseline and post 12-week questionnaire assessments. All participants underwent a 12-week exercise program 3 times/week for 90 minutes/session. We calculated differences in baseline and post 12-week quality of life through 5 questionnaires: Functional Assessment of Cancer Therapy - General (FACT-G), Social Support, Insomnia Severity Index, Brief Fatigue Inventory, and Body Image after Breast Cancer (BIBCQ) and assessed the intervention's efficacy by comparing the baseline and post 12-week scores using paired t-tests.

Results:

The difference between baseline and post 12-week quality of life are presented in Table 1. 7/13 questionnaires showed statistical significance: FACT-G Emotional, FACT-G Functional, Insomnia Severity Index, BIBCQ Vulnerability Scale (VS), BIBCQ Body Stigma Scale (BSS), BIBCQ Limitation Scale (LS), and BIBCQ Body Concern Scale (BCS). Interestingly, 4/6 of the BIBCQ questionnaires showed statistical significance: BIBCQ VS, BIBCQ BSS, BIBCQ LS, and BIBCQ BCS.

Summary:

Our study showed improvement in all metrics evaluated in breast cancer survivors who underwent the personalized exercise program. Specifically, multiple questionnaires including body image were improved with exercise which further exemplifies the impact of lifestyle changes on quality of life measures and is an important adjunct to future cancer survivorship studies.

Table 1: Summary of questionnaires with overall significant improvements

Questionnaire	n/22 (%) improvement	p-value (significant p<0.05 in bold)
FACT-G Physical	12/22 (54.5%)	0.097
FACT-G Social/Family	8/22 (36.4%)	0.612
FACT-G Emotional	12/22 (54.5%)	0.048
FACT-G Functional	13/22 (59.1%)	0.003
Social Support	12/22 (54.5%)	0.577
Insomnia Severity Index	14/22 (63.6%)	0.002
Brief Fatigue Inventory	13/22 (59.1%)	0.138
BIBCQ VS	17/22 (77.3%)	0.004
BIBCQ BSS	15/22 (68.2%)	0.022
BIBCQ LS	18/22 (81.8%)	0.048
BIBCQ BCS	18/22 (81.8%)	0.001
BIBCQ Transparency Scale (TS)	14/22 (63.6%)	0.244
BIBCQ Arm Concerns Scale (ACS)	13/22 (59.1%)	0.481

Disclosure(s):

Lauren Imai, n/a: No financial relationships to disclose

Kirsten Baron, BS: No financial relationships to disclose

Matthew Toyama, BS: No financial relationships to disclose

Ian Pagano, PhD: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-05-31

Early integrated rehabilitation helps smoking cessation in 467 breast cancer patients – a comparison between the intervention and control group in a prospective study

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Background: Tobacco related illnesses are important public health issues worldwide. Cigarette smoking effects cancer risk and cardiovascular risk. Smoking cessation confers substantial benefits on health. Our aim was to determine whether the early introduction of integrated rehabilitation from the beginning of cancer treatment is associated with the smoking cessation in breast cancer patients. **Material and Methods:** The subjects of our prospective study were 467 female breast cancer patients (29-65 (mean 52) years of age), who participated in the pilot study on the individualized integrated rehabilitation of breast cancer patients in 2019-2022 and were followed for at least one year. The control group included 282 patients and the intervention group 185 patients. The patients completed three questionnaires (EORTC QLQ - C30, B23 and NCCN) before and one year after the beginning of cancer treatment. The control group obtained the same rehabilitation as was offered to all breast cancer patients in our hospital before the start of our prospective study. The multidisciplinary rehabilitation team reviewed the documentation of all the patients from the intervention group before and one year after the beginning of cancer treatment and recommended appropriate interventions according to the patient's difficulties. The integrated rehabilitation coordinator referred patients for additional interventions in compliance with the institute's clinical pathway (psychologist, general practitioner, clinical nutritionist, physical rehabilitation, kinesiologist-guided online exercises, gynecologist, analgesia, vocational rehabilitation). Smokers were referred to a smoking cessation workshop organized by a health promotion center within community health centres. Data on the patients' demographics, disease extent, cancer treatment and prevalence of tobacco smoking before and one year after the beginning of cancer treatment were collected and analysed using the chi-square and ANOVA test. **Results:** There were no differences between the control and the intervention group of patients in terms of age, education, disease extent, surgical procedures, systemic cancer treatment, or radiotherapy. There were no differences between the groups in the prevalence of smoking before the treatment. Before the cancer treatment, smoking was present in the intervention and control group in 22% and 27% ($p=0.22$), respectively. However, one year after the beginning of cancer treatment, smoking was less common in the intervention group in comparison to the control group of patients ($p=0.004$). Smoking was present in the intervention and control group in 10% and 20%, respectively. **Conclusions:** Early integrated rehabilitation helps the smoking cessation in breast cancer patients.

Disclosure(s):

Nikola Besic, MD, PhD: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-05-32

Does Aggregation Hide Place of Death Disparities for Asians with Breast Cancer?

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Introduction: Place of death (PoD) studies are often used to motivate and monitor progress on health inequities for persons with cancer. It remains unclear whether aggregation of Asian race masks disparities in health equity for care at the end of life.

Methods: De-identified death certificate data were obtained via the National Center for Health Statistics. All adult (>18 years of age) breast cancer deaths from 2018 to 2019 were included. Multinomial logistic regression was used to test for differences in place of death associated with sociodemographic variables.

Results: From 2018 through 2019, 81,772 died from breast cancer in the United States. Overall, persons of Asian descent were less likely to die at home compared to White patients. Disaggregation noted significant differences in likelihood of hospice facility use. For example, Filipino race was approximately 5 times more likely to utilize hospice facilities (CI 3.764, 8.718; $p < 0.001$) compared to Whites, whereas Chinese race was significantly less likely (OR 0.49, 95% CI 0.307 to 0.627, $p < 0.001$). American Indian (OR 0.006), Asian Indian (OR 0.016), and Samoan (0.011) were the least likely to die in a nursing facility. While trends were overall similar when compared to White, Black and Hispanics, the likelihood of PoD among Asian subgroups were significantly different.

Conclusion: Our data highlights notable differences in PoD only apparent with disaggregation of Asian race. While this study remains exploratory in nature, and reasons to explain these disparities are necessary, disaggregation of the Asian Pacific Island category is imperative to unmask disparities to improve health equity among all indigenous populations.

Association Between Race and Place of Death for Patients with Breast Cancer

Table 1: Number of deaths due to breast cancer in 2018 and 2019, by race. Odds ratios for the association between race and place of death from multinomial regression.

	N	N (%)				Home v. Hospital		Hospital v. Hospital		Nursing Facility v. Hospital	
		Hospital	Home	Hospice	Nursing Facility	OR [95% CI]	P	OR [95% CI]	P	OR [95% CI]	P
AIAN	N = 342	136 (39.8)	161 (47.1)	41 (12)	4 (1.2)	0.983 [0.666, 0.149]	< 0.001	0.481 [0.569, 1.219]	0.228	0.036 [0.002, 0.061]	< 0.001
Asian Indian	N = 340	138 (40.6)	152 (47.6)	29 (8.5)	11 (3.2)	0.982 [0.665, 0.103]	< 0.001	0.593 [0.294, 0.853]	0.012	0.016 [0.008, 0.029]	< 0.001
Black	N = 12700	8921 (88.7)	4010 (39.3)	1880 (14.8)	1289 (10.1)	0.992 [0.062, 0.097]	< 0.001	1.978 [0.973, 1.194]	0.15	0.051 [0.047, 0.055]	< 0.001
Chinese	N = 352	238 (43.1)	217 (39.3)	31 (8.7)	60 (10.9)	0.994 [0.683, 0.077]	< 0.001	0.439 [0.207, 0.627]	< 0.001	0.049 [0.031, 0.056]	< 0.001
Filipino	N = 726	34 (4.7)	262 (39.1)	69 (9.5)	360 (49.7)	0.528 [0.376, 0.772]	< 0.001	5.729 [3.764, 8.748]	< 0.001	2.07 [1.481, 2.952]	< 0.001
Guamanian	N = 23	7 (30.4)	19 (82.2)	3 (13)	1 (4.3)	0.12 [0.047, 0.305]	< 0.001	1.211 [0.312, 4.694]	0.782	0.028 [0.003, 0.227]	< 0.001
Hawaiian	N = 29	7 (23.9)	14 (53.8)	3 (11.5)	2 (7.7)	0.14 [0.056, 0.366]	< 0.001	1.259 [0.312, 4.889]	0.783	0.026 [0.012, 0.209]	< 0.001
Hispanic	N = 26922	13169 (60.8)	2667 (11.4)	9367 (39.1)	420 (1.7)	0.916 [0.015, 0.017]	< 0.001	2.909 [1.833, 2.201]	< 0.001	0.006 [0.005, 0.007]	< 0.001
Japanese	N = 249	46 (19.2)	117 (48.8)	34 (14.2)	43 (17.9)	0.178 [0.126, 0.250]	< 0.001	2.985 [1.327, 3.277]	0.004	0.183 [0.12, 0.278]	< 0.001
Korean	N = 166	54 (32.7)	71 (43)	26 (15.8)	14 (8.5)	0.992 [0.664, 0.131]	< 0.001	1.259 [0.844, 2.187]	0.267	0.051 [0.028, 0.091]	< 0.001
>1 race	N = 644	129 (20)	271 (42.1)	45 (7)	199 (30.9)	0.147 [0.118, 0.182]	< 0.001	0.985 [0.695, 1.368]	0.93	0.201 [0.24, 0.378]	< 0.001
Samoa	N = 39	17 (43.6)	18 (45.2)	3 (7.7)	1 (2.6)	0.074 [0.038, 0.144]	< 0.001	0.498 [0.145, 1.704]	0.267	0.011 [0.002, 0.066]	< 0.001
Vietnamese	N = 161	92 (59.1)	74 (46)	13 (8.1)	11 (6.8)	0.982 [0.666, 0.115]	< 0.001	0.362 [0.218, 1.056]	0.079	0.024 [0.018, 0.055]	< 0.001
White	N = 28863	1919 (4.8)	27473 (88.9)	680 (1.7)	9621 (24.6)	1.0 (ref)		1.0 (ref)		1.0 (ref)	

† Association between death in a given location compared to the reference category (Non-Hispanic White).

Disclosure(s):

- Naveena Lall, MD:** No financial relationships to disclose
- Alexandra Noveihed, MD:** No financial relationships to disclose
- Qasim S. Hussaini, MD:** No financial relationships to disclose
- Amanda L. Blackford, ScM:** No financial relationships to disclose
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- Ramy Sedhom, MD:** No financial relationships to disclose

12/9/2022

7:00 AM - 8:15 AM

P6-05-33

Distress Reduction and Physical Activity Enhancement by Mobile Support Group in Breast Cancer Survivors: a randomized controlled study

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Purpose Improving physical activity (PA) and reducing mental distress are important issues in the treatment of cancer survivors. This study aimed to investigate the effect of a mobile app-based community on enhancing PA and decreasing distress in breast cancer survivors. Methods We conducted a single-center, prospective, non-blinded, randomized controlled study. Subjects who got breast cancer surgery were allocated to a control group or a app-based community group (intervention) where members were able to share their daily physical activities. Daily walk steps and weekly distress scores using app-based Distress Thermometer (DT) questionnaires were collected from participants for 24 weeks. To examine the differences in levels of distress and weekly step counts for 6 months, we used a t-test method and multivariable regression modeling. Results From Jan 2019 to Apr 2020, a total of 202 participants were enrolled in this study. The intervention group showed a significant increase in weekly steps by 4,496 for 6 months ($p < 0.001$). The participants in the intervention group showed a significantly lower rate of above mild distress ($DT \geq 3$, $\beta[B] = -0.731$, $p < 0.001$) and above moderate distress ($DT \geq 5$, $B = -0.558$, $p < 0.001$) compared to those in the control group for 6 months. Conclusions The mobile app-based community is an effective and less resource-intensive tool to increase PA and decrease distress in breast cancer survivors.

Disclosure(s):

Il-Yong Chung, M.D.: No financial relationships to disclose

Miyeon Jung, n/a: No financial relationships to disclose

Sae Byul Lee, M.D., Ph.D.: No financial relationships to disclose

Jong Won Lee, n/a: No financial relationships to disclose

Sei Hyun Ahn, M.D., Ph.D.: No financial relationships to disclose

Haekwon Chung, n/a: Swallaby Co.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

12/9/2022

7:00 AM - 8:15 AM

P6-05-34

Depression and Psychological Distress in Breast Cancer Patients

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Introduction:

Patients with breast cancer are at increased risk for depression and suicide compared to the general population. Breast cancer is unique among other cancers in that some treatments aim to decrease levels of estrogen, a hormone that is intricately linked to mood regulation. The trauma of diagnosis, invasive treatments, and hormone dysregulation all possibly contribute to poor mental health outcomes. Understanding risk factors associated with depression and distress are important for timely interventions.

Methods:

We performed a retrospective chart review of breast cancer patients seen at Froedtert & MCW Cancer Center Breast Care Clinic between 2019 and 2020. The present study had two aims. The primary aim was to identify breast cancer patient populations at increased risk of depression and psychological distress. Patient populations were distinguished by tumor pathology, patient demographics, and types of treatment interventions. The secondary aim was to identify demographic and clinical variables associated with changes in self-reported distress and depression. Univariate and multivariate analysis of demographic and clinical variables was performed in relation to Patient Health Questionnaire (PHQ) and The National Comprehensive Cancer Network (NCCN) Distress Thermometer scores.

Results:

Data from 197 patients was analyzed. Patients with a history of depression scored significantly higher on distress screening (mean= 4.4 \square 3.0, $p=0.004$) versus patients without psychiatric history (mean 2.8 \square 2.9). Patients under 50 years old reported higher levels of distress than patients over 70 years old ($p=0.031$, $\beta=-1.0$). Self-reported distress declined significantly with increased time from initial diagnosis ($p=0.043$; $p=0.006$ at 2 years). Distress was significantly higher prior to initiation of radiation versus during and immediately following therapy ($p=0.028$). A history of depression, younger age, passage of time, and temporal relationship to radiation treatment were not associated with significant differences in self-reported depression on multivariate analysis. Distress and depression screening scores were not significantly impacted by surgery or chemotherapy ($p=0.5$; $p=0.11$ respectively).

Conclusion:

Patients with a known history of depression and age less than 50 reported significantly higher levels of distress but not depression associated with diagnosis of breast cancer. Distress exhibited a greater downward trend than depression following initiation of oncologic intervention. The results of this study indicate that breast cancer patients are susceptible to significant fluctuations in psychological distress. In contrast, clinically relevant depression screening scores were less frequent and less subject to deviation.

Table 1: Multivariate analysis

Table 1: Multivariate Analysis

Characteristic	Distress				PHQ			
	N	Beta	95% CI ¹	p-value	N	Beta	95% CI ¹	p-value
Age at dx (grouped)				0.048				0.059
<50	157	----	----		115	----	----	
50-59	138	0.22	-0.58, 1.0	0.6	97	-0.23	-2.1, 1.6	0.8
60-69	117	-0.50	-1.3, 0.28	0.2	95	-1.4	0.06	0.061
70+	92	-1.0	-2.0, -0.09	0.031	69	-0.87	0.88	0.3
Time since Dx				0.043				0.5
<6mo	184	----	----		164	----	----	
6mo- 1 yr	100	-1.0	-2.0, -0.10	0.030	77	-1.1	-2.7, 0.51	0.2
1-2 yrs	144	-1.3	-2.2, -0.34	0.008	97	-0.83	-2.7, 1.0	0.4
2+ yrs	76	-1.6	-2.7, -0.44	0.006	38	-0.70	-2.9, 1.5	0.5
History of depression?				0.004				0.5
No	407	----	----		298	----	----	
Yes	97	1.3	0.42, 2.2	0.004	78	0.57	-1.3, 2.4	0.5
Radiation therapy				0.068				0.2
None/ 90+ days before	284	----	----		214	----	----	
<90 days before	63	0.55	-0.36, 1.5	0.2	59	0.28	-0.78, 1.3	0.6
During/ 90 days after	21	-1.2	-2.3, -0.23	0.028	14	0.54	-1.9, 3.0	0.7
90+ days after	136	-0.21	-1.0, 0.54	0.6	89	-0.95	-2.0, 0.11	0.079

¹CI= Confidence interval

Dx= diagnosis. Significant p-values are bolded.

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7:00 AM - 8:15 AM

P6-05-35

Cost-effectiveness of CDK4/6 inhibitors in the first-line treatment of HR+/HER2-metastatic breast cancer in postmenopausal women in Panama.

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Background: 4/6 kinase-dependent cyclin inhibitors have been approved for use in combination with first-line aromatase inhibitors in patients with hormone-sensitive, Her 2neu negative metastatic breast cancer. These agents have significantly improved progression-free survival compared to monotherapy aromatase inhibitors. The purpose of this study was to evaluate the cost-evaluation of each of these new agents (palbociclib, ribociclib, and abemaciclib) in the first line in Panama with the perspective of the National Oncological Institute. Methods: A partition survival analysis was carried out that includes three states (free of progression, progression, and death) with cycles of one month and a time horizon of 7.5 years. The efficacy data were taken from pivotal clinical trials, and the costs were estimated locally. A deterministic and probabilistic sensitivity analysis of the Monte Carlo was performed. Results; According to the base case, the update of each of these strategies involved an increase of USD 355,184 per additional QALY for ribociclib with Letrozole compared to Letrozole; USD 944,148 / additional QALY for Palbociclib plus Letrozole; and USD 223,956 for Abemaciclib plus Letrozole, when compared with Letrozole, all above the availability threshold to pay 50,000 / QALY. Conclusion: Despite the improvement in progression-free survival, none of the strategies have proved cost-effectiveness in our setting. Price negotiations, cost reduction, and risk-sharing agreements between pharmaceutical companies and payers might improve access to new drugs in countries with limited resources.

Disclosure(s):

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7:00 AM - 8:15 AM

P6-05-36

Cost-effectiveness of CDK4/6 inhibitors as a First line Therapy for Metastatic Breast Cancer. A Mexican Cohort.

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Cost-effectiveness of CDK4/6 inhibitors as a First Line Therapy for Metastatic Breast Cancer. A Mexican Cohort.

BACKGROUND.

Breast cancer is the most frequent neoplasm worldwide, as reported by GLOBOCAN 2020, there were 2.2 million new cases per year and 680,000 deaths. In Mexico, it represents the leading cause of death from cancer in women, and therefore represents a public health problem in our country. The standard treatment for patients with hormone receptor-positive, her2-negative breast cancer is endocrine therapy with an aromatase inhibitor plus a CDK4/6 inhibitor (CDK4/6i+AI), however access to these therapies is difficult and limited resources in developing countries, lead to treatment strategies such as aromatase inhibitors alone (AI) or chemotherapy

(ChT) still being used. However, management with ChT involves an increase in the use of resources due to cost per infusion, use of premedication and granulocyte colony-stimulating agents.

OBJECTIVE

The aim of this study was to provide an economic evaluation of CDK4/6i+AI compared with AI alone or ChT as a first line in MBC to better understand its value from the healthcare point of view in a developing country.

METHODS.

We designed a retrospective cost-effectiveness analysis of three different therapies CDK4/6i+AI, AI alone and ChT administered as first-line therapy for patients with MBC.

RESULTS.

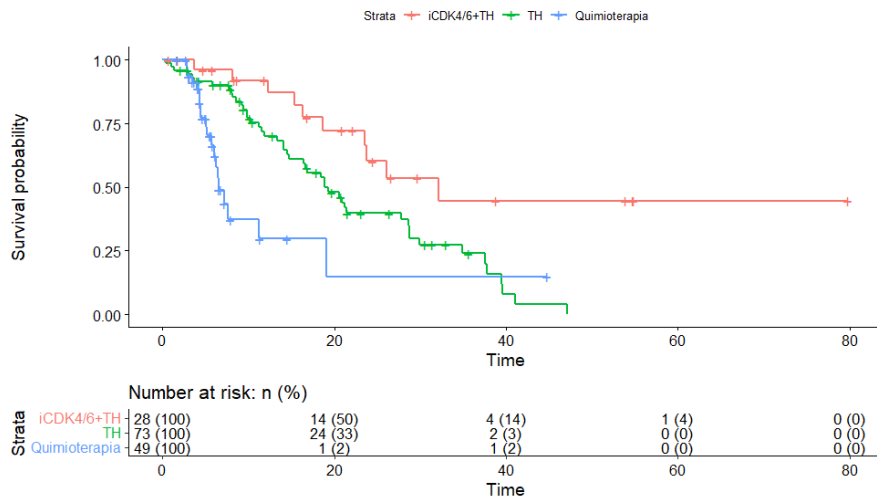
A cost-effectiveness analysis was performed on a retrospective cohort of 150 MBC patients (march 2011 to April 2020) with a follow-up of at least 2 years. The median age at diagnosis was 55 years old. The utilization of health care resources was retrieved from clinical charts. Only direct costs associated with pre-progression, progression, and management of adverse events were considered and expressed on current USD.

Seventy-six percent were diagnosed with de novo stage IV disease, 66% were postmenopausal and 76% had ductal histology. The most common sites of metastasis were visceral 55% and 29% had only bone metastases. We identified 3 treatment groups: (1) CDK4/6i+AI, 18.66% (28/150), (2) AI, 48.66% (73/150) and (3) ChT, 32.66% (49/150). The median PFS of iCDK4/6 + TH was 32.10 months compared with 18.87 (95%CI: 16.4, 28.7) months for the AI group and 6.57 months for chemotherapy. The HR of iCDK4/6+TH vs HT was 0.357 (95%CI: 0.18-0.72) and that of iCDK4/6+TH vs chemotherapy was 0.09 (95%CI: 0.04-0.22). Median OS survival was not reached in any arm. The most frequent adverse events grade 3 were fatigue 10.71%, neutropenia 32.14%, diarrhea 7.14%, myalgias 3.57% and arthralgias 3.57% in the CDK4/6i +AI group, fatigue 2.74% and arthralgias 4.11% in AI group and fatigue 20.41%, neutropenia 18.37%, nausea 10.2%, diarrhea 6.12%, myalgias 2.4% and headache 2.4% with chemotherapy. PFS was used as the outcome for the cost-effectiveness analysis, with 5 years of follow-up, CDK4/6i+AI offer an incremental efficacy of 1.4 years in PFS compared with AI and 2.43 years with ChT, they are related to an incremental cost of \$28,151.61 and \$26,720.47 concerning AI and ChT, respectively. The ICER for CDK4/6i+AI compared to AI is \$20,108.29 and \$10,996.07 compared to chemotherapy.

CONCLUSION.

CDK4/6i+AI increase years of life gained when compared to AI and chemotherapy. Is a cost-effective treatment in our institution because it is less than two GDP per capita. CDK4/6i+AI is the standard treatment around the world even in develop countries like Mexico.

PFS 3 arms



Disclosure(s):

Maritza Ramos-Ramírez, MD, MSc, N/A: No financial relationships to disclose
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12/9/2022

7:00 AM - 8:15 AM

P6-05-37

Comparing Changes in Depression and Anxiety Levels of Breast Cancer Patients throughout a Course of Radiation Therapy

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An estimated 32.2% and 41.9% of breast cancer patients experience depression and anxiety, respectively. However, due to differences in the understanding of radiotherapy and variability in the severity of side effects, responses of patients with breast cancer receiving radiation therapy may vary at different time points and differ in comparison to other patients with breast cancer. This study sought to describe the changes in levels of depression and anxiety experienced by English and Spanish-speaking patients throughout a course of radiation therapy for breast cancer along with the impact of different variables on these levels to better understand and quantify potential gaps.

Eligibility criteria included English and Spanish-speaking females, ages 18 or older, undergoing radiation therapy treatment for breast cancer at Boston Medical Center. Pre- and post-treatment surveys were completed before and after delivery of radiation therapy. Survey included sociodemographic questions along with the standardized PHQ-4 questionnaire, which uses a maximum total score of 12, to assess anxiety and depression. Results were analyzed using a least means square procedure.

A total of 60 participants completed pre- and post- treatment surveys. Total baseline distress mean (BDM) was 3.32 (SD= 3.55) and final distress mean (FDM) was 3.22 (SD= 3.78). English-speaking patients comprised 70% (n=42) of the sample and had a BDM of 3.40 with an adjusted change mean (ACM) decrease of 0.48. Spanish-speaking patients comprised 30% (n=18) of the sample, with a BDM of 3.11 and an ACM increase of 0.79, differences in ACM trended toward significance with a p-value of 0.083. Sociodemographic characteristics included: race, ethnicity, marital status, education level and longest residency. Additional variables surrounding social determinants of health included housing and food insecurity, which showed statistically significant increasing distress with increased insecurity at baseline.

While our study showed a higher BDM among English-speaking patients in comparison to Spanish-speaking patients, results showed that Spanish-speakers' distress increased throughout treatment as opposed to English-speakers. Most of our patient population was English-speaking, though approximately one third Spanish-speaking and our participants were also primarily Black, non-Hispanic, never married, had a high school or associate level

education, and had their longest residence in the US. Although the majority did not report housing or food insecurity, both had increasing DM with increased insecurity, with statistically significant results. As the number of Spanish-speakers in the US continues to increase, it will be important to continue assessing potential differences in cancer care. In addition, an understanding of the changes of distress throughout radiation treatment could help inform future interventions that address these disparities.

Baseline distress values and adjusted change in overall score by sociodemographic factors

	N	Mean (SE)	Overall P	Pairwise comparison, P			Adjusted Change Mean* (SE)	Overall P
				1 vs. 2	1 vs. 3	2 vs. 3		
Overall	60	3.32 (0.46)	-	-	-	-	-0.10 (0.35)	-
Language								
English	42	3.40 (0.55)	0.772	-	-	-	-0.48 (0.39)	0.083
Spanish	18	3.11 (0.84)					0.79 (0.60)	
Race								
1. White	16	3.13 (0.90)	0.965	0.961	0.988	0.994	-0.60 (0.63)	0.086
2. Black	28	3.43 (0.68)					-0.51 (0.48)	
3. Other	16	3.31 (0.90)					1.12 (0.63)	
Hispanic Identity								
No	40	3.25 (0.57)	0.839	-	-	-	-0.59 (0.40)	0.038
Yes	20	3.45 (0.80)					0.88 (0.56)	
Marital status								
1. Never married	22	3.82 (0.76)	0.376	0.987	0.393	0.494	-0.08 (0.56)	0.810
2. Married	20	3.65 (0.79)					-0.38 (0.59)	
3. Divorced/Separated/Widowed	18	2.33 (0.84)					0.18 (0.63)	
Education								
1. < High School	12	3.25 (1.04)	0.897	0.981	0.972	0.889	0.65 (0.75)	0.533
2. High School/Associate	36	3.47 (0.60)					-0.33 (0.44)	
3. Bachelors/Masters/Doctorate	12	2.92 (1.04)					-0.17 (0.76)	
Country								
United States	35	3.51 (0.60)	0.614	-	-	-	-0.30 (0.44)	0.486
Foreign	25	3.04 (0.72)					0.18 (0.52)	
Housing worry								
1. Never	30	2.13 (0.61)	0.007	0.384	0.001	0.190	-0.79 (0.48)	0.112
2. Sometimes	16	3.50 (0.83)					0.18 (0.64)	
3. Always	14	5.64 (0.89)					1.07 (0.72)	
Food worry								
1. Never	37	2.24 (0.54)	0.003	0.198	0.003	0.245	-0.54 (0.44)	0.194
2. Sometimes	13	4.08 (0.90)					0.08 (0.72)	
3. Always	10	6.30 (1.03)					1.30 (0.87)	

Abbreviations: N= total number of respondents; SE= standard error

*The change in score from the first week of treatment to the final week was calculated as (final treatment score - first treatment score).

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12/9/2022

7:00 AM - 8:15 AM

P6-05-38

Breast Density Notification: Impact on anxiety, breast cancer worry, and self-perceived risk among Latinas at a federally qualified medical center.

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Mammographic breast density (MBD) has been shown to be a strong, independent risk factor for breast cancer (BC) irrespective of race/ ethnicity. Given the risk association of MBD and its potential to mask tumors on a mammogram, state and federal laws have mandated that women receive information regarding their personal MBD in their mammography reports. However, concerns have been raised regarding the impact of MBD notification on patient anxiety, especially written information for women who experience health disparities such as racial/ethnic minorities, lower health literacy, limited English proficiency and lower socioeconomic status. We performed a randomized controlled clinical trial to examine the impact of three different written and interpersonal approaches to MBD notification on patient anxiety, BC worry, and self-perceived BC risk, among Latinas receiving routine mammography screening at a federally qualified medical center (FQHC). We hypothesized that interpersonal education would reduce anxiety and worry, relative to the written notifications alone. The study was performed at the Baseline Clinic of Mountain Park Health Center, a FQHC in Phoenix, AZ. Women between ages 40 and 74 years presenting for screening mammogram were eligible. After providing signed informed consent, participants were randomized equally to usual care (UC- mailed notification letter); enhanced care (notification letter and MBD educational brochure designed for this study); interpersonal care (notification letter, brochure, promotora education via telephone). A stratified block randomization procedure was used with age > 50 years (yes vs no), ethnicity (Hispanic vs non-Hispanic), and language preference (Spanish vs. English) as strata. Study participants completed surveys at the time of enrollment/ pre-intervention (T0), at two weeks to six months after intervention was delivered (T1), and about one year after randomization (T2). Anxiety state was measured using the state anxiety subscale of the State-Trait Anxiety Inventory scale (STAI-S) (range from 20-80). BC worry was probed using the question: "How frequently do you worry about getting breast cancer someday". The self-perceived lifetime risk of BC was rated between 0% (no chance of BC) to 100% (definitely will get BC). The proportion of participants with an increase or persistence of higher level for each outcome between time points was compared between the three study groups. The study was approved by the Mayo Clinic Institutional Review Board. 1332 Latina women were enrolled and randomized between October 2016 and October 2019. All completed the baseline (T0) survey, 928 completed T1, 632 completed T2, and 516 completed both T1 and T2 surveys. At study entry, majority of the participants were young (64.1% between age 40-49 years), had no family history of breast cancer (81.0%), had less than high school education (68.8%), and were married or partnered (67.8%). At T0, the mean (SD) anxiety STAI score was 32.5 (11.1); 51.8% with moderate or severe anxiety (score > 30). With regard to BC worry, 41.3% reported worrying "sometimes", "often", or "almost all the time". Further, 25.4% reported a self-perceived lifetime risk of developing BC of >10% while only 6.6% had a Gail model estimated lifetime risk score of >10%. There was no significant difference in changes in anxiety, BC worry or self-perceived risk from T0 to either T1 or T2 surveys between the intervention groups. In summary, this study found high levels of baseline anxiety and BC worry (despite the majority being 40-49 years old and having no family history of BC) which persisted regardless of how notification and education were delivered. Future work is needed to improve the understanding of factors that could lower anxiety and BC worry and improve risk perception in this population.

Disclosure(s):

Karthik Ghosh, M.D., M.S., F.A.C.P.: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-05-39

Black Breast Cancer Survivors' Sociocultural Perspectives of Beauty, and Use of Personal Care Products Containing Endocrine Disrupting Chemicals

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The passage of H.R. 2116 (CROWN Act) prohibits hair texture and style discrimination based on race or national origin, thus, theoretically reducing structural barriers to economic mobility. Regardless, hair is synonymous with Black women's identities. Possibly due to society's afro-political ideologies of beauty, Black women tend to use more hair products compared to other racial groups. These standards include social structures that affect self-mediated worth, as well as structural and interpersonal racism based on appearance and societal status. The use of personal care products containing endocrine disrupting chemicals (EDCs) has been shown to increase Black women's breast cancer risk. The Black identity, hair product use, and breast cancer scale (BHBS) was developed to measure the sociocultural constructs associated with Black women's hair product use and perceived breast cancer risk. The purpose of this study was to validate the BHBS and examine hair product use among Black breast cancer survivors.

Methods: Participants (N=162) completed a 27-item survey between 2020 and 2022 via a community-based participatory research project—Bench to Community Initiative. Principal component analyses (PCA) and confirmatory factor analysis (CFA) were used to establish the underlying component structures and determine the model fit. Chi-square tests were used to determine associations between BHBS subscales and product use, with a p-value < 0.05 defined as statistically significant. Products evaluated included washout and leave-in conditioners, salon, and do-it-yourself (DIY) relaxers, and salon and DIY hair dyes. Response options were used daily through several times a year (daily–yearly), used but stopped, and never used. Results: Participants were African American (90%) and African or Caribbean (10%) Black breast cancer survivors. The mean age (standard deviation [SD]) and stage of diagnosis (SD) was 37.4 ± 8.8 and 1.9 ± 0.97 , respectively. PCA yielded two components that accounted for 63% of the total variance in the model. Five items measuring sociocultural perspectives about hair and identity (subscale 1 [S1]) accounted for 28% of the total variance ($\alpha = 0.73$, 95% CI 0.71, 0.82). Six items assessing perceived breast cancer risk related to hair product use (subscale 2 [S2]) accounted for 35% of the total variance ($\alpha=0.86$, 95% CI= 0.81, 0.94). CFA confirmed the two-component structure (Root Mean Square Error of Approximation = 0.034; Comparative Fit Index = 0.93; Tucker Lewis Index = 0.89). On average, participants used hair products daily–yearly, including conditioners (64%), relaxers (32%), and hair dyes (33%). The use of salon relaxers was significantly associated with BHBS subscales (S1 and S2). Similarly, salon hair dye was significantly associated with S2 of the BHBS. Discussion: The BHBS is a valid measure of sociocultural perspectives associated with hair product use and perceived risk for Black breast cancer survivors. Given that hair remains an important cultural expression within the afro-political confines of identity, the health impacts of hair products containing EDCs used to craft these identities should be considered in intervention planning.

Disclosure(s):

Jared Bailey, BS: No financial relationships to disclose

Marissa Ericson, PhD: No financial relationships to disclose

Tiah Tomlin-Harris, MS: Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Patient Advisory Board (Ongoing)

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7:00 AM - 8:15 AM

P6-05-40

Aqua polo: Preliminary feasibility and efficacy study of a programme of adapted, supervised water polo to reduce fatigue and improve women's psychological and social recovery after breast cancer treatment. A mixed-method design.

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Introduction : Physical activity has been shown to have many benefits, including reducing cancer-related fatigue (CRF) and improving psychological and physical recovery from breast cancer. Some authors have shown the benefits of aquatic practice, while others have detailed the benefits of group and supervised practice. We hypothesise that an innovative sports coaching proposal could allow a significant adherence of patients and contribute to their health improvement. The main objective is to study the feasibility of an adapted water polo programme (aqua polo) for women after breast cancer. Secondary we will analyse the effect of such a practice on patients' recovery and to study the relationship between coaches and participants.

The use of mixed methods will allow to question precisely the underlying processes. Methods and analysis : This is a prospective, non-randomised, monocentric study with a sample of 24 breast cancer patients after treatment. The intervention is a 20 week programme (1 session per week) of aqua polo in a real sports setting. The variables measured are patient participation, quality of life (QLQ BR23), CRF (R-PFS) and post-traumatic growth (PTG-I) as well as different variables to observe physical capacity (strength with dynamometer, step-test and arm amplitude). The quality of the coach-patient relationship will be evaluated (CART-Q) to explore its dynamics. Participatory observations and interviews will be carried out to report on the interactions between the coach and the participants during the sessions. Ethics and dissemination : Study procedures have been approved by the Institutional Review Board of the Institute (IPC 2019-028) and the National Ethics Committee (SI:20.01.20.54741). Consent is given in person to each participant. The information collected on the participants contain only a non-identifiable study identifier. The results of this protocol will be published in a scientific paper and communicated to the medical staff of the medical center. Trial registration number ID-RCB: 2019-A03003-54 Keywords: Quality of the relationship, Aquatic exercise, Quality of life, Sport

Disclosure(s):

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Agnès Tallet, n/a: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-05-41

Advocate-BREAST: Advocates and Patients' Advice to Enhance Breast Cancer Care Delivery, Patient Experience and Patient Centered Research by 2025

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Background: The high-level aims of the Advocate-BREAST study are to study and improve the overall experience of patients with breast cancer (BC) through education, shared decision making, and patient-centered clinical trials. Assessing areas of unmet need in care delivery and research as identified by patients with BC will direct future research and help us improve the patient experience. Methods: In April 2022, an electronic RedCap survey was circulated to 6,918 BC survivors (stage 0-4 disease) enrolled in the prospectively consented Mayo Clinic Breast Disease Registry (MCBDR), which includes rural-dwelling women often underrepresented in cancer care delivery research. The questionnaire asked about satisfaction with multiple aspects of cancer care delivery and the education and support patients receive(d) regarding practical, financial, emotional, societal and spiritual concerns linked to BC. Patients were also asked to rank potential Quality Improvement (QI) projects in order of the likelihood the proposal could improve quality of life for BC patients and their families. Questions regarding clinical trial participation, use of integrative medicine and perspectives on medical second opinions were also included. Responses were collected via anonymous local language questionnaires. Results: The survey received 2,451 responses from MCBDR enrollees. 13% of

respondents had Ductal Carcinoma in Situ (DCIS), 83% had early breast cancer (EBC) (Stage 1-3) and 4% had metastatic breast cancer (MBC). Mean age was 64 (SD 11.9), and mean time in months since diagnosis was 93 (SD 1.42). 69.3 % of patients received all care at Mayo Clinic; 24.7% at Mayo and another healthcare organization, and 6% at a non-Mayo site. Although the overall experience of care was generally good/excellent (> 90 %), gaps were perceived in terms of information provision, continuity of care (including survivorship care after 5 years), navigating care transitions, and timely access to mental health resources. The main severe symptoms patients recalled in year 1 were hair loss, eyebrow/eyelash thinning, hot flashes, sexual dysfunction and cognitive issues. The main concerns patients recalled in the first year following diagnosis were fear of BC recurrence and spread as well as of dying, practical and emotional concerns for family members if they were to die of BC, and their emotional health. Patients were most dissatisfied with information and support related to management of lymphedema, sexual dysfunction, eyebrow/eyelash thinning, and peripheral neuropathy. Respondents overwhelmingly voiced the need for the following QI projects: i) lifetime access to online patient educational resources: including summary “cheat sheets”; ii) educational, practical, emotional and holistic support programs for MBC patients, and iii) BC Wellness Programs for EBC and MBC patients (endorsed by 82.6%; 82.4% and 81.9% of respondents, respectively). Predictors in terms of age, time since diagnosis, and cancer stage that may account for satisfaction with care, concerns, or QI preferences will be reported at the meeting. Of 20% of patients who saw an Integrative Medicine provider, 85% were satisfied/very satisfied with the care received. Of ~40% of patients who received a second opinion regarding their BC diagnosis and treatment plan, 96% found this beneficial. 47% of respondents had participated in a clinical trial, which is higher than seen in the general population such that conclusions may not be generalizable. Of those who had not participated in a study, 30% reported that they were unsure if they would participate in a trial if offered, and 9% reported that they would decline same. Conclusion: Understanding the lived experiences of persons with BC is essential to improve quality of care. Patients with early and advanced BC desire holistic care, continuity of care, concise educational resources and early psychological support.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-05-43

Validity of EQ-5D-5L for women with breast cancer

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Background: The EuroQol- 5 Dimension (EQ-5D) is a generic patient-reported outcome measure widely used to capture meaningful change in health-related quality of life between treatments to inform drug and health technology reimbursement decision making. We investigated the construct validity of EQ-5D-5L in women with breast cancer.

Methods: This study included adult women diagnosed with stage I to IV breast cancer, who completed the EQ-5D-5L and the Edmonton Symptom Assessment System (ESAS) during outpatient clinic visits at two academic cancer centres in Toronto. We evaluated construct validity through assessing known-group validity and convergent / divergent validity. For known-group validity, the primary analysis tested the hypothesis that EQ-5D-5L could adequately discriminate between patients with metastatic disease and early-stage disease; secondary analyses addressed utility values between women in breast-cancer associated health states. A suggested minimally important difference (MID) for the Canadian scoring of the EQ-5D-5L is 0.037; we evaluated whether the lower bound of the 95% confidence interval (95%CI) exceeded this value. In terms of convergent / divergent validity, the primary analysis tested the hypothesis that EQ-5D-5L mean utility values for each health state (HS) would be at least moderately correlated with ESAS total symptom distress score (SDS) ($|r| > 0.30$) using Wilcoxon rank-sum tests and Spearman's correlation tests. Construct validity was considered as acceptable if the hypotheses of the primary analysis are satisfied.

Results: We recruited 549 women, 406 (74%) with early-stage disease and 143 (26%) with metastatic disease (HS5), with a mean age of 57 (SD 12); 412 (75%) had been diagnosed with breast cancer in the 7 years prior to recruitment and were receiving active treatment for their cancer.

The mean utility value for early-stage breast cancer was 0.84 (95% CI 0.83-0.86) and for metastatic breast cancer (0.78, 95% CI 0.76-0.81). This difference was 0.060 (95% CI 0.036 to 0.085, $p < 0.001$) with the lower bound of the confidence interval slightly less than the prespecified MID (0.037). There was no significant difference between the mean utility value for women in the first year after primary breast cancer diagnosis (HS1), and women in their second to fifth year after a primary breast cancer treated with curative intent (HS3) or between women in HS1 and women in their sixth and following years after a primary breast cancer treated with curative intent (HS4). EQ-5D-5L also did not discriminate between women in HS3 and HS4.

For convergent / divergent validity, there was a negative correlation between utility values and ESAS physical, emotional and total SDSs. EQ-5D-5L and ESAS total SDSs correlation coefficients were higher than 0.30 for all health states.

Conclusion: EQ-5D-5L met criteria for convergent/divergent validity in women with breast cancer. The tests for discriminant validity were equivocal, suggesting more research is needed for assessing construct validity with a larger sample size.

Table 1- EQ-5D-5L Utility Values

Health State	N (%)	Mean (95%CI)	Std Dev	Median (IQR)	Min-Max
Total Study Population	549 (100)	0.83 (0.82-0.84)	0.13	0.87 (0.11)	0.13-0.95
Women with early-stage Breast cancer	406 (74%)	0.84 (0.83-0.86)	0.12	0.87 (0.10)	0.13-0.95
Women with metastatic breast cancer	143 (26)	0.78 (0.76-0.81)	0.14	0.81 (0.20)	0.29-0.95
Early-Stage Breast Cancer Health States	N (%)	Mean (95%CI)	Std Dev	Median (IQR)	Min-Max
First year after diagnosis primary breast cancer (HS1)	146 (27)	0.85 (0.83-0.86)	0.12	0.87 (0.08)	0.23-0.95
First after local recurrence or diagnosis new primary (HS2)	13 (2)	0.78 (0.65-0.90)	0.21	0.87 (0.12)	0.13-0.95
2 nd to 5 th year after a primary breast cancer (HS 3)	185 (34)	0.84 (0.83-0.86)	0.11	0.87 (0.10)	0.21-0.95
6 th and following years after a primary breast cancer (HS 4)	62 (11)	0.86 (0.82-0.89)	0.14	0.90 (0.10)	0.36-0.95

N= number; Std Dev= standard deviation; IQR= interquartile range; CI= confidence interval

Disclosure(s):

Sofia Torres, n/a: No financial relationships to disclose

Maureen Trudeau, n/a: No financial relationships to disclose

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Nicholas Mitsakakis, n/a: No financial relationships to disclose

Ahmed Bayoumi, n/a: No financial relationships to disclose

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7:00 AM - 8:15 AM

P6-05-44

REASONS FOR CHOOSING DELAYED RATHER THAN IMMEDIATE CONTRALATERAL PROPHYLACTIC MASTECTOMY IN PATIENTS WITH UNILATERAL BREAST CANCER.

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Background: Rates of contralateral prophylactic mastectomy (CPM) have more than doubled in the past decade amongst breast cancer patients irrespective of inherited genetic predisposition related to high penetrance genes. Increasing numbers of women with unilateral breast cancer are opting for removal of both the affected ipsilateral and unaffected contralateral 'normal' breast even when suitable for breast conserving surgery. Reasons for requesting CPM include prevention of recurrence, peace of mind and moving on after breast cancer. Some women seek CPM as a delayed procedure but factors influencing this are poorly understood. Methods: A retrospective analysis examined patients undergoing CPM as either an immediate or delayed procedure with or without breast reconstruction (BR) at a single tertiary referral centre between January 2009 and December 2019. A cross-sectional survey was undertaken that was compiled and based on validated questionnaires and responses to defined statements generated using a 5-point Likert scale (1 = strongly disagree to 5 = strongly agree) with calculation of mean scores and standard deviation (SD). This questionnaire explored patient's decision-making process in terms of timing of CPM and any BR and was supported by subjective free-text boxes to gauge qualitative and quantitative aspects of the patient-related decision-making process. Those patients who consented to participate were provided with access to an online questionnaire. Results: Amongst this cohort of 39 delayed CPM patients, there were 6 decliners and therefore questionnaires were issued to the remaining 33 patients. The response rate was 67% (22/33) and the most common reason for seeking delayed CPM was to allow completion of adjuvant treatment recommendations (including radiotherapy/chemotherapy) before surgery on the unaffected breast [mean score 2.91; SD 1.0]. This avoided risk of delay in commencement of adjuvant treatment consequent to potential complications of contralateral surgery (especially with BR). The second most important reason for choosing delayed CPM was unavailability of genetic test results at the time of therapeutic mastectomy [mean score 2.64; SD 1.4]. The third most common reason was a subsequent change in family history cancer history after their personal breast cancer diagnosis that often prompted genetic testing [mean score 2.55; SD 2.7]. Several patients cited a shorter recovery time as a strong reason for requesting delayed CPM. Conclusion: Factors determining delayed CPM are patient-driven and this accords with documented reasons for women seeking CPM in general. Patients tend to make decisions about CPM based on two main themes relating to either 'fear' of cancer or a desire to 'take control'. Temporal factors are important in the context

of a delayed procedure and relate to subsequent availability of genetic test results and changes in family history in relatives who were otherwise unaffected at the time of initial diagnosis. Completion of all cancer treatments prior to delayed CPM (with BR) can be advantageous when implant-based BR is planned at the time of an immediate CPM. Radiotherapy can increase capsular contracture rates and surgical complications can delay start of chemotherapy. CPM should be offered as a potentially delayed option with informed discussion of risks and benefits.

Disclosure(s):

Chien Lin Soh, BA: No financial relationships to disclose

Samantha Muktar, MBBS, MRCS, BMedSci: No financial relationships to disclose

Charles M Malata, BSc(HB), MB ChB, MRCS LRCP, FRCS(Glasg), FRCS(Plast): No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-05-45

Providing Educational Resources during the Pandemic for Advanced Breast Cancer Patients

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Significance and Background: Metastatic Breast Cancer (MBC) or Advanced Breast Cancer (ABC) is multifaceted and requires high levels of support and resource utilization. The ABC Program at MD Anderson Cancer Center began in 2014 with a goal to increase the quantity and quality of life for patients living with MBC. It offers emotional support, personalized visits with a nurse practitioner navigator, access to clinical trials, specialty clinics, tailored patient education and innovative care projects. Prior to COVID-19, the ABC Program held a 90-minute quarterly town hall series featuring 2-3 presenters and topics of patient interest. In response to COVID-19, it pivoted to a weekly virtual 60-minute educational series called "ABCs of Healthy Living in Challenging Times" that is for patients with breast cancer, caregivers, faculty, staff, community members and advocates. Purpose: To address COVID-19 social-distancing related isolation and changes to healthcare, build community, empower patients, and educate on diverse topics including patient services, treatment, symptom management and quality of life. Interventions and Evaluation: The series was facilitated by a nurse practitioner navigator via Zoom. A distribution list created from town hall meetings was the basis for the series' notices and has grown by referrals, word of mouth and marketing opportunities; it began with less than 150 people and has grown to more than 550 people. The facilitator offered a format where the attendees and speakers could interact visually and verbally with each other. From 4/2020 to 6/2022, 104 webinars were held for 2,546 attendees for an average of 24 attendees each week. Topics covered were side effect management/quality of life/healthy lifestyle (26%), patient education/empowerment (18%), treatment (19%), clinical trials/research (11%), quality of life related to COVID-19 (8%), COVID-19 (7%), innovation projects (4%), palliative/end of life care (7%), and financial/disability concerns (3%). The series was evaluated using the Qualtrics survey software (n=53). Respondents said that the series has positively influenced their interactions with healthcare providers (65%), how patients with MBC think about their cancer experiences (65%) and provided an opportunity to connect with others like themselves (65%). Respondents stated actions taken based on the series: shared the information with family/friends (77%), joined or remained in a support group (34%), spoke with a provider for

information and services (32%), requested an appointment with the ABC Program or other specialty clinics (26%), started a new healthy behavior (21%), joined a clinical trial (11%), or started using a patient reported outcome tool (9%). The series served mostly patients living with MBC (70%), established patients at MD Anderson (38%) or patients at MD Anderson as well as a community cancer center (17%). Most respondents indicated that they attended about half of the time, usually or always (60%) and are very or completely satisfied with the series (92%). Demographics of the respondents were White (77%), Black (13%), Asian (4%) and Hispanic (16%). Discussion: The ABC Program pivoted to COVID-19 by offering services virtually. The virtual series has allowed for more digestible patient education, varied presentations, and participation for those living outside of Houston, TX. Peer support and continuing education are imperative dynamics for patients to use their voice to impact their overall quality of life. The series has impacted attendees with a change in behavior when speaking with their clinical team, awareness and utilization of support resources, and starting healthy behaviors. While the series was created in response to demands of COVID-19, it effectively addressed psychosocial and educational needs and overall quality of life of MBC patients. The series was an easy intervention to initiate with lasting changes relative to the effort and resources required.

Disclosure(s):

Ginny T. Kirklin, MPH: No financial relationships to disclose

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Debu Tripathy, MD: AstraZeneca: Fees for lectures (educational) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing); GlaxoSmithKline: Consulting (Ongoing); Novartis: Clinical research support (paid to institution) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing); OncoPep: Steering committee (Ongoing); Pfizer: Consulting (Ongoing)

12/9/2022

7:00 AM - 8:15 AM

P6-05-46

Project SOAR (Speaking Our African American Realities): A qualitative study of the Strong Black Woman schema in the breast cancer context

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Background: Marked disparities exist for African American women, relative to non-Latina white women, in the five-year survival rate for breast cancer. Black women breast cancer survivors also demonstrate relative disadvantage in specific quality of life (QOL) domains, persisting through at least two years after diagnosis. Although Black women have higher QOL in the spiritual domain relative to white women, disparities include lower physical QOL, as well as more pronounced depressive symptoms, perceived stress, fear of dying, unmet supportive care needs, and financial distress, with younger Black women (< 50 years) particularly at risk. African American breast cancer survivors also report receiving too little information from their oncologists during diagnosis, treatment, and follow-up care. Sociodemographic and medical factors only partially explain the QOL disparities. The goal of Project SOAR (Speaking Our African American Realities), a community-academic partnership, is to interrogate the potential relevance of the Strong Black Woman (or Black Superwoman) schema in the breast cancer context. The schema involves historically grounded expectations to prioritize caregiving over self-care, suppress emotions, present an image of strength, decline support, and strive to achieve success without adequate resources. Method: Black women were recruited via relevant email listservs and flyers distributed at local breast cancer events to take part in a study "to understand the unique experiences of African American women and their views on the Strong Black Woman concept as it applies during their breast cancer experience." Eligibility criteria were self-identification as being: 1) an African American woman (or a Black woman living in the United States); 2) diagnosed with breast cancer (any stage, any diagnosis duration); 3) at least 21 years old; and 4) able to communicate in English. Three Gatherings (i.e., culturally curated focus groups) were held as half-day experiences in intimate settings (e.g., private homes, a church) in three California cities (Sacramento, Oakland, Los Angeles). Gatherings provided an entirely Black women's space to discuss the breast cancer experience and the relevance and consequences of the Strong Black Woman schema, break bread together, and engage in an inspiring activity. Reflexive thematic analysis was conducted on the Gatherings transcripts with

a critical realist, contextualist approach. Results: All participants (N = 37; age range = 30-94 years; M = 59 years) had heard of the concept of the Strong Black Woman. Reflexive thematic analysis yielded six themes: 1) historical legacy of Strong Black Woman; 2) navigating intersecting Strong Black Woman identities; 3) everyday challenges encountered on the battlefield by Strong Black Women; 4) Strong Black Woman in action during the breast cancer journey; 5) the complexities of seeking and accepting support; and 6) the liberated Strong Black Woman. Participants linked both negative and positive consequences with the Strong Black Woman schema. Negative consequences included the oncologic team and others expecting them to be strong and not to need support, as well as expectations of themselves to suppress emotions and to continue caring for others to the neglect of caring for themselves. Positive consequences included engaging in self-advocacy in the oncologic context, having a sense of resilience, and redefining strength to include expressing emotions and accepting help from others. Conclusion: Qualitative analysis revealed the relevance of the Strong Black Woman schema in the breast cancer context, as well as its negative and positive consequences. Future research can assess whether oncologic professionals' awareness of the schema is useful in ensuring they offer support and refer Black women diagnosed with breast cancer to culturally relevant supportive resources.

Disclosure(s):

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7:00 AM - 8:15 AM

P6-05-47

Preimplantation genetic testing for BRCA gene mutation carriers - the future of health care in Poland?

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Introduction

Genetic background is rarely the cause of breast cancer incidence. Mutations in genes that increase the risk of breast cancer (most commonly BRCA1/2) are diagnosed in about 5-10% of patients. The lifetime risk of breast cancer in BRCA1/2 gene mutation carriers is 80%, and for ovarian cancer from 40-60%, while the chance of passing the mutation to offspring is 50%. The use of pre-implantation genetic testing (PGT-M) of the embryo during in vitro treatment prevents the transfer of mutated gene associated with an increased risk of cancer to the child. The significantly limited availability and high cost of PGT-M in Poland prevent its widespread use. The aim of the survey was to assess interest in PGT-M by female carriers of mutations in genes that increase cancer risk in Poland.

Material and Methods

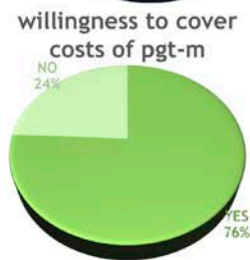
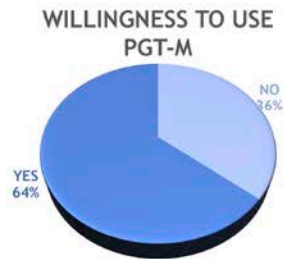
The survey covered 103 persons, 102 with diagnosed mutations in genes that increase cancer risk. The questionnaire consisted of 22 questions regarding: age and gender of the patients, carriage of mutations in genes that increase the risk of cancer (age of mutation diagnosis, type of mutation, preventive measures taken, carriage of mutations in the family, incidence of cancer among relatives, and care of relatives during illness), and knowledge of pre-implantation diagnosis and attitudes regarding the use of PGT-M to avoid passing the defective gene to offspring.

Results

The study included 101 women (98.1%) and 2 men (1.9%), with a median age of 38 years (22-74). Fifty-two (50.5%) were diagnosed with cancer: 50 with breast cancer and 2 with ovarian cancer. Eighty-one subjects (78.6%) were diagnosed with a mutation in the BRCA1 gene, seventeen (16.5%) in the BRCA2 gene, three (2.9%) in the CHEK2 gene, two (1.9%) in the TP53 gene and one (1%) in the PALB gene. The median age of mutation diagnosis was 34 years (18-66). A significant proportion of patients took prophylactic measures, sixty-one (59.2%) underwent risk-reducing mastectomy (RRM), and forty-six (44.7%) risk-reducing salphingo-oophorectomy (RRSO). Ninety-five subjects (92.2%) declared regular visits to a genetic counseling center. Thirty-two persons (31.1%) had a family history of cancer (1-5 members in the family), mainly in 1st degree relatives – parents and siblings (about 60% of cases), the predominant cancers were breast cancer (106 cases), ovarian cancer (38 cases) and prostate cancer (7 cases); eighty-two family members died of cancer, seventy-five (72.8%) respondents accompanied family members in the dying process. Twenty-six individuals (25.2%) knew what PGT-M was, information was obtained from an oncologist (11), gynecologist (7), geneticist (6), other patients (6) and most often from the Internet (17). Seventy-four respondents (71.8%) had children. Thirty-three (32%) declared that information about carrying a mutation in a gene that increases cancer risk influenced their decision to have offspring. Sixty-eight (64.1%) of the respondents, with prior knowledge of PGT-M and with the availability of the method, would have used the diagnosis in combination with in vitro fertilization to avoid passing the defective gene to offspring. Fifty subjects (48.5%) were willing to cover the costs of this procedure.

Conclusions

PGT-M in combination with in vitro fertilization is a safe and effective method of preventing the transfer of a defective gene to offspring. Due to the lack of availability and high cost of the procedure, it is not available in daily clinical practice among carriers of mutations in genes that increase the risk of cancer in Poland. Their own incidence of cancer, multiple incidences in family members and involvement in the dying process may influence patients' decisions to have offspring and motivate them to seek out centers offering PGT-M. The results of this survey indicate the need to offer pre-implantation testing to patients despite the lack of reimbursement and to increase its availability in Poland.



Disclosure(s):

Joanna Kufel-Grabowska, clinical oncologist: No financial relationships to disclose

Amira Podolak, molecular biology specialist: Urteste: Salary (Ongoing)

Mikołaj Bartoszkiewicz, clinical trials specialist: No financial relationships to disclose

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7:00 AM - 8:15 AM

P6-05-48

Perceptions About Breast Cancer in North Africa: A Social Listening Project

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Background

Social media platforms are a versatile platform used for exchange of information. It is increasingly being used by patients, caregivers, and physicians to interact and engage among themselves and with healthcare organizations. Breast cancer is the most commonly diagnosed cancer in the world, with ~2.3 million cases in 2020 alone. Hence, it is vital to understand the perceptions about breast cancer from a wider lookout to bridge the gaps in patient management.

The objective of this study was to understand the trends in social media conversations and current perceptions about breast cancer in the North African countries.

Methods

Artificial Intelligence (AI) technologies hosted by Brandwatch (a social analytics tool) were used to scan 100M websites to analyze publicly visible online conversations about cancer between November 1, 2018 and October 31, 2021. Conversations from 6 North African countries i.e. Algeria, Egypt, Morocco, Sudan, Tunisia, and Western Sahara were analyzed in 3 languages (Arabic, English, and French).

Conversations were filtered to isolate breast cancer and related mentions. To isolate the voice of breast cancer patients and their caregivers, manual review of all non-news content in which pronouns appeared within 7 words proximity of disease terms was carried out.

Results

A total volume of 53,354 conversations (43,785 Arabic, 6,161 English, and 3,408 French) on breast cancer were analyzed.

Breast cancer was the most discussed cancer type, contributing to 63% of Arabic, 61% of English, and 66% of French conversations among total cancer related conversations. Egypt led the volume of breast cancer related conversations in Arabic and English, followed by Sudan. Morocco led the volume of conversations in French, followed by Tunisia. For all 3 languages, the proportion of male authors dominated the volume of conversations as compared to female authors (60% of Arabic, 54% of English, and 56% of French). A total volume of 590 (347 Arabic, 158 English, and 85 French) conversations about breast cancer were identified as patient related. Twitter was the most popular platform for Arabic and English-speaking populations.

The most discussed topic about breast cancer was identified to be 'Pink October' or 'Breast Cancer Awareness Month'.

Across all languages, impact on mental health and financial security was a significant patient concern. Many people reached out directly to the online community for financial support. In Arabic conversations, female patients expressed concern about impact on their relationship with their spouse (or future spouse) due to their condition. Patient conversations about the

BRCA gene (BRCA) were also observed. However, there is little evidence about the extent of awareness among patients or their caregivers. There were scarce mentions about male/transgender breast cancer among conversations. Discussions about raising awareness, early detection, and self-checking of breast cancer were also identified.

Conclusion

Breast cancer was the most discussed type of cancer in North African countries. Patients and caregivers sought financial support on social media platforms. Based on types of conversations identified, it can be inferred that patients do not actively seek information about treatments and cancer management on social media.

These insights can be utilized to engage patients, caregivers, patient advocacy groups, and influencers to address concerns and disseminate accurate and simplified information for mass consumption.

Types of Patient Conversations

Table 1: Types of Patient Conversations*

Sr. No.	Conversation Category	Total	Arabic	English	French
1	Financial impact	36	15	13	8
2	Disease related	15		7	8
3	Request for moral support	24	07	7	10
4	Impact on mental health	34	05	24	5
5	Impact on personal life	32	32	0	0
6	Impact on social life	03	02	0	1
7	Request for information	2	0	1	1
8	Screening/ diagnosis conversation	80	44	17	19

Financial impact – This category included conversation in which patients and/or their caregivers have requested for financial support or have expressed concerns over the cost of treatment.

Impact on mental health – This category included conversations from patients about how breast cancer has affected their mental well-being and the associated emotions

Impact on personal life – This category included conversations about impact of breast cancer on patients' relationships with their spouse and their family. This category also included conversations about impact of breast cancer on marriage prospects.

Impact on social life – This category included conversations on the negative effect of breast cancer on patient's social relations and social interactions.

* Retweets and reshared posts included

Disclosure(s):

Amel Ladjeroud, n/a: Pfizer Inc.: Consulting Fees (e.g., advisory boards) (Ongoing)

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12/9/2022

7:00 AM - 8:15 AM

P6-05-49

Modeling a public-private grant initiative to address breast cancer care disparities at the community level

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Background: Breast cancer disparities between Black and White women have persisted in the US, with breast cancer death rates 40% higher in Black women compared to White women (American Cancer Society Cancer Facts & Figures for African American/Black People 2022-2024). Education and interventions at the community level can potentially reduce racial gaps, particularly in curbing late-stage diagnoses that disproportionately affect Black women with breast cancer. Together, the American Cancer Society (ACS) and Pfizer Global Medical Grants (Pfizer) developed a collaborative model to support health systems in engaging communities to reduce breast cancer disparities between Black and White women. This collaboration aimed to identify novel interventions and provide foundational support for these communities to advance their work in bridging the gap in breast cancer disparities. Methods: This collaborative grant program divided project responsibilities, in which Pfizer provided funding and ACS provided project oversight and technical support. An advisory committee provided input on the areas of most need, impact and project direction. Funding applicants were required to partner with local organizations to implement evidence-based initiatives for education and/or quality improvement within the respected community. The grant award selection committee comprised of experts in the field, including breast cancer survivors and individuals from racial/ethnic minority groups. In response to a Request for Proposals, over 100 applications were systematically reviewed based on the National Cancer Institute grant selection process. The committee selected 9 grantees with innovative proposals addressing breast cancer disparities for Black women along the cancer-care continuum. Bi-annual progress reports were used to measure progress, with a final report to mark projects' impact and reach. The COVID-19 pandemic presented numerous obstacles during the project period and the ability to convene with partners virtually through web-based sessions helped to foster opportunities for collaboration and knowledge sharing among leaders in cancer disparities research. Results: The projects occurred from January 2020 to June 2022, with no-cost extensions given to accommodate COVID-19 pandemic delays. During this period grantees successfully completed project goals in one of three areas: screening, identifying areas of need and education. Approximately 10,000 patients and 200

healthcare professions were impacted among three projects focused on increasing mammography efforts in Black women during the project period. Three projects incorporated surveys and focus groups to identify novel areas for intervention/need and interviewed over 350 patients and over 60 health care professionals. The remaining three grantee projects that focused on education successfully implemented advertisement campaigns and lecture series to target patients and healthcare professionals. The projects selected under this model independently completed their goals within the project period while also laying a foundation to continue work in reducing disparities along the cancer care continuum with their enhanced community partner relations. Additionally, the project period also provided opportunities for external collaborations and discussion among all grantees through 8 ACS-coordinated online sessions and 3 summits. Conclusions: Projects selected by the public-private grant initiative model can enhance community relationships and provide infrastructure to continue work along the cancer care continuum. We believe this collaborative competitive grant program can be used for future efforts to address breast cancer and other health disparities at the community level. Similar collaborative funding projects related to prostate and pan-tumor disparities have been launched and are currently ongoing.

Disclosure(s):

Emily C. Marlow, PhD, MS: Pfizer: My postdoctoral fellowship is supported through ACS by a grant from Pfizer. (Ongoing)

Kristen Wehling, MPH: Pfizer: Grant funding for developing external grant research program (Ongoing)

Karla Wysocki, MA: Pfizer: Salary (Ongoing)

Jacqueline Waldrop, MS: Pfizer Inc.: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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12/9/2022

7:00 AM - 8:15 AM

P6-05-50

Lobular Breast Cancer Alliance Inc. Survey of Individuals with Metastatic Invasive Lobular Carcinoma

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Background: The Lobular Breast Cancer Alliance Inc. (LBCA) is committed to raising awareness of the distinctive characteristics of invasive lobular carcinoma (ILC) and promoting and funding ILC research. Comprising 15% of all breast cancers, ILC tumors often form in a linear, sometimes diffuse fashion both within the breast and in metastatic sites, making them difficult to diagnose, monitor, and treat. LBCA surveyed individuals living with metastatic ILC (mILC) about their experiences with detection and monitoring of mILC. Methods: LBCA conducted an anonymous, online survey of persons living with mILC using SurveyMonkey. The survey was shared with LBCA newsletter subscribers, sister organizations, and via social media. Survey questions asked about metastatic site locations, imaging and monitoring modalities, and patient experience with disease progression and clinician discussions about mILC. An independent IRB review determined the study was exempt from full IRB review. Results: 241 people living with mILC completed the survey. 77% were from the US and Canada. 71% were between 35-64 years of age. 41% had been diagnosed with de novo metastatic ILC. Bone was the most common site of initial metastasis with 75% diagnosed de novo (DN) and 59% diagnosed with a distant recurrence (DR). GI metastases (including metastases to stomach, colon, bowel, peritoneum, or rectum) were reported by 11% of the DN and 14% of the DR groups, respectively. Unusual sites for breast cancer metastasis (to genitourinary organs, eye, or skin) were reported by 11% of the DN and 16% of the DR groups. Metastatic progression was reported by 47% of respondents including to bone (42%), to the liver (22%), and 40% reported progression within the initial metastatic site. 36% of individuals with DN mILC reported progression as compared to 54% among those with a DR. Both groups reported living with mILC for similar durations (on average 3.9 years for DN; 3.3 for DR). 36% of respondents reported that at least one imaging modality failed to visualize one or more of their metastatic sites at initial diagnosis of mILC. 54% of respondents with bone metastases and 19% of those with GI metastases indicated their metastases had not been visualized by standard imaging modalities. 48% of all surveyed stated their mILC was an unexpected or an incidental finding made during another medical procedure, of those, 64% were bone metastases. 25% of respondents whose metastases progressed indicated imaging failed to detect one or more of their sites of progression. In both the DN and DR groups, the most frequently utilized tests and/or procedures used to monitor for progression or changes in metastases were routine blood and tumor marker tests. Respondents with DN mILC reported an average 12 months between first report of symptoms and mILC diagnosis. Those with DR reported an average 8 months between symptom reporting and diagnosis. 42% of all respondents reported that a doctor had told them what symptoms to report at any time. 58% of respondents reported feeling that non-oncologists caring for them (primarily PCPs, radiologists, and gastroenterologists) needed to be better informed about ILC. Conclusion: Surveyed individuals confirmed the perception that mILC can occur in unique locations and be difficult to diagnose and that mILC may be challenging to monitor, and standard surveillance methods may fail to visualize mILC. While a large percent of respondents reported that their mILC diagnoses were unexpected or incidental findings during another medical procedure, this may be due to different understandings of "incidental." This and the fact that more respondents with DR mILC reported progression than those with DN mILC warrant further study.

Disclosure(s):

Laurie B. Hutcheson, M.S.: No financial relationships to disclose

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(stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Medtronic: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Merck: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Organon: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Teva: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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12/9/2022

7:00 AM - 8:15 AM

P6-05-51

Best Quality of Care from a Distance (BQual-D): Maintaining high quality care for hormone receptor positive (HR+) metastatic breast cancer (MBC) during the COVID pandemic, patient participation and satisfaction with the program.

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Background During the COVID pandemic, we designed and implemented a program, called BQual-D, to maintain high quality care for patients with HR+, HER2 negative MBC who were taking oral anti-cancer therapy and needed to shelter at home. This program augmented available clinical resources with (1) trained nurse coaches to manage side effects, improve adherence, monitor for cancer progression and screen for psychological distress via telehealth, and (2) a care coordinator to arrange blood testing at local labs to facilitate timely medication dose adjustments. BQual-D served patients from August 2020 through April 2021. Here, we describe survey results assessing patient (pt) satisfaction with BQual-D. **Methods** Pt's satisfaction surveys included questions rated on a Likert scale (1 "strongly disagree" to 5 "strongly agree") with questions regarding the following: satisfaction with the quality of the nurse coaching calls; perception that the nurse coach listened to what they were trying to convey; whether or not their needs were met by the nurse coaching calls; whether they felt that they received adequate explanation regarding the nurse coaching calls; whether they would recommend the nurse coaching calls to a friend; perception of whether or not the nurse coach was negative or critical towards them; whether or not they would do it over (i.e., if they would return to the nurse coaching calls); whether or not they felt that the nurse coach was friendly or warm toward them; they were able to more effectively deal with care and symptoms; they felt free to express themselves; they were able to focus on what was of real concern to them; the nurse seemed to understand what they were thinking and feeling. Patients were also asked how much the calls helped with their care and symptoms. Descriptive statistics are reported (i.e., frequencies and means). Results 84 pts were screened and contacted for the BQual-D program. Of the 64 pts who responded, 52 (81.3%) were interested and enrolled in BQual-D; 12 (18.8%) declined. Among those who enrolled, 1 voluntarily withdrew, and 7 withdrew due to change in treatment. Participants had a mean age of 65 (range 36 – 88 yrs) and the following racial distribution - Caucasian/White (38, 73.1%), Black or African American (12, 23.1%), American Indian (1, 1.9%) and American Indian or Alaskan Native (1, 1.9%). Satisfaction surveys were received from 32 (50%) pts. Results of surveys regarding patient satisfaction with the nurse coach were generally positive. Pts agreed or strongly agreed that they were satisfied with the quality of the nurse coaching calls (94%), the nurse coach listened to what they were trying to convey (94%), their needs were met by the nurse coaching calls (91%), they understood the purpose of the call (90%), and they would recommend the nurse coaching calls to a friend (88%). The majority (74%) agreed or strongly agreed that they were able to more effectively deal with their care and symptoms after the nurse coach calls. When asked how much the calls helped their care and symptoms, 61% indicated that they made things a lot better, 19% indicated that they made things somewhat better, 16% indicated that they made no difference. One patient indicated that the calls made things somewhat worse. **Conclusions** During the COVID pandemic, when sheltering at home was encouraged, patient satisfaction with BQual-D, which provided additional health resources (nurse coaches, care coordinator) to support pts on oral therapy for HR+ MBC, was high. Resources needed to implement BQual-D should be explored as a way of providing additional support for pts to minimize the requirement for in-person visits. **Funding:** Supported by a grant from Pfizer.

Disclosure(s):

Gretchen Kimmick, MD, MS: Biotheranostics: Virtual Advisory Board (Terminated, March 23, 2021); Immunomedics: Virtual Advisory Board (Terminated, October 1, 2020); Pfizer: Research Grant (Terminated, May 31, 2022); Research-To-Practice: interview (Terminated, November 19, 2021); Springer Nature: Royalty (Ongoing); UpToDate: Royalty (Ongoing)

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Jeremy Force, DO: Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing), Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); G1 Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); OncoSec: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); PRIME: Consulting Fees (e.g., advisory boards) (Ongoing); Rain Therapeutics: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Veracyte: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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7:00 AM - 8:15 AM

P6-05-52

Addressing Healthcare Gaps and Disparities in Electronic Medical Record Messages: A Quality Improvement Project Among Breast Cancer Patients

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Introduction: Despite evidence that utilization of Electronic Medical Record (EMR) messaging positively impacts patients with cancer, there is little research on who uses EMR messaging and for what purpose.

Methods: Sociodemographic and MyChart usage data was collected from Epic to identify patterns of EMR messaging by patients at an academic breast center. Study eligibility included breast cancer patients who completed a visit and sent at least one message to a provider during the study period (May 2021- May 2022). Chi-square and t-tests were used to describe differences between users and non-users of EMR messaging. ANOVA and chi-square were used to describe differences between race/ethnicity. Analyses were performed in R version 4.2 and $p < 0.05$ was considered statistically significant.

Results: A total of 4069 patients who had MyChart account activated were included in the analysis sample. Of those, 3575 (87.9%) were messaging users and 494 (12.1%) were non-users. The mean age of users was significantly lower compared to the non-users (57.7 vs 61.2, $p < .001$). There were statistically significant racial/ethnic differences ($p < 0.001$) by user status with 83.9% and 9.5% of users being non-Hispanic White (NHW) and non-Hispanic Black (NHB) respectively. Among non-users 69.6% were NHW and 21.1% were NHB. There were also significant differences in preferred language ($p < 0.001$) and payor ($p < 0.001$) by user status. 99.2% of users were English speaking and 96.8% of non-users were non-English speaking. 54% and 38%, and 6.5% of users had Managed care, Medicare, and Medicaid respectively as their payor. Whereas 36.9%, 51%, and 10.5% of non-users had Managed care, Medicare, and Medicaid respectively. Lastly, there were statistically significant racial/ethnic differences in the types of messages sent among EMR users.

Conclusions: There are significant differences in race/ethnicity among EMR users and non-users, and racial/ethnic differences in the types of messages sent among EMR messaging users. We believe that these differences may be in part due to disparities in access or comfort in using EMR. Future directions include conducting interviews with minority patients who are users and non-users of EMR messaging to identify barriers and gaps in use.

Table 1. Patient Characteristics

	Non-User (N=494)	User (N=3575)	Total (N=4069)	P value
AGE YEARS				< 0.001
Mean (sd)	61.188 (15.993)	57.710 (14.463)	58.132 (14.699)	
Range	16 - 99	17 - 97	16 - 99	
SEX				0.031
Female	484 (98.0%)	3541 (99.0%)	4025 (98.9%)	
Male	10 (2.0%)	34 (1.0%)	44 (1.1%)	
RACE/ETHNICITY				< 0.001
Non-Hispanic White	344 (69.6%)	2998 (83.9%)	3342 (82.1%)	
Non-Hispanic Black	104 (21.1%)	341 (9.5%)	445 (10.9%)	
Hispanic	26 (5.3%)	110 (3.1%)	136 (3.3%)	
Other	20 (4.0%)	126 (3.5%)	146 (3.6%)	
COUNTY				< 0.001
Other WI county/Out of State	69 (14.2%)	296 (8.3%)	365 (9.1%)	
Milwaukee county	232 (47.8%)	1701 (48.0%)	1933 (47.9%)	
Waukesha county	103 (21.2%)	1023 (28.8%)	1126 (27.9%)	
Washington/Ozaukee County	36 (7.4%)	279 (7.9%)	315 (7.8%)	
Racine/Kenosha County	45 (9.3%)	248 (7.0%)	293 (7.3%)	
PREFERRED LANGUAGE				< 0.001
English	478 (96.8%)	3545 (99.2%)	4023 (98.9%)	
Spanish	9 (1.8%)	12 (0.3%)	21 (0.5%)	
Hmong	0 (0.0%)	4 (0.1%)	4 (0.1%)	
Russian	2 (0.4%)	3 (0.1%)	5 (0.1%)	
American Sign Language	0 (0.0%)	2 (0.1%)	2 (0.0%)	
Other	5 (1.0%)	9 (0.3%)	14 (0.3%)	
INTERPRETER NEEDED				< 0.001
No	477 (97.0%)	3551 (99.3%)	4028 (99.0%)	
Yes	15 (3.0%)	24 (0.7%)	39 (1.0%)	
PAYOR				< 0.001
Managed Care	180 (36.9%)	1922 (54.0%)	2102 (52.0%)	
Medicaid	51 (10.5%)	230 (6.5%)	281 (6.9%)	
Medicare	249 (51.0%)	1353 (38.0%)	1602 (39.6%)	
Other	8 (1.6%)	51 (1.4%)	59 (1.5%)	
MEDICARE				< 0.001
N	242 (49.0%)	2186 (61.1%)	2428 (59.7%)	
Y	252 (51.0%)	1389 (38.9%)	1641 (40.3%)	
MEDICAID				< 0.001
N	389 (78.7%)	3155 (88.3%)	3544 (87.1%)	
Y	105 (21.3%)	420 (11.7%)	525 (12.9%)	
DUAL COVERAGE				< 0.001
N	445 (90.1%)	3417 (95.6%)	3862 (94.9%)	
Y	49 (9.9%)	158 (4.4%)	207 (5.1%)	

Characteristics of users and non-users of EMR messaging. Chi-square and T-test for significance were performed to assess the difference between groups. P< .05 was considered significant.

Table 2. Message Type by Race/Ethnicity

	Non-Hispanic White (N=2998)	Non-Hispanic Black (N=342)	Hispanic (N=110)	Other (N=126)	Total (N=3575)	P value
General Questionnaire Submission						< 0.001
No	630 (21.1%)	133 (39.3%)	24 (21.8%)	27 (21.4%)	814 (22.9%)	
Yes	2355 (78.9%)	205 (60.7%)	86 (78.2%)	99 (78.6%)	2745 (77.1%)	
History Questionnaire Submission						< 0.001
No	2177 (72.9%)	290 (85.8%)	89 (80.9%)	112 (88.9%)	2668 (75.0%)	
Yes	808 (27.1%)	48 (14.2%)	21 (19.1%)	14 (11.1%)	891 (25.0%)	
Appointment Cancel Request						0.005
No	1616 (54.1%)	158 (46.7%)	48 (43.6%)	75 (59.5%)	1897 (53.3%)	
Yes	1369 (45.9%)	180 (53.3%)	62 (56.4%)	51 (40.5%)	1662 (46.7%)	
Appointment Schedule Request						0.597
No	1199 (40.2%)	129 (38.2%)	41 (37.3%)	56 (44.4%)	1425 (40.0%)	
Yes	1786 (59.8%)	209 (61.8%)	69 (62.7%)	70 (55.6%)	2134 (60.0%)	
Customer Service Request						0.384
No	2779 (93.1%)	323 (95.6%)	102 (92.7%)	118 (93.7%)	3322 (93.3%)	
Yes	206 (6.9%)	15 (4.4%)	8 (7.3%)	8 (6.3%)	237 (6.7%)	
Information Update Request						0.222
No	2352 (78.8%)	258 (76.3%)	91 (82.7%)	106 (84.1%)	2807 (78.9%)	
Yes	633 (21.2%)	80 (23.7%)	19 (17.3%)	20 (15.9%)	752 (21.1%)	
Medication Renewal Request						0.005
No	2483 (83.2%)	262 (77.5%)	81 (73.6%)	101 (80.2%)	2927 (82.2%)	
Yes	502 (16.8%)	76 (22.5%)	29 (26.4%)	25 (19.8%)	632 (17.8%)	
Questionnaire Series Submission						0.357
No	2965 (99.3%)	338 (100.0%)	109 (99.1%)	126 (100.0%)	3538 (99.4%)	
Yes	20 (0.7%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	21 (0.6%)	
Questionnaire Submission CC						< 0.001
No	475 (15.9%)	68 (20.1%)	24 (21.8%)	35 (27.8%)	602 (16.9%)	
Yes	2510 (84.1%)	270 (79.9%)	86 (78.2%)	91 (72.2%)	2957 (83.1%)	
User Message						0.306
No	1773 (59.4%)	217 (64.2%)	67 (60.9%)	80 (63.5%)	2137 (60.0%)	
Yes	1212 (40.6%)	121 (35.8%)	43 (39.1%)	46 (36.5%)	1422 (40.0%)	

Types of message sent by race/ethnicity. ANOVA and chi-square were used to describe differences between race/ethnicity and type of message sent. $P < .05$ was considered significant.

Disclosure(s):

Meghan Conroy, BS: No financial relationships to disclose

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Aprill Dawson, PhD: No financial relationships to disclose

Anna Beckius, MS: No financial relationships to disclose

Heun Min, BS: No financial relationships to disclose

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P6-05-53

“ANDEAN CARAVAN” & “MAUCHIS PLATFORM”: 1st MOBILE CLINIC AND 1st ARTIFICIAL INTELLIGENCE PLATFORM AGAINST CANCER IN PERU

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Science, Technology and Society have been related for many years with the goal of providing technological advances for the service of human development. Healthcare has not been immune to this influence and today there are numerous examples that promote the management of various diseases. Therefore, it is important to incorporate this technology into our daily lives, which will allow us to interact quickly and easily with various sectors of Peruvian society, regardless of their level of education or physical location. In this context, Technology and Innovation have become great allies in reinforcing health education and raising awareness of the importance of preventing and reducing the risks caused by cancer. By modifying some lifestyles for "healthy" ones, we would reduce the number of sick people. Knowing that in our country, 11 women die every day from breast and cervical cancer, totally preventable diseases that no one should die from; and that the government is completely overwhelmed in its preventive work, we decided to approach the mining industry. Together, we managed to create a "MOBILE CLINIC", an itinerant bus that will deliver medical care and perform oncological screening tests (Mammography, Ultrasound, Colposcopy and/or Laboratory Tests) to women from vulnerable populations in the communities that are within the area of influence of formal mining in Peru. Similarly, during these meetings all residents will be taught about the use of our Artificial Intelligence platform "MAUCHIS", (www.mauchis.org). Mauchis is the first and only free Platform available 24 hours a day, 365 days a year in Latin America for the prevention of cancer accessible from Whatsapp (+51 1 994003265) and/or Facebook Messenger. This service is free, no payment will be accepted and no institution or company is promoted.

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Mauricio León Rivera, n/a: No financial relationships to disclose

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P6-05-54

"Clinical Trials are Space Travel": Moderators of Recurrence Stress among Breast Cancer Oncologists

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Background: Being an oncologist means accepting that some patients will have disease recurrence despite the most expert treatments. The universality of that experience, however, does not negate the potential for decisional regret and emotional distress on the part of the physician. The broad scale movement towards treatment optimization in medicine likely complicates this experience, as enrollment in de-escalation clinical trials inevitably means that the patient will receive less than the current standard of care. The objective of this study was to assess physician perceptions of potential emotional distress and decisional regret following patient recurrence through exploring the broad range of factors that either moderate or exacerbate those experiences. Methods: Physicians who treat breast cancer in academic and community settings across the United States participated in a qualitative interview designed to assess physician perspectives regarding patient enrollment in de-escalation clinical trials. Purposive sampling techniques were utilized to construct a balanced sample (sex, time in practice) of 39 participants. A subsection of the interview schedule centered on the experiences of decisional regret and distress surrounding patient recurrence. Interviews were recorded, transcribed, and analyzed in order to identify shared themes. Two independent coders performed a content analysis, identifying and recording factors that impact the level of distress that the physician may feel. Results: Thirty-six physicians provided in depth responses regarding their experience when a patient recurs. A total of 21 factors that affected recurrence stress were identified and spanned broad categories including patient features, disease biology, the design of the clinical trial, and characteristics of the physician. All participants expressed willingness to enroll patients in de-escalation-focused clinical trials. However, approximately half of the sample indicated that the experience would be worse after enrollment in a de-escalation trial than after a traditional intensification trial, and a quarter admitted that patient recurrence after a de-escalation trial would impact their decision making regarding future patient enrollment. Individuals not likely to experience distress emphasized having a strong trial rationale, informed patient consent, and engaging in shared decision-making, while greater distress centered on the fear of “not doing enough” and the patient missing out on necessary treatment. Conclusions: Many factors contribute to the experience of physician decisional regret and emotional distress after patient recurrence. Although most physicians recognize the importance of de-escalation focused clinical trials, a significant proportion indicated a greater potential for distress following patient recurrence in such trials and offered insight into how trial design and the process of patient enrollment can be improved to minimize potential distress.

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7:00 AM - 8:15 AM

P6-05-55

Financial Toxicity Outcomes on a Phase I 5-fraction Partial Breast Irradiation Protocol for Early Stage Breast Cancer

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Purpose/Objectives: Accelerated partial breast irradiation (APBI) has been shown to have both acceptable oncologic and cosmetic outcomes for early stage breast cancer following breast-conserving surgery (BCS). Given the demonstrated financial toxicity (FT) of conventional radiation treatments on breast cancer patients, we wanted to quantitatively assess the FT on patients treated with APBI in our phase I five fraction stereotactic APBI (S-PBI) trial, which could be generalized across APBI treatment regimens. **Methods:** A phase I dose escalation trial of S-PBI for early stage breast cancer following BCS was conducted. Women age > 18 years with in-situ or stage I-II (AJCC 7) invasive breast cancer < 3 cm following BCS with > 2 mm margins were treated with S-PBI in 5 fractions to a total dose of 30 to 40 Gy over 2.5 Gy increments (Clinical trials.gov ID NCT01162200). One month following completion of treatment, patients were asked to complete our novel "Patient Perspective Cost and Convenience of Care Questionnaire" developed at our institution. **Results:** Of 75 patients enrolled and treated, questionnaire data was available for 66 patients. Our trial encompassed a wide spectrum of annual household incomes, with 25.5% of patients (n=14/55) reporting income of less than \$30k and 45.5% (n=25/55) reporting incomes of more than \$80k. Educational status was also well represented with 53.1% completing at least some college (n= 34/64), 25% holding post graduate or professional degrees (n=16/64), and 21.9% patients reporting a high school equivalent or less (n=14/64). Overall 48.4% of patients (n=30/62) said that oncologic treatment did not present a financial burden; however, 29.0% (n=20/62) patients reported a somewhat to significant financial burden. Neither household income nor patient education status predicted perceived FT. Of the 6 patients (9.7%) who reported significant FT, 5 reported travelling at least 25 miles one way for treatment with 2 of these patient travelling over 175 miles. Half of the patients reported having private insurance for medication (49.2%, n=32/65), 33.8% had governmental coverage (n=22/65), 6.1% had both private and government coverage, 7.7% had no coverage (n=5/65), and 3.0% were unsure of their coverage (n=2/65). Only 1 of the 6 patients with significant FT had no coverage. Over half of the patients (54.2%, n=34/62) reported a co-pay during their treatment with a median out of pocket cost of \$300 for treatment (range \$10-10000, n=16). Over half of the patients were working full or part time during treatment (54.2%, n=32/59). All 26 patients that were working full time had to take time off work for treatment (median of 5 days, range 0.25 days – 10 days). Over a third of these patients (34.6%, n=9) had to use vacation time or unpaid time off. There was an additional patient who reported months off without pay. Additionally, 24.2% of patients (n=15/62) reported they had family or friends take time off work due to the patient's treatment. Finally, patients were surveyed on the treatment related disruption to their daily activities and enjoyment of life rated on a scale 0-10, with 0 being no disruption, median values were 3 and 1, respectively. Patients also reported a median score of 10 (scale 0-10, 10 being most satisfied) on satisfaction with treatment time. **Conclusions:** In this cohort of patients, interestingly FT was significant primarily in the 10% of patients who traveled a significant distance for these treatments. However, despite this, and the fact that patients were undergoing cytotoxic cancer therapy, impressively, all patients were uniformly satisfied with treatment time (median score of 10), and most did not express significant disruption to their life. We plan to explore the impact of further reducing treatment fractions (with our single fraction S-PBI studies) on FT and quality of life in future studies.

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Ambrosia Simmons, MD PhD: No financial relationships to disclose

David Sher, MD: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-05-56

Current Status and Focus of Breast Reconstruction Research in China and Abroad-A Bibliometric Study

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Objective: The aim of this study was to conduct a bibliometric and visual analysis of breast reconstruction related research at China and abroad published in the past five years, to understand the research status and development trend in this field, to discuss the focus of research in different countries and different disciplines, and to provide reference for other researchers. Methods: Relevant literatures about breast reconstruction were retrieved from the Web of Science Core Collection. The VOS viewer 1.6.15 software was used to extract the authors, countries, institutions and keywords to generate network maps of high-yield authors, institutions and high-frequency keywords clustering network. Results: 4,815 documents meeting the requirements were retrieved, which showed an upward trend in the past five years. Regarding the discipline, 838 documents (17.40%) were published by breast surgery and Cancer Surgery, 3308 (68.70%) were published by plastic surgery, and 669 (13.90%) were jointly published by both types of researchers. A total of 161 clinical trials were registered in the US clinical trial registry (ClinicalTrial.gov), of which intervention trials accounted for the highest proportion (107, 66.46%), followed by observational trials (54, 33.54%) and patient registry (4, 2.48%). Regarding country distribution, the United States conducted the largest number of breast reconstruction-related clinical trials (45, 27.95%), followed by China (22, 13.66%), Italy (12, 7.45%), France (11, 6.83%), the Netherlands (9, 5.59%). The top ten institutions

contributed 983 articles (20.41%), and the institution with the highest number of publications was MD Anderson Cancer Center (144, 2.99%), followed by Harvard Medical School (139, 2.89%), Sloan-Kettering Cancer Center (125, 2.60%), Stanford University (113, 2.35%) and University of Michigan (102, 2.12%). The author with the largest number of documents was Bernard T. Lee of Beth Israel Deaconess Medical Center (BIDMC), with 56 papers and 540 citations. The most cited author was Andrea L. Pusic of Brigham and Women's Hospital, with 48 papers and 1,332 citations. Chinese authors published 310 documents, accounting for 6.44%. There were differences in the disciplines of the main authors between China and abroad. In China, authors from breast surgery published a larger proportion of documents (138, 44.52%), while the number of documents published by authors of plastic surgery (129, 44.52%) and the joint publication of both types of authors (43, 13.87%) was relatively small. However, foreign documents mainly came from authors of plastic surgery (74.74%). There were more cooperative groups (155) formed by major foreign authors, and joint publishing between groups was more frequent; while Chinese author formed only 16 cooperative groups with less cooperation. Keyword cluster analysis showed that top five keywords were flap, implant, breast cancer, immediate breast reconstruction, tissue. In breast surgery publications, top five keywords were breast cancer, breast reconstruction, complications, implant, immediate breast reconstruction, while in plastic surgery publications top five keywords were flap, implant, tissue, breast cancer, infection. Authors from breast surgery focus more on oncology-related issues in breast reconstruction, while in plastic surgery, more attentions were paid on autologous tissue reconstruction. Conclusion: Breast reconstruction had gradually attracted the attention of Chinese and foreign researchers. Compared with foreign countries, there were problems such as lack of high-quality research and less cooperative research in China. There were differences in the research focus of breast reconstruction between China and abroad, which is mainly related to the differences in the disciplines of researchers.

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7:00 AM - 8:15 AM

P6-05-57

Developing and feasibility testing a web-based intervention (ePainQ) to support post-operative pain and symptom self-management following surgery for breast cancer

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Background: Breast cancer is the most commonly diagnosed women's cancer with 2.3 million new global cases diagnosed in 2020. The global rise in survivorship has resulted in a significant health and economic burden on society. Breast cancer survivors report being overwhelmed physically and emotionally with treatment adverse effects. Recommendations include self-management support and personalised follow-up to meet patient needs. Persistent post-surgical pain (PPSP) is the most common negative consequence of breast surgery, often relating to inadequate acute post-surgical pain management. An unintended consequence of day surgery is reduced post-operative pain monitoring. There is a need to ensure appropriate support and pain monitoring alongside preparation, behavioural change and expectation management. Web-based interventions (WBI) could be a potential solution. A mixed-methods approach was used to develop a WBI to capture patient self-reported post-operative symptoms and provide individualised self-management advice. Methods: An audit and service evaluation revealed a 46% PPSP rate and identified opportunities where advice could support improved self-management. Developing the WBI (ePainQ) comprised a scoping review, systematic review, and development study with all results informing the development of ePainQ. ePainQ comprised two parts; a website containing supportive information and a post-operative symptom questionnaire. Intervention questions included pain, swelling, infection, functionality and QoL. Advice was generated for each question with different levels, based on CTCAE grading agreed with clinicians. A feasibility study prospectively tested ePainQ for acceptability, usability and perceived usefulness. Feasibility study aims were assessing uptake, retention, follow up and completion rates and acceptability of ePainQ. Study arms: usual care (cohort) or intervention (ePainQ). Intervention: daily online symptom questionnaire for 2 weeks commencing the day after surgery. Participants received immediate advice based on the severity of the reported symptoms, either self-management advice or in cases of clinical concern, advice to contact the hospital team. Reports were immediately available to HCPs as

ePainQ was linked to the electronic patient record. Data collection: baseline, 2 weeks, 3 and 9 months post-operatively. Outcome measures: EORTC C30, and BR23, EQ-5D, HADS and BPI. Patient Activation was measured at baseline and 9 months. Results: 69 patients recruited over 8 months; 60 intervention and 9 cohort. Mean age: 57.7yrs (SD 9.8; range 38-82). Recruitment rate was 63%. IT issues prevented 12/60 using ePainQ but engagement of the 48/60 active participants was 89.6%. 40/48 completed a usability scale in which • 97.5% highlighted ePainQ as easy to use • 95% reported not needing any technical support • 90% felt very confident using ePainQ Outcome measures: 69/69 (100%) completion at baseline and 2 weeks. No active withdrawals with 13/69 passive withdrawals by 9 months. 67 participants (97.1%) consented to an interview invite with 14/67 interviews conducted. Participants were a mix of compliance rates to be reflective of the study and capture both positive and negative feedback. Feasibility study results demonstrated that ePainQ was perceived to be simple, easy to use and not requiring much learning to use effectively. All pre-set criteria for progression to a phase III RCT were met. Conclusion: ePainQ was designed in response to patient identified needs. The feasibility study established that ePainQ was accepted, used, and liked by participants who interacted with it. Even participants with limited use felt they had benefited from the advice. Results demonstrated patient positivity towards ePainQ suggesting recruitment rates could be increased if research capacity was improved and higher retention rates if IT issues were resolved and daily reporting duration was slightly reduced.

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7:00 AM - 8:15 AM

P6-05-58

Comparing Patient-Reported Outcomes for Same-day Discharge and Inpatient Admission After Mastectomy

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Background: Same-day discharge after mastectomy has been demonstrated to be safe in appropriately selected candidates. However, the association between same-day discharge after mastectomy and quality of life (QOL) is unclear. Patient-reported outcome (PRO) measures represent important indicators of QOL among patients undergoing treatment for breast cancer. In this study, we aimed to evaluate the effect of same-day discharge after mastectomy on PROs.

Methods: We performed a retrospective review of a prospectively collected, longitudinal PRO registry of female breast cancer patients treated at an academic breast center between June 2019 and June 2022. Patients were invited to complete the BREAST-Q module, a validated PRO questionnaire measuring QOL domains such as psychosocial wellbeing, physical wellbeing, satisfaction with their surgeon, and satisfaction with their medical team. Preoperative and 2-week postoperative questionnaire responses were analyzed in this study. Patients who had a mastectomy with or without reconstruction were included in this analysis. Those who underwent immediate reconstruction with autologous tissue were excluded as these operations are not conducive to same-day discharge. Patients were divided into two groups: the first was discharged on the date of surgery while the second was admitted to the hospital for a minimum of one night. Clinical and demographic factors were collected from a review of the electronic medical record. The primary endpoints were mean satisfaction scores as well as differences between postoperative and preoperative scores for the psychosocial and physical wellbeing domains. T-tests were used to evaluate differences between groups. A multiple regression model was fit to adjust for the effects of relevant clinical and demographic factors.

Results: A total of 104 patients within the registry underwent mastectomy during the study period and were offered questionnaires. Of these, 58 completed both the preoperative and 2-week postoperative questionnaire (56% response rate); 20 (34%) in the same-day discharge group and 38 (66%) in the inpatient admission group. The groups were similar in age, stage, American Society of Anesthesiologists' classification group, body mass index, frequency of unplanned readmission or reoperation, and receipt of bilateral mastectomy, axillary lymph node dissection, post-mastectomy reconstruction, and neoadjuvant chemotherapy. Mean patient satisfaction scores and mean changes in psychosocial and physical wellbeing scores were similar between the groups 2 weeks after surgery (Table 1). After controlling for age, type of reconstructive operation, receipt of unplanned reoperation, and preoperative score, same-day discharge did not have a significant effect on satisfaction with the surgeon (Beta=-4.3, p=0.37), satisfaction with the medical team (Beta=0.2, p=0.97), physical wellbeing score (Beta=-0.1, p=0.99), or psychosocial wellbeing score (Beta=8.0, p=0.15).

Conclusions: Patients who are discharged from the hospital on the same day of a mastectomy display similar levels of satisfaction with their care team and similar short-term trends in physical and psychosocial wellbeing compared to those who are admitted to the hospital. While further data are being accrued, these early results suggest patients tolerate same-day discharge after mastectomy well.

Table 1

	Same-day Discharge Mean change in score from baseline (SD) N=20	Inpatient Admission Mean change in score from baseline (SD) N=38	Significance (P value)
Satisfaction with Surgeon	87.5 (17.5)	90.0 (15.9)	0.58
Satisfaction with Medical Team	94.4 (12.8)	94.2 (12.3)	0.95
Psychosocial Wellbeing – Change from Preoperative Score	-14.2 (27.4)	-5.8 (22.3)	0.23
Physical Wellbeing – Change from Preoperative Score	-28.4 (26.2)	-26.6 (31.4)	0.83

Patient-reported outcomes at 2 weeks after mastectomy for patients discharged on the date of surgery compared to those admitted inpatient

Disclosure(s):

Sudheer Vemuru, MD: No financial relationships to disclose

Kathryn Colborn, PhD: No financial relationships to disclose

Laura Leonard, MD: No financial relationships to disclose

Victoria Huynh, MD: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-05-59

Clinical Characteristics and Prognosis of Postpartum Breast Cancer

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Background: Postpartum breast cancer (PPBC) is a not well-established subset of breast cancer, and only few studies address its poorer prognosis. However, there are previous studies that PPBC is associated with worse outcome with higher rates of metastasis than in young women's breast cancer (YWBC). The purpose of this study was to analyze the clinical characteristics and prognosis according to the onset period of PPBC, Materials and methods: 208,780 breast cancer patients from the online Korean Breast Cancer Society (KBCS) registry database between January 2000 and December 2014 were reviewed retrospectively. Premenopausal women aged 20 to 50 years who underwent breast cancer surgery were included. According to the diagnosis period of breast cancer, it was classified into groups diagnosed within 5 years (PPBC < 5) after delivery, between 5-10 years ($5 \leq \text{PPBC} < 10$), and after 10 years (PPBC ≥ 10). Results: The patients in PPBC < 5 group showed a younger and more advanced stage compared to other groups, and the expression of estrogen receptor (ER) and progesterone receptor (PR) was lower and the HER2 positive rate was higher. PPBC < 5 group had worse survival rate compared to nulliparous and other group (5-year cumulative survival; PPBC < 5 group, 89% vs. nulliparous group, 97.3% vs. $5 \leq \text{PPBC} < 10$ group 93%). In multivariate analysis, PPBC < 5 group was associated with worse survival rate (Hazard ratio 1.55, 95% CI 1.148-2.094, $p=0.004$) after adjustment for age at diagnosis, breast cancer stage, ER and HER2 status, Ki-67 level, and chemotherapy. Conclusion: We demonstrated that patients with breast cancer diagnosed within first five years after delivery had aggressive characteristics and a worse survival rate. In order to improve the survival rate of PPBC, the cause should be identified and new therapeutic strategy should be established.

12/9/2022

7:00 AM - 8:15 AM

P6-05-59

Developing a Community Standard of Care for Individuals Diagnosed with Breast Cancer Patients Across Oregon

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Early in the pandemic, cancer centers across the nation and Oregon canceled their cancer support programs as non-essential medical care. Breast cancer patients were forced to look elsewhere for essential assistance and community support to move along their cancer journeys.

Pink Lemonade Project (PLP), a Vancouver, WA based community based nonprofit, helped fill the gaps and expanded its local support for breast cancer patients. A virtual format allowed PLP to serve more individuals with our psychological, emotional and financial support programs. Next, PLP convened an informal coalition of all the local breast cancer support organizations including those that offer breast cancer support programs, community including dragon boating and rowing, and others that serve broader communities and more people of color.

Then, as Komen National announced its restructuring, and closed the Oregon-Southwest Washington affiliate in Spring 2021, Pink Lemonade Project stepped up again to maintain two locally-grown Komen programs that met critical community need--the MBC Dinner Series and the Treatment Access Program (TAP), a transportation assistance program that served all of Oregon and reduced the geographic barrier to care.

Through the coalition, PLP heard patients express concern that they were receiving outdated information and were struggling more to find needed support and resources from their providers. Understandably, nurse navigators and social workers could not maintain and/or

update patient resources while they assisted COVID patients. The goal of the coalition was to increase communication across the organizations and to share more event schedules for the ease of patients to understand what support programs are available.

This session, delivered by an all breast cancer patient panel, will give an overview of Pink Lemonade Project; its programs that helps with psychological, emotional, community and financial support for breast cancer patients, survivors and those living with metastatic breast cancer; and will highlight the results from the patient point of view of the systematic review of the contents of 6 regional health systems new patient binders and present recommendations for consistent, community-wide content for all future breast cancer patients.

The project's main strength was that Pink Lemonade Project could draw upon on an existing coalition of local, community-based breast cancer organizations to help update and standardize breast cancer support information from the patient point of view. Then by acting as a neutral convener, PLP could request and receive the binders from all the region's healthcare providers to help standardize and update the community resources across all the region's cancer centers. The result is that any new breast cancer patient, regardless of where their access to care is, can receive consistent community-based information and resources.

Another result of this project showed the importance of the partnership of healthcare and human service agencies, especially in a post-pandemic world. As the pandemic continues to strain healthcare, community-based nonprofits have a unique role to help coordinate community resources and improve the quality of life for those affected by breast cancer.

Developing a Community Standard of Care for Individuals Diagnosed with Breast Cancer Across Oregon

Pink Lemonade Project/OHSU Community Partnership Program Grant:
Developing a community standard of care for those diagnosed with breast cancer across Oregon.

Background/Introduction

Early in the pandemic, cancer centers across the nation and Oregon suspended their cancer support programs as non-essential medical care. Breast cancer patients were forced to look elsewhere for essential assistance and community support.

Pink Lemonade Project (PLP) helped fill the gaps and expanded its local support for breast cancer patients. A virtual format allowed PLP to serve more individuals with our psychological, emotional and financial support programs.

Furthermore, as the local Komen affiliate closed on March 31, 2021, Pink Lemonade Project stepped up to maintain two locally-grown Komen programs that met critical community need—the MBC Dinner Series and the Treatment Access Program (TAP), a transportation assistance program that served all of Oregon and reduced the geographic barrier to care. Healthcare staff across Oregon have been strained and unable to maintain and update resource information for breast cancer patients.

Program Goals and Objectives

Goals/Objectives:

1. Activate existing, local breast cancer coalition to gather and update information about community resources & peer supports for those diagnosed with breast cancer.
2. Serve as a neutral convener and invite nurse navigators and oncology social workers to combine and compile individual health systems' health and community support information available and distributed to patients.
3. Pilot disseminating newly developed, comprehensive community support information to participants of the Treatment Access Program (TAP) and test whether patients who need transportation assistance and are interested in additional emotional and psychological community supports, when offered.

Methods-Project Design

Target Population: Breast cancer patients and breast cancer providers across Oregon.

Activities/Interventions:

- Coalition of local breast cancer support organizations.
- Hold information sessions for healthcare providers on PLP programs and especially how to complete financial and program applications.
- Comprehensive review of 6 healthcare partners' breast cancer patient binders and welcome information by patients.
- Provided recommendations of standardized topics and information for healthcare systems to include in their patient information binders.

Time frame of the project: September 2021- June 2022
Evaluation tools: follow up tracking, interviews, pre/post tests- trainings sessions, surveys of binder content

Results

Objective 1:

- An average of 10 Portland breast cancer organizations regularly attended the 4 collaboration meetings from 5/2021 to 6/2022, sharing organization activities and events. Collaboration also pooled resources to light Morrison Bridge pink for Breast Cancer Awareness Month as sign of tribute to departing Komen and to recognize healthcare workers tireless effort to help breast cancer patients during the pandemic.

Key Breast Cancer Coalition Partners:

Objective 2:

- Binders were collected from Compass Oncology, Kaiser Permanente, Legacy, OHSU, PeaceHealth Southwest Medical Center, and Providence.
- 11 breast cancer patients completed surveys evaluating the content and organization of the binders, including a Spanish native-speaker and survivor and two patients living with metastatic breast cancer.
- PLP compiled and updated a list of community and national resources and returned the standardized resource information back to all participating health systems.
- 67 health professionals from 15 organizations/health systems across Oregon were trained on PLP programs and resources, and on how to complete applications for Pink Lemonade Project's financial aid programs, including Treatment Access Program and Pink Practicables.

Objective 3:

- As of 3/31/22, 126 breast cancer patients across Oregon had received TAP assistance.
- As of 3/31/22, 33 people had completed the survey (25% of total).
- We talked with 7 patients who returned the survey, and then provided additional support information. Other patients did not return messages.

Conclusions

The project's main strength was that Pink Lemonade Project could draw upon an existing coalition of local, community-based breast cancer organizations to help update and standardize breast cancer support information from the patient point of view. Then by acting as a neutral convener, PLP could request and receive the binders from all the region's healthcare providers to help standardize and update the community resources across all the region's cancer centers. The result is that any new breast cancer patient, regardless of where their access to care is, can receive consistent community-based information and resources.

Another result of this project showed the importance of the partnership of healthcare and human service agencies, especially in a post-pandemic world. As the pandemic continues to strain healthcare, community-based nonprofits have a unique role to help coordinate community resources and improve the quality of life for those affected by breast cancer.

Due to current program design of TAP and contract with 21Info, PLP does not receive adequate patient contact information to make pilot a success, but in future as a HIPAA-compliant entity, PLP could try again.

Key Partners/Funders/Acknowledgements

Key Healthcare Partners:

- 21Info, Compass Oncology, Kaiser Permanente, Legacy, OHSU, PeaceHealth SW Medical Center, Providence and Legacy

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Breast Cancer Awareness Month
Morrison Bridge Lighting
Friday, October 1st • 6:00 pm

Pink Lemonade Project poster session

Disclosure(s):

Susan Stearns, MBA, MA: Allergan-Natrelle: grant to support Pink Lemonade Project' programs (Ongoing); Oregon Health and Science University Knight Cancer Institute: grant (Terminated, July 31, 2022)

Thalia Williams, n/a: Allergan-Natrelle: grant to support PLP's programs (Ongoing); OHSU Knight Cancer Institute: grant (Terminated, July 31, 2022)

Lisa Peters, n/a: Allergan - Natrelle: grant (Ongoing); OHSU Knight Cancer Institute: grant (Terminated, July 31, 2022)

Sonja Trytko, n/a: Allergan - Natrelle: grant (Ongoing); OHSU Knight Cancer Institute: grant (Terminated, July 31, 2022)

12/9/2022

7:00 AM - 8:15 AM

P6-05-60

People with metastatic breast cancer face barriers to finding information and support

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People with metastatic breast cancer face barriers to finding information and support Background FORCE, a national nonprofit organization developed a health communication tool to help patients assess research relevance, key findings, and the quality of media reporting on cancer to support informed and shared health decision-making. People with metastatic breast cancer (mBC) are a priority population. Methods The organization conducted a survey about awareness of and access to breast cancer information and supportive services for people living with metastatic breast cancer. The organization promoted the survey through e-mail and social media, and a network of partner organizations that serve the metastatic breast cancer community. The survey invited respondents to volunteer to participate in focus groups and a follow-up survey in order to support efforts to serve this priority population. Results and Conclusions While interest in clinical trials was high, many users reported that they do not know how to find an appropriate clinical trial. A majority of the 335 respondents were interested in information about clinical trials, treatment side effects, research findings, long-term health issues, diet/exercise, fatigue, and emotional health. Three quarters of the respondents indicated that they had never participated in a clinical trial, 67% indicated they would be interested in participating in the future, and about 40% indicated they did not know how to find a

clinical trial recruiting people with metastatic breast cancer. Approximately one-third of participants were unable to obtain referrals to services they sought. Other barriers to services included lack of insurance coverage, lack of availability, and the COVID-19 public health emergency. Focus group responses indicate that women with mBC find the health communication tool to be useful, and appropriate in language, images, and tone. Results indicate that women with mBC are interested in finding information about clinical trials and other topics related to treatment side effects and quality of life. FORCE and partners are incorporating these results into tailored online resources to meet the needs of the mBC community.

12/9/2022

7:00 AM - 8:15 AM

P6-06-01

Development of a patient advocate training at UNC's Lineberger Comprehensive Cancer Center

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Development of a patient advocate training at UNC's Lineberger Comprehensive Cancer Center Introduction: Patient advocates are survivors, caregivers, or people affected by cancer who represent the patient experience and bring a nonscientific viewpoint to the research process. Based on a previous assessment of engagement related needs of researchers and patient advocates at UNC's Lineberger Comprehensive Cancer Center (LCCC), the need for a comprehensive training for patient advocates was identified to better facilitate collaboration in cancer research, including learning more about the role of patient advocates to prepare them for meaningful interactions with researchers. Purpose: To provide an engaging, empowering training for patient advocates involved in (or interested in becoming involved in) research projects with faculty and staff of LCCC. LCCC is committed to offering trainings that better equip researchers and patient advocates to meaningfully work together. This training will be the first step towards that goal and introducing patient advocates to patient advocacy, LCCC's programs and services, and working with researchers. Methods: Prior to designing the patient advocate training, we, the student team working with LCCC, created a Curriculum Adaptation

Plan and Diversity, Equity, and Inclusion (DEI) plan to include implementation steps along with questions to ask, items to consider, and examples organized by section. We then conducted three interviews with members of LCCC to collect qualitative data on existing, external patient advocate trainings and provide insight on best practices. Using our findings, we created a five-part training to better equip advocates for research partnership. We reviewed the training for health literacy and to ensure alignment with the Curriculum Adaptation and DEI plans. Lastly, we facilitated a one-hour focus group via Zoom with experienced patient advocates to receive feedback on the training. As a result, we integrated key changes into the final training to encourage participants that all comments and questions are welcome, add clear definitions of patient advocacy, and include an optional activity reviewing research abstracts. Results: We developed a training to engage patient advocates involved or interested in becoming involved in research projects at LCCC. Training objectives include understanding LCCC's goals and the role of patient advocacy, building a sense of community and passion for advocacy, and gaining confidence in providing feedback on research materials. The training consists of a facilitator script and outline, PowerPoint slide deck, handouts, and an evaluation survey to be delivered in a two-hour hybrid synchronous format. Training content is organized into five parts: Welcome and Introductions, Purpose of Training and Introduction to LCCC, What is Patient Advocacy at LCCC?, Practice Giving Feedback, and Conclusion. The training is designed to be skills-based, consisting of group discussions, an interview with a current patient advocate-researcher pair, and the opportunity for participants to make suggestions on research materials. Recommendations: Based on our recommendations, LCCC will offer the training as onboarding for new patient advocates with the option for seasoned patient advocates to attend as a refresher. An individual with direct involvement with patient advocates and researchers will lead the training. To tailor to varying patient advocates' experience and knowledge, more advanced research examples based on participants' experience in advocacy should be included. LCCC will use this training and consider ways to provide iterations of the training in other languages and engage individuals from different cultural backgrounds disproportionately burdened by cancer and not commonly involved in patient advocacy. We propose a scale-up implementation at other institutions to adapt this patient advocate training.

Disclosure(s):

Kathryn L. Kennedy, MPH: No financial relationships to disclose

Angelica M. Mejia, MPH: No financial relationships to disclose

Emily K. Walton, MPH: No financial relationships to disclose

Joia Freeman, MPH: No financial relationships to disclose

Alice Lu, MPH: No financial relationships to disclose

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7:00 AM - 8:15 AM

P6-07-01

Costs of breast cancer recurrence after initial treatment for high risk early breast cancer using SEER-Medicare linked data

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Background:

Despite the good prognosis with treatment for most patients with hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) early breast cancer (EBC), ~ 20–30% of patients experience locoregional or distant disease recurrence. To assist in value assessments of novel therapies in the adjuvant setting, this study aimed to determine the costs of treated breast cancer recurrence following treated EBC.

Methods:

This retrospective study analyzed linked patient data from the US Surveillance Epidemiology and End Results (SEER) registry (2010-2014) and Medicare claims (2009 to 2019, which included data from Part A, B, and Prescription Drug Events [Part D]). Data were analyzed for patients aged ≥ 65 years with HR+, HER2-, node-positive EBC at high risk of recurrence (consistent with monarchE trial high risk criteria). Treated recurrences were defined based on

treatment events/procedure codes, including surgery, radiation and systemic therapy, after a 90-day gap following the last treatment for initial EBC. Recurrences were classified based on Medicare claim diagnosis codes or SEER registry data. Extra cost was defined as cost attributable to treated recurrence. Cumulative extra costs were estimated by calculating cost differences between patients with treated vs non/untreated recurrence. Cumulative extra costs were analyzed over the first 6 years following first treated recurrence, a duration which ensured adequate sample size. Costs were inflated to 2021-US\$.

Results:

We identified 3081 eligible patients (mean age at diagnosis 74.5±7.1 years, 97.4% female, 87.8% White). We identified 964 patients with treated recurrence (distant=432, locoregional=128, contralateral=9, unclassified=347) and 2117 patients with non/untreated recurrence. Six-year cumulative extra costs were higher for patients with distant recurrences (\$168,656) than for patients with locoregional recurrences (\$96,465) (Table 1).

Conclusions:

Cost of recurrence in patients with high risk EBC is considerable, particularly in patients with distant recurrences. Most patients who recurred in this population experienced distant recurrence. Delaying or preventing recurrence may reduce long term costs in these high risk EBC patients.

Table 1: Mean cumulative extra costs attributable to treated recurrence

[SEER CoR Abstract Table 1.tif](#)

Disclosure(s):

Alexandra S. Vitko, n/a: Eli Lilly and Company: Full-time employee (Ongoing), Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

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7:00 AM - 8:15 AM

P6-08-01

A cost-consequence analysis of pertuzumab in the neoadjuvant treatment of high-risk HER2+ Early-Stage Breast Cancer (EBC): health-economic considerations for drug availability in Italy

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Introduction: Neoadjuvant pertuzumab+trastuzumab+chemotherapy (TPC) combo is a well established treatment for HER2+ high-risk (EBC) as recommended by International and National guidelines. However, notwithstanding EMA approval, in some European countries (i.e Italy and France) pertuzumab drug-access is prevented by the NHS decision not to reimburse the drug in a value-driven sustainability balance. This study aims to estimate the cost and consequences of TPC vs. the same combo w/o pertuzumab (TC) in the neoadjuvant treatment of high-risk HER2+ eBC to better understand the value of TPC regimen.

Methods: With a Markov model, we simulated the costs and consequences associated to TPC or TC neoadjuvant treatments, using 5 years time horizon and Italian Lombardy region Health System point of view. The model includes nine health states: Neoadjuvant treatment; Surgery; Invasive disease-free Survival (IDFS) with pathological complete response (pCR), IDFS with residual disease (RD), non-metastatic recurrence, remission, first-line treatment and subsequent-lines for metastatic cancer, and death. Transition probabilities and utilities were

derived from relevant clinical trials and literature. For each neoadjuvant treatment, the model estimates: direct (drug, administration, hospitalization, disease management), indirect (patients' loss of productivity), total costs and different outcomes, as cumulative incidence of metastatic recurrence, days of work lost, days with activity impairment, IDFS life years, and quality adjusted life years (QALY). Costs and outcomes were estimated per 100-treated patients. An alternative scenario analysis with a 10-year time horizon and a deterministic sensitivity analysis was performed to assess the impact of model time horizon and parameters value.

Results: The estimated costs and outcomes for TPC and TC are reported in Table 1. TPC produces a total direct cost reduction of €75,630 per 100-treated patients, a small increase of TPC neoadjuvant treatment costs (+4.8%) is offset by the lower cost of metastatic treatment and management (-20.4%). Considering also the indirect costs, TPC is associated to a cost reduction of €124,956 per 100-treated patients. The cost saving is associated to a reduction of 5-year cumulative incidence metastatic recurrence (8.32% vs 10.42%, -20.14%), a reduction of days of work loss (-548 days) and days with activity impairment (-283 days) and a 10.5 QALY gained per 100-treated patients. Using a 10-year time horizon, the value of TPC compared to TC increases. Probabilities of pCR with TPC and TC were the parameter with the higher impact on model results.

Conclusion: Use of TC instead of TPC in high-risk HER2+ EBC derives a marginal savings (4.8%) according to the first year of our cost-consequence analysis. However, this negligible savings comes with the need for a heavily and long-lasting adjuvant cytotoxic therapy escalation because of a lower clinical activity of TC vs TPC. Moreover, according to medium-term cost-consequence analysis (5 years) the early negligible savings is overwhelmed by the subsequent increase in costs for the patients' management, because of the lower clinical efficacy of TC vs. TPC. In Italy, the lack of pertuzumab in the neoadjuvant setting of high-risk HER2+ eBC is questionable; our results support the opportunity to reconsider the pertuzumab availability in Italy and reduce inequalities within Europe.

Cost and consequences of neoadjuvant treatments for high-risk HER2-Positive Early-Stage Breast Cancer: trastuzumab+pertuzumab+chemotherapy (TPC) vs trastuzumab+chemotherapy (TC)

[Table 1.tif](#)

IDFS, Invasive disease-free Survival; QALY, quality adjusted life years.

Disclosure(s):

Alberto Zambelli, MD: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Eli-Lilly: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Exact Sciences: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Gilead: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); Istituto Gentili: Consulting Fees (e.g., advisory boards) (Terminated, June 30, 2022), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Terminated, June 30, 2022); MDS (Merck Sharp&Dome): Consulting Fees (e.g., advisory

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12/9/2022

7:00 AM - 8:15 AM

P6-08-02

Developing a Patient-Centered Video Intervention to Improve Uptake of Genetic Testing for Cancer Among Black Americans: The Stakeholder's Perspective

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Introduction Advances in genetic testing have contributed to improvements in our approach to early detection, prevention, and treatment of breast cancer. All populations, however, have not equally benefited from the scientific advances. Cancer genetic testing can directly impact the health and wellbeing of entire families. Uptake of cancer genetic testing continues to be significantly lower among Black patients with unequal access, fear, and medical mistrust all contributing to this disparity. Objective: To address the racial disparity in genetic testing uptake we are developing a short patient-centered video intervention to inform, educate, and

encourage Black women and men to consider genetic testing when recommended by a provider. Methods To begin, we created a 15-minute video using data from a recently completed video-based qualitative interview study that included 47 people who have a known genetic or inherited cancer risk. We reviewed coded transcripts of participants' study videos, with a prioritization of the perspectives of the Black participants about learning about their cancer risk due to a hereditary predisposition, their decision making around genetic testing, and testing experiences. From this review, we created a montage video of short segments from 9 patients (4 of whom were Black). Next, we conducted qualitative stakeholder interviews with 10 Black patients who had undergone genetic testing for cancer within the last year and 10 oncologists and genetic counselors involved in genetic testing (mix of Black and non-Black providers). All participants were made aware that our goal is to develop a video intervention. Interviews were conducted via zoom, with interviewees being shown the montage in segments, followed by questions about why people choose to test (or not), barriers to and concerns around testing. We also asked for thoughts about what information might be important to improve chances of uptake of genetic testing for Black patients. Participants were also asked about whether patient-centered videos were an appropriate intervention strategy, and if so, the preferred voices and messages to be included. Results Initial analysis of the qualitative interviews shows strong support for an intervention focused on patient-centered videos, indicating possible acceptability and clinical utility of this approach. Relatability and representation were mentioned as key, though there was not agreement as to whether all patients need to be Black in an intervention targeting a Black audience. Patients described appreciating seeing other patients discuss genetic testing as a mechanism to reduce risk by facilitating early detection. Patients also felt that describing possible benefits for children and future generations could be a powerful message, and noted that given the widespread fear of cancer, the authenticity of the patients' perspectives could provide important reassurance. In contrast, patient discussions of their specific problems with insurance and other barriers to testing were identified as possibly problematic for this approach, without explicit identification of solutions. Both providers and patients identified a need for factual information about inherited cancer risk, and the processes and implications of genetic testing alongside experiential content. Patients may not be best placed to deliver such information as it is usually outside of their expertise. Conclusions This developmental work suggests the potential impact of incorporating the patient voice into interventions to increase uptake of cancer genetic testing. Based on this work, we are planning to interview more patients to develop a video-based intervention that will combine information around inherited risk, testing, finances and implications of testing and patients' perspectives that will then be evaluated in a randomized clinical trial.

Disclosure(s):

Katherine C. Smith, Professor: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-08-03

Barriers to enrolling in observational trials for patients with stage IV breast cancer.

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Title: Barriers to enrolling in observational trials for patients with stage IV breast cancer.

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Background and Purpose

Increasing research data support the existence of barriers and discrepancies to oncology interventional clinical trial enrollment rate based on patients' social-economic status. However, few studies examined if such discrepancy exists in observational trials. We hypothesize the enrollment discrepancy remains the same in specimen collection only protocols, and several factors including health literacy and religious belief contribute to such discrepancy.

Methods

Data was collected from March 1st, 2022, to July 7th, 2022, as part of an ongoing pilot study examining circulating tumor DNA (ctDNA) from patients diagnosed with stage IV metastatic breast cancer starting a new line of therapy treatment (BCM protocol number H- 48751). This study was selected as specimen collected is part of normally scheduled standard of care clinical labs and beyond informed consent does not require any additional patient commitment for participation. This study was performed across both county and private practice sites: 1) Smith Clinic-Harris Health System 2) Baylor Saint Luke's Medical center (BSLMC); respectively.

Correlations for independent variables potentially affecting enrollment were assessed to estimate the association between patient participation and socio-economic factors like religious affiliation and level of formal education received. Free-form text responses were collected from patients who declined study participation.

Results

Fourteen eligible candidates were asked to participate in the observational trial to determine whether serial changes in ctDNA ratio correlate with the results of first monitoring patients via imaging at three months. Out of 14 patients approached, 5 patients (36%) declined. Interestingly, all five patients who declined were from Smith Clinic- Harris Health System, while all BSLMC patients agreed to enroll. Based on the free-text response of why patients declined the ctDNA study, we identified a total of 4 different categories: Language barriers, low health literacy, religious objection, and disinterest in research. Using these four categories, we continue to collect data to improve our understanding of barriers in observational trial enrollment.

Conclusion

Low literacy and other socioeconomic factors serve as barriers to enrollment in observational trials for patients who suffer from stage IV breast cancers. In our preliminary data, we also noted that these barriers are only relevant for patients who are treated at the county hospital. An investigation to recognize low literacy and religious affiliation as barriers to poor trial accrual is ongoing.

Reasons to declining participation in observational trial.

Reason	(n = %)
Language barrier	20
Low health literacy	40
Religious objection	20
Disinterest	20

Disclosure(s):

Maria L. Machado Heredia, IMG: No financial relationships to disclose

Alphi Kuriakose, BS: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-08-04

Geographical variation of social deprivation, cardiovascular and other comorbidities in 226,516 patients with early breast cancer in England: results from a National Registry Dataset Analysis

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Background In England, as for many countries, there are geographical variations in treatment uptake and outcomes for patients with early breast cancer (EBC). It is important such inequalities are addressed. The co-existence of cardiovascular disease (CVD) in patients with early breast cancer (EBC) may complicate treatment choices, lead to deviations from standard of care, and be associated with worse cancer and CVD outcomes. Social deprivation is also associated with increased incidence of co-morbidities, reduced cancer treatment rates, and worse cancer survival. If there are regional differences in rates of CVD/ co-morbidities and social deprivation these may explain observed differences in treatment uptake and cancer outcomes in EBC. Therefore, in this analysis we evaluated rates of CVD and social deprivation in a large population of patients with EBC in 20 English Cancer Alliances. Methods Cancer registry data as part of The Virtual Cardio-Oncology Research Initiative (VICORI) were used to identify patients diagnosed with stage I-III breast cancer diagnosed between 2013 - 2018 in England. National data (hospital records and national cardiovascular audit databases) were used to describe CVD prevalence (CVDp), Index of Multiple Deprivation (IMD), and Charlson Comorbidity Index (CCI). Patient, disease, tumour, and treatment characteristics were allocated into Cancer Alliance tertiles according to CVDp (minimum (< 33.3rd percentile); middle (33.3rd – 66.6th percentile); maximum (>66.6th percentile)) with approximately equal patient numbers in each group. The disease burden was depicted in bar charts and regional variation as heat maps of England. The percentage of patients in the most deprived quintile of income domain of the IMD were plotted. Funnel plots were used to investigate variations in regional CVD rates based on a logistic regression model. Results Data from 226,516 patients with stage I-III breast cancer with a mean age of 62.5 (+/- 13.7) were included in the analysis. 78,833 patients were assigned to the minimum (37.0%; 95% CI 36.7 – 37.2), 74,443 to the middle (35.5%; 95% CI 35.3 – 35.7), and 73,240 to the maximum (34.7%; 95% CI 34.5 – 34.9) tertile. Geographical variation between Cancer Alliances was demonstrated for CVDp (6% - 9.5%), IMD (2%- 30%), and CCI ≥ 4 (8.2% - 9.5%). Variation of CVDp revealed a South/North gradient between Cancer Alliances towards higher percentage, with centrifugal tendency from London. These findings were consistent with a similar pattern seen for variation in IMD quintiles with higher prevalence of most socioeconomic deprived patients located in cancer alliances in the North compared to the South of England. Regional variation was less obvious for CCI. After adjusting for age, TNM stage, IMD, and CCI, differences in the standardised CVD ratio persisted for some cancer alliances suggesting that other factors than those adjusted for are likely accountable for the higher CVDp seen in some Cancer Alliances. An adjusted ordinal logistic regression model demonstrated that older age (aged >75), white ethnicity, and social deprivation were associated with a higher risk of CVDp ($p < 0.001$). Conclusions This study highlights significant geographical variation of social deprivation, CVDp, and other comorbidities in early breast cancer patients in England which may contribute to the variability in treatment received and breast cancer survival in different regions within the country.

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7:00 AM - 8:15 AM

P6-08-05

Racial and Economic Disparities in Social Support and Symptom Distress among Women Diagnosed with Early-Stage Breast Cancer

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Introduction: Social support (SS) is predictive of symptom distress among patients with breast cancer (BC) during the treatment and post-treatment phases. There is evidence of racial and economic disparities in SS seen among patients with cancer. Little is known about how race and income influence SS among patients with BC.

Objectives: 1) To describe SS in women with early-stage BC prior to or at their first chemotherapy treatment (i.e., baseline); 2) To examine how SS varies by race, income level, ability to meet basic financial needs at baseline; and 3) To examine the association between SS and symptom distress at baseline.

Methods: This secondary analysis employed a descriptive, correlational, comparative design

with data from the baseline time point of SEMOARS: The Symptom Experience, Management and Outcomes According to Race and Social Determinants of Health (R01-MD012245), a multi-site, repeated, multi-method study comparing the symptom experience and management in Black and White women with early-stage BC. Inclusion criteria were female, Black or White race, age at least 18 years and prescribed chemotherapy for BC stages 1–3. Measures included self-reported race; income level measured by annual income (low: < \$29,999; medium: \$30,000 to \$69,999, high: ≥ \$70,000) and affordability of basic needs (single item: yes or no). The Interpersonal Support Evaluation List includes four subscales (possible range 0-30), assessing the perceived availability of support (emotional, tangible, self-esteem, and belonging). The Symptom Distress Scale measures the current experiences of 11 symptoms and their severity (possible range: item:1-5; total score:13-65). Descriptive, comparative, correlational, and regression analyses were used.

Results: Participants (N=248; mean age 52.9±12.3 years) were 58.9% White and 41.1%, Black, 54% married/partnered, 57.3% employed, 70.8% had some college education, and 98% insured. Half of the sample (50.5%) reported high income, 30.3% reported medium income, and 19.2% low income. One-fifth (18.5%) reported an inability to afford basic needs. Income and race are moderately correlated, with Black patients more likely to have low income (39.5% vs. 7.6) and less likely to have high income (22.4% vs. 66.7%) (Cramer's V=.472; p<.001). On average, patients reported moderately high levels of SS (emotional=26±5; tangible=25±6; self-esteem=23±4; belonging=25±5). Compared to White patients, Black patients reported lower levels of SS: emotional (24.4 vs. 27.0; p<.001), tangible (24.3 vs. 25.8; p=.02), and belonging (24.3 vs. 25.6; p=.02). Using one-way analysis of variance with multiple comparisons there were significant differences in SS by income level, where patients with low income had lower SS levels (all subscales) when compared with patients of high income (all p<.001) and lower tangible SS when compared with medium income (p=.005). Patients with a medium income had lower emotional and tangible SS when compared with those having high income (p=.003; .022; respectively). Inability to afford basic needs was associated with lower SS (all subscales; p<.01). For all SS subscales lower SS was associated with worse symptom distress (r= -.213;p=.004 to r= -.265; p<.001). Adjusting for race and income (high vs. low and medium; low vs. medium and high), lower scores for each SS subscale, except belonging, were predictive of higher symptom distress scores (all p<.05).

Discussion: For this cohort, Black race, low income, and inability to afford basic needs were associated with lower levels of baseline SS. Regardless of race and income, poor baseline emotional, tangible, and self-esteem SS were significantly correlated with increased symptom distress.

Future Directions: SS is a predictive marker of symptom distress as patients begin BC chemotherapy. Interventions to increase SS in Black and/or low-income women with BC at the patient, clinic, and community level are needed.

Coefficients of associations for individual social support subscales with symptoms distress adjusting for race and income level

Coefficients of associations for individual social support subscales with symptoms distress adjusting for race and income level

Variable	b	95% CI	p	ΔR^2	Adjusted R^2
Emotional SS and Symptoms Distress					
				0.036	0.128
Constant	28.49	22.19 – 34.79	<0.001		
Race	-.213	-2.59 – 2.12	0.845		
Income level(Low [†])	-4.34	1.50 – 7.19	0.003		
Emotional SS	-0.29	-0.52 – -0.06	0.014		
Tangible SS and Symptoms Distress					
				0.034	0.126
Constant	27.58	21.78 – 33.38	<0.001		
Race	-0.72	-3.06 – 1.62	0.545		
Income level(Low [†])	3.82	0.85 – 6.78	0.012		
Tangible SS	-0.25	-0.46 – -0.05	0.017		
Self-esteem and Symptoms Distress					
				0.031	0.123
Constant	28.09	21.64 – 34.54	<0.001		
Race	-0.96	-3.31 – 1.41	0.428		
Income level(Low [†])	4.15	1.25 – 7.046	0.005		
Self-esteem	-0.29	-0.55 – -0.04	0.023		
Belonging and Symptoms Distress					
				0.014	0.105
Constant	25.61	19.30 – 31.93	<0.001		
Race	-0.66	-3.03 – 1.71	0.583		
Income level(Low [†])	4.44	1.52 – 7.37	0.003		
Belonging	-0.18	-0.41 – 0.05	0.125		

Notes: n=175; SS: social support; race was categorized as (0= Black; 1= White); [†]income level was categorized as (0=medium and high; 1=low: reference)

Notes: n=175; SS: social support; race was categorized as (0= Black; 1= White); income level was categorized as (0=medium and high; 1=low: reference)

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P6-08-06

Uncovering gaps in patient-provider perceptions of triple-negative breast cancer care: Addressing disparities through education-advocacy partnerships

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Background: Providers and patients alike are unaware of the racial disparities that exist in triple-negative breast cancer (TNBC), which occurs at twice the rate in women of the African Diaspora (WAD) compared to White American women. WAD tend to be diagnosed at a more advanced stage, use under-resourced health care settings or encounter bias in their care, and experience higher rates of TNBC-related mortality. An historically difficult-to-treat breast cancer subtype, the TNBC landscape is changing with an influx of clinical data and newly approved treatments. An educational initiative was designed to heighten awareness of new therapies, including antibody drug conjugates, empower patients in their care, and to align on addressing disparities in TNBC care. Methods: Two, 1-hour online, interactive, video-based programs were designed for patients and providers. The patient/caregiver program was hosted on CancerCoachLive in April, 2022 and the provider program on OMedLive in May, 2022 and remains on-demand until May 2023. With a focus on addressing disparities in care, 78% of patients/caregivers attending the patient program were of African descent. The initiative was conducted in collaboration with TOUCH, the Black Breast Cancer Alliance and the National Breast Cancer Foundation. Four real-world patient accounts of TNBC navigation and management were embedded in the patient program; and represented women of Caucasian, African, and Native American ethnicity. While practice and knowledge gaps among HCPs, and knowledge gaps of patients were assessed, we report on the analysis of 'tethered', behavioral, practice pattern, and perception questions assessed across the patient and provider programs. Results: As of June 2022, 200 providers and 29,389 patients/caregivers participated in the ongoing activities. Post education, participants in the provider program anticipated the education would positively impact practice behavior (86%) while patients/caregivers reported greater confidence in discussions with their treatment team (92%). Pre- and post-evaluation of strategies addressing disparities revealed improvements in 'ensuring access to care through integration of care coordinators or social worker as part of the healthcare team.' Provider assessment of barriers to enrollment in clinical trials uncovered the top barrier as 'lack of trials at my institution' (33%) and the top barrier to integration of new therapies as 'lack of knowledge regarding evidence-based strategies' (44%). Misalignments in patient-provider perceptions were observed. 'Patient lack of interest' was a provider-identified barrier to clinical trials, yet 60% of patients/caregivers reported that they were 'very likely' to participate in a clinical trial if eligible. Similarly, differences were seen in the ranking of topics of highest interest regarding treatment decisions. Lastly, patient- vs provider-identified care challenges were not aligned. Themes from the real-world patient accounts provided greater context for the misalignments observed. Conclusions: Assessment and alignment of patient-provider care perceptions has potential to impact clinical practice behaviors, patient/caregiver communication and confidence,

and treatment/clinical trial knowledge for effective TNBC management. This educational partnership facilitated assessment of attitudes, perceptions, and barriers to care that can further guide how disparities in care for patients with TNBC are addressed. This 'tethered' approach to education was successful in empowering patients in shared decision-making, initializing changes in clinical practice, and gaining patient-provider insights in TNBC management. This activity was supported by an educational grant from Gilead Sciences, Inc

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-08-07

Reasons for Reduced Willingness to Participate in Clinical Trials During the COVID-19 Pandemic: The Translational Breast Cancer Research Consortium (TBCRC) 057 Survey

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Background:

Historically, less than 10% of adult patients with cancer enroll in clinical trials, however, enrollment dropped further at the onset of the COVID-19 pandemic. Barriers to trial participation during the pandemic have not been reported. As part of the TBCRC 057 survey on the impact of the pandemic on willingness to participate in breast cancer trials, we assessed reasons for reluctance to participate in trials during the pandemic.

Methods:

US residents who self-reported a breast cancer diagnosis were eligible to complete the online survey 8/6/21-9/30/21. Respondents indicated whether they were current trial participants and, if not, their willingness to consider participating in a trial during the pandemic using a 5-point scale (0-not at all willing to 4-definitely willing). Respondents who were not current trial participants and who were not “definitely willing” to consider participation during the pandemic were characterized as “reluctant” and asked to select reasons for their reluctance from a checklist. Pandemic-related anxiety was assessed on an 11-point scale (0-no anxiety to 10-worst anxiety possible). Respondents indicated how the option to conduct trial activities online would affect their decision to participate in a trial (much less likely, somewhat less likely, would not affect my decision, somewhat more likely, or much more likely). In exploratory analyses, we evaluated whether pandemic-related anxiety and favorable reactions towards opportunities to conduct trial activities online were associated with reluctance to consider trial participation during the pandemic due to fear of SARS-CoV-2 exposure. Means were compared with two sample t-tests and proportions with Fisher’s exact tests.

Results:

Of 385 survey respondents, 185 (48%) were characterized as reluctant to consider trial participation during the pandemic. Among these 185, median age was 55 (range 25-80), 85.7% were non-Hispanic White, 48.1% had metastatic disease and 44.2% received care at academic centers. Reasons for reluctance to consider trial participation during the pandemic cited by $\geq 15\%$ of the 185 reluctant respondents are shown in the Table. Respondents who selected fear of exposure to SARS-CoV-2 as a reason for their reluctance to consider participating in a trial during the pandemic had higher mean pandemic-related anxiety (7.0 vs 5.2, $p < 0.001$). These respondents were more likely to indicate telemedicine doctor visits ($p=0.01$), virtual consents ($p=0.001$) and online study questionnaires ($p=0.001$) would make them somewhat or much more likely to participate in trials than respondents who did not select fear of exposure to SARS-CoV-2 as a reason for their reluctance.

Conclusions:

Reasons for reluctance of patients with breast cancer to consider participation in clinical trials during the pandemic are multifactorial. Although concerns about safety and efficacy remain prominent, fear of exposure to SARS-CoV-2 drives unwillingness to participate in >25% of reluctant patients. Trial accrual may benefit from incorporation of electronic activities when possible.

Table

Reason	N (%)
Worry about not getting best treatment	88 (47.6)
Worry about side effects	82 (44.3)
Worry about delaying cancer treatment	58 (31.4)
Fear of exposure to SARS-CoV-2	51 (27.6)
Financial concerns	49 (26.5)
Health insurance concerns	45 (24.3)
Do not want to spend time away from home/family	32 (17.3)
Too overwhelmed	32 (17.3)

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P6-08-09

Self-identified race and Area Deprivation Index in patients with invasive lobular carcinoma of the breast: associations with tumor characteristics and event free survival

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Objectives: Investigators have shown a relationship between race/ethnicity and survival in invasive lobular carcinoma (ILC), the second most common type of breast cancer. While non-white patients with ILC were shown to have worse outcomes, there are no data evaluating the impact of socioeconomic factors. Herein we evaluated the relationship between self-reported race and socioeconomic factors with tumor features and outcomes in early-stage patients with ILC. Methods: We used chi-squared tests, t-tests, the Kruskal-Wallis test, multivariate Cox proportional hazards models, and tests for trend in Stata 16.1 to evaluate race, area deprivation index (ADI), and event-free survival (EFS) in a single institution cohort of patients with stage I-III ILC. Race was self-reported and categorized as black, white, or other. ADI was ascertained from a publicly available database using measures of income, education level, employment, and housing quality to provide information about neighborhood adversity. ADI was evaluated in quintiles, with quintile 1 signifying the least resource deprived neighborhoods, and quintile 5 signifying the most resource deprived. Tumor receptor subtype was defined by estrogen receptor (ER), progesterone receptor (PR), and HER2 status. Body mass index (BMI) of 18.5-24.9 kg/m² was categorized as normal, 25-29.9 kg/m² as overweight, and ≥ 30 kg/m² as obese. Results: Of 823 patients in our institutional database, self-reported race/ethnicity data

were available for 808, with 28 (3.5%) identifying as black, 638 (79.0%) as white, and 142 (17.6%) as other. ADI data were available for 816 patients, with 174 (21.3%) in quintile 1, 210 (25.7%) in quintile 2, 110 (13.5%) in quintile 3, 163 (20.0%) in quintile 4, and 159 (19.5%) in quintile 5. Tumor receptor subtype differed by ADI, with patients in the highest ADI category (most resource-deprived) being most likely to have ER positive, PR positive, and HER2 negative tumors (81.8% in ADI category 5 versus 69.0% in ADI category 1, $p=0.001$). Those in higher ADI categories were also more likely to have lymphovascular invasion (9.2% in ADI category 5 versus 4.3% in ADI category 1, $p=0.008$), and were less likely to present with stage I disease (55.5% in ADI category 5 versus 67.9% in ADI category 1, $p=0.002$). BMI was not associated with tumor characteristics, but was significantly associated with ADI, with a significant trend towards higher BMI in areas of higher ADI ($p < 0.001$). Among patients who self-identified as black, age at diagnosis was significantly higher compared to those identifying as white or other (mean age 65.8, 59.9, and 58.0 years respectively, $p=0.0074$). There were no differences in tumor receptor subtype, grade, presence of LVI, or stage by self-identified race. Black-identifying patients were significantly less likely to have the lowest ADI category (0% versus 22.6% and 20.4% in white and other categories respectively, $p=0.016$), and were significantly more likely to have elevated BMI (79.2% overweight/obese versus 47% of white and 41.5% of other patients, $p=0.003$). On univariate analysis, self-identified black race, elevated ADI, and overweight/obesity were each associated with significantly worse EFS. However, in a multivariate model containing all three predictors, only overweight/obesity remained significantly associated with worse EFS (hazard ratio 1.6, 95% confidence interval 1.1-2.3, $p=0.022$). Conclusions: Although prior investigators identified a relationship between non-white race and worse outcomes in patients with ILC, our data show complex relationships between many factors that impact breast cancer outcomes. The relationship between race and EFS was mitigated by ADI and obesity, suggesting that race is not an independent predictor of outcome in patients with ILC.

Disclosure(s):

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P6-08-10

Cash, Commercial Negotiated Prices, and Correlations with Neighborhood Poverty Levels for Shoppable Breast Cancer Services

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Introduction: On January 1, 2021, the Centers for Medicare and Medicaid Services (CMS) implemented the Hospital Price Transparency Final Rule to promote price competition and improve hospital care affordability. Hospitals in the US are required to disclose, among other items, the cash prices and the payer-specific negotiated prices for CMS-specified, high-volume common services. We investigated the compliance rate and descriptive costs for breast cancer services in the central New Jersey region. Methods: We collected CMS-specified hospital services representing 4 unique Current Procedural Terminology (CPT)/diagnosis related group codes (screening mammography, US guided biopsy, mastectomy, partial lumpectomy). Cash prices and payer-specific negotiated prices for these services were obtained from Turquoise Health, a data service company that specializes in collecting pricing information from hospitals. We collected the median cash price, the proportion of hospitals for which the cash price was lower than its median commercial negotiated price, interquartile ranges (IQR) for cash prices across all services by practice type, and the correlation between cash price of service and neighborhood poverty level. Results: 106 hospitals in a 50-mile radius from central New Jersey were reviewed, representing 22 academic and 84 community clinics. Of these, only 4 hospitals disclosed both their cash price and commercially negotiated price for all services. Overall, there was a correlation for mammography cash price and neighborhood level of poverty (Rs -0.34, p = 0.026). No correlations were noted for the other services. Cash prices varied substantially across hospitals, as evidenced by large IQR for US-guided biopsy \$ 1877.19 (1647.05 – 5388.2), mastectomy \$6417.00 (4847.34 – 48166.69), and lumpectomy \$3820.00 (3021.76 – 17041.84) in academic centers. When compared to community hospitals, academic institutions were more likely to set their cash prices below negotiated insurance prices. Discussion: Of the 106 hospitals investigated, only 4 disclosed both their cash price and commercially negotiated price. As evidenced by the negative correlation between the cash median cash price of screening mammography and neighborhood level of poverty, hospitals encourage entry into the health system. Unfortunately, downstream costs for diagnosis and treatment are unpredictable and present major challenges in preventing financial toxicity and assuring health equity. Because of its descriptive nature, this study was unable to identify factors or outcomes

associated with the cash price variation. Uninsured or underinsured patients who choose to take the cash price offered by hospitals remain extremely vulnerable.

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P6-08-11

Hyperglycemia in Hispanic MBC patients treated with alpelisib: single institution retrospective study

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Background: PIK3CA mutations are found in up to 40% of hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) metastatic breast cancers (MBC). Alpelisib is an orally bioavailable PIK3CA inhibitor approved in combination with fulvestrant based on the SOLAR-1 study. However, uptake has been limited due to toxicity concerns, most commonly hyperglycemia (grade ≥ 3 was 37% in SOLAR-1 and 28% in the BYLieve study, which evaluated alpelisib after progression on a CDK 4/6 inhibitor). Patients with uncontrolled type 2 diabetes (T2DM) were excluded from both studies [defined as fasting plasma glucose (FPG) level >140 mg per deciliter, or a glycosylated hemoglobin (HgbA1C) level of $>6.4\%$]. Of note, both trials enrolled a majority of non-Hispanic White (NHW) patients. Disparities regarding prevalence of diabetes has been reported among Hispanics (H). The Centers for Disease Control and Prevention reports that H are more likely to have T2DM than NHW (approximately 17% vs 8% respectively). Our study aims to characterize the incidence and management of hyperglycemia in H MBC patients treated with alpelisib. Methods: A retrospective chart review was performed to include patients with HR+ HER2- MBC with a documented PIK3CA mutation treated with alpelisib in combination with fulvestrant at Miami Cancer Institute from 2019-2022. Patients were identified using pharmacy records and the COTA real-world database (RWD, an analytics platform enabling investigation of longitudinal RWD). Cases were excluded where the start date was unclear, or treatment was given for a diagnosis other than breast cancer. Based on available data in the medical record, patients were categorized as H or NH. Descriptive statistics were used to describe variables in both groups of patients. Results: Of 46 patients

identified, 34 were included in the final analysis (17 H and 17 NH). The median age was 63 y (range 32-87). The most common PIK3CA mutation identified was H1047R (41.2% of H and 23.5% of NH; $p > 0.05$). Starting body mass index (BMI) was higher in H compared to NH (29.9 vs 24.8; $p < 0.05$). Starting FPG was the same for both groups (115 mg/dL), and within the first two weeks on treatment the highest FPG was higher in H vs NH (250 mg/dL vs 157 mg/dL; $p > 0.05$). H also had the highest peak glucose when compared to NH (333.8 mg/dL vs 217.8 mg/dL; $p < 0.05$). Furthermore, by the end of treatment H had a higher FBG than NH (247.4 mg/dL vs 118.0 mg/dL; $p < 0.05$). Overall, any grade hyperglycemia occurred in 70.6% (82.4% H, 58.8% NH; $p > 0.05$, with high rates of grade 3/4 hyperglycemia in both groups (53% H 41% NH; $p > 0.05$). A higher percentage of H patients required more than one anti-hyperglycemic medication as compared to NH (41% vs 12%; $p > 0.05$). Hispanics time on treatment was shorter compared to NH (151 vs 240 days; $p > 0.05$). Disease progression was the most frequent reason for treatment discontinuation in both groups 52.9%. However, more H patients discontinued alpelisib due to hyperglycemia (23.5% vs 5.9%; $p > 0.31$). Conclusions: Despite starting treatment with similar FPG levels, H had a higher peak plasma glucose level compared to NH. Although not statistically significant, likely due to a small sample size, the rates of hyperglycemia within two weeks of treatment was higher in H than NH. Furthermore, H required the use of more antiglycemic medications and had higher discontinuation rates. Therefore, there is a heightened need to increase education and awareness of glucose monitoring in H during treatment with alpelisib. Further prospective studies are warranted to better define the optimal management of hyperglycemia in H patients.

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7:00 AM - 8:15 AM

P6-08-12

Toward Comprehensive Cancer Prevention for Women Experiencing Homelessness: Demonstrating the Need for Onsite Mammography, Education, Navigation, and Cross Cancer Screenings

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Background: Persons experiencing homelessness (PEH) rarely receive regular preventative health care or consistent cancer screenings. Late stage detection of cancer and barriers to care are prevalent among PEH. Novel programs such as onsite mobile mammography services represents an approach to improve breast cancer disparities among women experiencing homelessness (WEH) and allows for understanding of barriers to cancer screening amongst WEH and to develop best practices. Objectives: During onsite mobile mammography events at shelters for WEH, develop best practices for improving breast cancer screening utilization while

developing approaches to increase use of other cancer screenings. **Methods:** In 2022, the Cleveland Clinic performed onsite mobile mammography screening events at area shelters and day centers. All seven screening events included onsite mammography, breast health education, and patient navigation. After WEH completed the education session, they completed the mammogram. Subsequently, at two events, patients had an opportunity for further consultation with an advanced practice provider (APP) including discussing additional screening tests (ex. colorectal, lung, cervical cancer) beyond mammograms with referrals as needed. Consultations also discussed approaches to reduce cancer risks with further education, referrals for dental care, and assistance securing a primary care provider (PCP). **Results:** At the events that included consultations, 30 patients received mammograms and 80% (n=24) of patients chose to speak with the APP. Patients seeking consultation were 21-73 years old and identified as Black/African American (n=5), White (n=16), and other (n=3). Topics of discussion included mammograms (n=24, 100%), smoking cessation referral and /or lung cancer screening (n=16, 67%), colorectal cancer screening (n=11, 46%), and cervical cancer/HPV screening (n=11, 46%). Additionally, 46% of patients (n=11) were assisted with securing a PCP and 8% of patients (n=2) were referred for dental services. **Discussion:** Our preliminary data demonstrate that most WEH undergoing onsite mammography screening are willing to engage in consultation to discuss additional cancer screenings with many patients eligible for additional cancer screenings. Additionally, this approach provided access to PCPs. Three best practices for cross cancer screenings include: 1) Onsite mobile mammography is an appropriate entry point for addressing breast health and also cancer screening broadly. 2) An onsite approach allows for education beyond cancer screening to provide access to primary care and other wrap around services. 3) Clinicians provide credibility and trust when they attend onsite mobile mammography events. **Conclusion:** Beyond breast cancer screening, WEH benefit from onsite mobile mammography, which can serve as a gateway to cross cancer screenings and access to primary care. Addressing disparities in this population should include wrap around services such as smoking cessation and connection to a PCP. Future research should examine best practices for following up with patients and completing navigation through cross cancer screenings.

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12/9/2022

7:00 AM - 8:15 AM

P6-08-13

**Home-based treatment with subcutaneous (SC) trastuzumab - only a pandemic solution?
Real world evidence (RWE) analysis**

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Background The pandemic has accelerated the introduction of more flexible and cost-effective treatment forms. The efficacy of trastuzumab in the intravenous (IV) and SC forms is similar both in early and advanced HER2-positive breast cancer (BC) patients. Compared to IV administration, SC enables reduction of treatment costs and time, and saves equipment and human resources. SC formulation is more convenient for both patients and healthcare providers and may be implemented as a home-based therapy. Recently, systemic anticancer treatment (including chemotherapy) has been increasingly performed at home, improving patient comfort and reducing the burden on the healthcare system. Poland has already implemented home-based treatment with some biologic compounds; however, they have not included trastuzumab in BC patients. **Objectives** This RWE analysis aims to evaluate the organizational and therapeutic procedures related to the home-based treatment with SC trastuzumab and the attitudes of patients and healthcare providers to this approach. **Material and methods** The study

enrolled early HER2(+) BC patients treated with trastuzumab during the COVID-19 pandemic. Monitoring and treatment duration were consistent with SmPC and reimbursement regulations in Poland. The first 3-6 doses of SC trastuzumab (alone or in combination with CHT) were administered at a cancer center in outpatient and inpatient settings. Subsequent doses were administered at home by 3 qualified breast nurses. Post-injection follow-up was used for educational purposes. Data were analyzed with descriptive statistics. The study was reviewed and approved by the local Bioethics Committee. Results The analysis included 20 patients treated in two comprehensive cancer centers in Poland with a median age of 59 years (range, 36-72 years). Seven patients (35%) were professionally active. The average distance from the place of residence to the cancer center was 24 km (range, 2-65 km). A total of 232 doses were administered (mean 11.6 doses per patient; range 6-14), 133 doses at home and 99 at the cancer center. The overall tolerance of trastuzumab was good and consistent with the known safety profile described in Summary of Product Characteristics. Only 1 patient (5%) discontinued treatment prematurely due to decreased LVEF; another 19 patients completed treatment as planned. For 19 patients (95%), the benefits of SC treatment included time savings, the ability to continue working, and avoiding crowded places and infection risk. 2 patients (10%) considered the nurse's visit privacy disturbing, while 18 (90%) would recommend home-based drug administration. The average duration of a nurse's stay at home was 60 minutes (range 30 to 130 minutes). No logistical or technical problems were reported, except for occasional patient lateness. Nurses positively assessed the treatment provided in the nursing office, which was a source of additional knowledge, and experience. The overall impression of home-based therapy was positive for both patients and nurses. The limitation of the study is the declarative nature of the data. Conclusions Home-based treatment with SC trastuzumab should be pursued due to its safety, ease of organization, positive perception by patients and nurses, and reducing healthcare system resources. It can be particularly valuable for disabled patients who have difficulty reaching the hospital and professionally active patients. Specialized, trained nurses can self-sufficiently carry out part of the prolonged trastuzumab treatment, reducing physician involvement.

Disclosure(s):

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7:00 AM - 8:15 AM

P6-08-14

Breast Cancer Treatment Choices and Results in Hispanic Women Without Funding for Radiation

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Background: Although the survival rates for breast cancer have improved, there is still a disparity gap between Hispanic women and non-Hispanic women. Hispanic women in the US are vulnerable to cancer inequalities due to a plethora of barriers including disproportionate poverty, lack of health insurance, and citizenship status. A Surveillance, Epidemiology, and End Results analysis found that Hispanic women had lower rates of both early-stage breast cancer and receipts of radiation therapy (RT) after breast-conserving surgery than White women. For patients without private or government health insurance, charity and county indigent programs have variable levels of coverage, and some patients cannot access radiation services. The aim of this study is to identify disparities in breast cancer treatment for patients referred to the Travis County indigent cancer treatment program. Methods: We analyzed new referrals to the Ascension Seton Breast Clinic from April 2020 to January 2022. Demographics, disease stage, funding and treatments were extracted from medical records. We compared funding status at the time of referral vs time of surgery. We also analyzed the type of surgery elected and if RT was indicated and received. Results: We found that out of 242 referrals, 116 were diagnosed with a new malignancy. Of the 116, a total of 76 underwent breast surgery and RT was considered in 64 of these patients. 61% received RT. Of the remaining 25 patients, 16 patients elected simple mastectomies and 9 did not have funding to cover radiation (income was not low enough to qualify for RT benefit under the health district). Of the 9 women who did not have funding about 78% identified as Hispanic or Latino. 4 opted for simple mastectomies thus no longer needing RT, 3 received modified radical mastectomies without RT, 1 accessed charity funding for RT and 1 had lumpectomy without radiation and had recurrence of her breast cancer. Overall, the rate of breast conserving surgery was 43%. Discussion: The safety net system for patients in the US without access to private or government funding for healthcare is inherently limited. Costs of radiation treatment for cancer can be prohibitive for charity and indigent programs, but patients are forced to choose between mastectomy or risk a higher rate of recurrence. This data will be used to advocate for health district funding for this patient population.

Disclosure(s):

Maria De Los Leon-Camarena, MD: No financial relationships to disclose

Neha Reddy, MD: No financial relationships to disclose

Kimberly Ellison, DNP: No financial relationships to disclose

Boone Goodgame, MD: No financial relationships to disclose

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7:00 AM - 8:15 AM

P6-09-01

Treatment goals and quality of life (QOL) in a survey of patients with ER+/HER2-metastatic breast cancer (mBC)

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Introduction: In patients (pts) with ER+/HER2- mBC, insights into the foremost concerns regarding their mBC treatment goals and QOL are often assumed by providers but are vastly understudied. The objectives of this survey were to better comprehend treatment goals and QOL concerns in pts with ER+/HER2- mBC. Methods: The 42-question, online EQUALS (ESR1 QUALity of Life Survey) survey was sent to US subjects in June 2022 from 1) the Cure Media Group (n=6,625) by email, 2) private Facebook groups of pts with mBC and 3) members of a BC clinic. Subjects were eligible if they had ER+/HER2- mBC. A \$10 gift card was obtained at survey completion. Survey answers were summarized descriptively. Results: 213 pts completed the survey. Respondents had a mean age of 57 y (range, 31–83 y), and were mostly white (91%), living in an urban/suburban setting (75%), with a higher education degree (71%) and household income \geq \$75k (53%). Mean year of mBC diagnosis was 2018 (range, 1995–2022). Most common first-line mBC treatments were aromatase inhibitor (AI) + CDK4/6 inhibitor (CDK4/6i; 44%), AI alone (18%), or fulvestrant + CDK4/6i (16%); 54% had received chemotherapy in the metastatic setting. Pts most frequently received information about new mBC treatments from other people living with mBC (42%), followed by physicians (34%), social media (31%), or medical journals/conferences (28%). Two-thirds of pts (64%) reported good/very good QOL, with 12% reporting poor/very poor QOL. Common side effects mostly/moderately impacting QOL were: fatigue (74%), joint pain (64%), vaginal atrophy/dryness (56%), and vasomotor symptoms (47%). Most (84%) were comfortable/very

comfortable discussing side effects with their medical team (MT). Worry about disease progression occurred often: everyday (38%), a few times a week (21%) or month (18%), or only before scans (15%). Upon progression, pts worried more about efficacy of new treatment (76%) and having additional options (70%) than they did about side effects (33%). Pts' current treatment goals were: control cancer growth/spread (93%), prolong life (82%), maintain QOL (81%), tolerate side effects (61%), and relieve suffering/pain (57%); similar to their goals at diagnosis. Almost two-thirds of MTs addressed these goals at the beginning of treatment (63%) and continued annually (60%). Most pts (70%) were very concerned that their mBC diagnosis impacted their family although 81% felt supported at home. Since diagnosis, major/moderate life impacts were: side effects (82%), mental health/stress (78%), QOL (71%), inability to engage in activities (62%), and finances (61%). Most pts (64%) thought their mBC or treatment impacted their intimate/sexual relationship negatively and half (50%) worried about sexual intimacy. Only 44% of pts were comfortable discussing intimacy/sexual side effects with their MT. More pts were comfortable/very comfortable discussing sexual side effects with their MT if their oncologists were female (64%) vs male (51%), BC (73%) vs general (45%), or academic (70%) vs community hospital (52%) or office-based practice (49%). Most (92%) were concerned that their treatments may have a negative impact on their bones. Conclusion: In this survey of pts with ER+/HER2- mBC, >70% received information about new mBC treatments from other pts or social media vs physicians. Pts' primary concerns were disease control and treatment options, although treatment side effects had the most impact on QOL. Mental health/stress, intimacy and relationships, and bone health were also impacted. Respondents to online surveys in mBC may portray non-representative populations lacking diversity and attempts to diversify future research are much needed, and further efforts are ongoing to address this knowledge gap.

Disclosure(s):

Sarah L. Sammons, MD: ABBVIE: Contracted Research (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Bristol Myers Squibb: Contracted Research (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Foundation Medicine: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Seagen: Contracted Research (Ongoing); Sermonix: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing)

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Elizabeth Attias, ScD: Sermonix Pharmaceuticals: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

12/9/2022

7:00 AM - 8:15 AM

P6-09-02

Knowledge of tumor/blood genomic testing (NGS) and ESR1 mutations in a survey of patients with ER+/HER2- metastatic breast cancer (mBC)

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Introduction: In patients (pts) with ER+/HER2- mBC, acquired ESR1 mutations after endocrine therapy can lead to treatment resistance, metastasis, and poor prognosis. The objective of this survey was to understand the knowledge of NGS in pts with mBC.

Methods: The 42-question, online EQUALS (ESR1 QUALity of Life Survey) survey was sent to US subjects in June 2022 from 1) the Cure Media Group (n=6,625) by email, 2) private Facebook groups of pts with mBC and 3) members of a BC clinic. Eligible pts were those with ER+/HER2- mBC. At survey completion, respondents received a \$10 gift card. Survey answers were summarized descriptively.

Results: Of 236 pts who responded to the survey, 213 completed. Participants had a mean age of 57 y (range, 31–83 y), mean mBC diagnosis year of 2018 (range, 1995–2022), and were mostly white (91%), living in an urban/suburban setting (75%), with mean household income of ≥\$75k (53%), and higher education degree (71%). First-line mBC treatments were aromatase inhibitor (AI) + CDK4/6 inhibitor (CDK4/6i; 44%), AI alone (18%), fulvestrant + CDK4/6i (16%), chemotherapy (12%), selective estrogen receptor modulator (SERM; 4%) or other/clinical trial (7%). Second-line therapies were none (31%), AI + CDK4/6i (28%), fulvestrant + CDK4/6i (18%), or AI alone (12%). Of the 54% (114/213) who received chemotherapy in the metastatic setting, 34% (39/114) had received ≥3 lines of chemotherapy. Pt's oncologist gender (female 56%) and type (general [52%], breast cancer only [48%]) or setting (office [22%], community [35%], academic [43%]) of oncology practice were well balanced.

Most pts' oncologists (63%) had discussed tumor NGS by a blood test or tumor biopsy with them, but only 29% of them had explained liquid biopsy (assessment of circulating tumor DNA from a blood draw). Regardless, pts knew a lot/moderate amount about NGS (65%), less so of liquid biopsies (44%). NGS awareness by location was different with more suburban pts (73%) knowing a lot/moderate amount than urban (63%) or rural (59%) pts, and by income (>\$50k [68%], \$35k to <\$50k [61%], <\$35k [52%]), but not by age (< 50 y [71%]; 50-60 y [62%]; ≥60 y [69%]).

When asked if they knew what an ESR1 mutation was, about a third each knew a fair amount, a little bit, or did not know much; only 24% of pts thought they had been tested for an ESR1 mutation. ESR1 awareness (Table) differed by location, with more urban pts (40%) knowing a lot/moderate amount about ESR1 mutations vs rural (30%) or suburban (26%) pts, by income (>\$50k [32%], \$35k to <\$50k [28%], <\$35k [14%]) and by oncologist setting (academic [39%] vs office [23%] or community [24%]), but not by age. Slightly more pts had an ESR1 test in urban (26%) vs rural (20%) settings, and with higher (29%) vs lower (10%) incomes, but similar by age. Overall, most pts believed that ESR1 testing results could affect their treatment options/decisions (92%), were comfortable asking about NGS (94%), and would prefer a blood test over a tumor biopsy for more targeted mBC treatments (88%).

Conclusion: In this survey of ER+/HER2- pts living with mBC, most had some knowledge of NGS but knowledge of ESR1 mutations was lower. Discordance between physician discussion of NGS and liquid biopsies was observed. Awareness of NGS and ESR1 mutations analyzed by demographics data suggests socioeconomic disparities in pt education and knowledge. Further education on NGS and ESR1 mutations is needed as NGS testing is becoming an important aspect of mBC treatment.

Table. Awareness of ESR1 mutations based on demographics

n (%)	n	Do you know what an ESR1 mutation is?			Have you been tested for an ESR1 mutation?		
		Not really*	Know a little bit	Know a lot/moderate amount	Yes	No	Uncertain
Region							
Urban	53	15 (28)	17 (32)	21 (40)	14 (26)	16 (30)	23 (43)
Suburban	106	38 (36)	40 (38)	28 (26)	27 (25)	39 (37)	40 (38)
Rural	54	23 (43)	15 (28)	16 (30)	11 (20)	22 (41)	21 (39)
Age, y							
<50	48	15 (31)	18 (38)	15 (31)	13 (27)	15 (31)	20 (42)
50 to <60	76	28 (37)	26 (34)	22 (29)	18 (24)	29 (38)	29 (38)
≥60	89	33 (37)	28 (31)	28 (31)	21 (24)	33 (37)	35 (39)
Income, \$							
≥150k	36	16 (44)	9 (25)	11 (31)	12 (33)	11 (31)	13 (36)
100k to <150k	41	13 (32)	13 (32)	15 (37)	11 (27)	12 (29)	18 (44)
75k to <100k	37	13 (35)	13 (35)	11 (30)	12 (32)	12 (32)	13 (35)
50k to <75k	37	11 (30)	14 (38)	12 (32)	9 (24)	9 (24)	19 (51)
35k to <50k	18	6 (33)	7 (39)	5 (28)	1 (6)	11 (61)	6 (33)
25k to <35k	10	4 (40)	4 (40)	2 (20)	1 (10)	5 (50)	4 (40)
<25k	11	6 (55)	4 (36)	1 (9)	2 (18)	5 (45)	4 (36)
Oncologist setting							
Office-based	47	21 (45)	15 (32)	11 (23)	7 (15)	19 (40)	21 (45)
Community hospital	74	29 (39)	27 (36)	18 (24)	12 (16)	33 (45)	29 (39)
Academic hospital	92	26 (28)	30 (33)	36 (39)	33 (36)	25 (27)	34 (37)

*Never heard of it or heard of it but don't know what it is.

Disclosure(s):

Jane Meisel, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Terminated, October 1, 2021), Contracted Research (Terminated, October 1, 2021); Clovis Oncology: Consulting Fees (e.g., advisory boards) (Terminated, July 20, 2020); Genentech: Consulting Fees (e.g., advisory boards) (Terminated, September 29, 2021); Glaxo SmithKline: Consulting Fees (e.g., advisory boards) (Terminated, December 19, 2020); Novartis: Consulting Fees (e.g., advisory boards) (Terminated, March 10, 2022); Pfizer: Consulting Fees (e.g., advisory boards) (Terminated, June 4, 2022), Contracted Research (Terminated, June 4, 2022); Puma: Consulting Fees (e.g., advisory boards) (Terminated, August 11, 2020); Sanofi Genzyme: Consulting Fees (e.g., advisory boards) (Terminated, June 16, 2021); SeaGen: Consulting Fees (e.g., advisory boards) (Terminated, March 10, 2022), Contracted Research (Terminated, March 10, 2022)

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Elizabeth Attias, ScD: Sermonix Pharmaceuticals: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing), Salary (Ongoing)

12/9/2022

7:00 AM - 8:15 AM

P6-09-03

Examining recollections of Black women with breast cancer who participated in clinical trials: A grounded practical theory study of patient-provider communication

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Introduction: The presence of strong barriers to research participation for Black and Brown women is indisputable. However, existing evidence clearly supports the possibility of equal levels of participation among members of minoritized populations in past breast cancer clinical trials, demonstrating that while these participation barriers do undoubtedly exist, they are not always insurmountable. A main implication of this current study is that researchers should take greater strides to remove the onus of recruitment responsibility from racialized population members, and instead leave it with the providers, investigators, and health care teams who hold enough power to make change. **Purpose:** This project takes a grounded practical theory (GPT) approach to engage with Black women who have been diagnosed with breast cancer and have participated in a breast cancer clinical trial and explores their recollections of conversations with their providers. GPT focuses on reconstructing particular communication practices, highlighting both the important procedural role of communication in practice and its ability to present intricate complications that echo society's norms and values. The aim of this work is to investigate and analyze those patient-provider conversations to try to illuminate how providers can better engage these women in ways that will positively influence their perceptions of breast cancer clinical trial participation. **Methods:** The current study was part of a larger project examining the recruitment of Black women to breast cancer clinical trials. Fourteen women (N=14) from six different states in the U.S., all of whom self-identified as Black, Black American, or African American, agreed to be interviewed as part of a larger study. All participants had participated or were currently participating in a breast cancer clinical trial. The interviews yielded a wealth of interesting and potentially important additional data about Black female breast cancer patients and their communication experiences with their providers. Employing grounded practical theory as a framework helped increase insight into the patient-provider communication needs of Black women who have participated in a breast cancer clinical trial. **Results:** Findings were summarized into four categories: 1) the participants held differing perspectives and personal impressions toward their providers; 2) the women reflect on their individual breast cancer journeys through richly described incidences, describing searching for, and finding trials on their own, or being guided by healthcare providers who suggested a clinical trial for them; 3) each participant's shared details of their unique communication relationship with medical and research providers; and 4) the cultural aspects of participants' patient-provider communication, focusing primarily on their expressions of faith. These findings have important implications for health communication scholars, healthcare providers, and breast cancer clinical trial research principal investigators and team members. **Conclusion:** As opposed to the conclusion that one may draw from most published explanations of poor minority accrual to clinical trials, which appear to put the blame on the minoritized

population members themselves, the current work outlines the actions and non-actions of many providers, and suggests that adjusting to approaches that demonstrate more encouragement and acceptance of their patients might result in better clinical trial participation outcomes from these group members.

Disclosure(s):

Katherine E. Ridley-Merriweather, MA: No financial relationships to disclose

12/9/2022

7:00 AM - 8:15 AM

P6-09-04

Oncologist-reported Barriers and Facilitators to enrolling patients in optimization trials that test less intense cancer treatment

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Background: As outcomes improve in early-stage breast cancer, clinical trials are undergoing a paradigm shift from intensification trials (more therapy) to improve survival to optimization trials, which assess the potential for using less toxic therapy while preserving survival outcomes. However, little is known about physician perspectives in community and academic settings about possible barriers and facilitators that could impact accrual to optimization clinical trials and about the generalizability of future findings. **Methods:** We conducted a qualitative study with semi-structured interviews of medical oncologists from different academic and community practices to assess their perspectives on optimization trials. Interviews were audio-recorded and transcribed. Three independent coders utilized a content analysis approach to analyze transcripts using NVivo. Major themes and exemplary quotes were extracted. **Results:** Forty-six physicians were approached from 3/31/21-11/5/21; 39 oncologists from different oncology practices across 17 states completed interviews, 7 either declined or did not respond to email requests. Physician characteristics were balanced: men vs. women (49% vs 51%) and community oncologist vs. academic oncologist (49% vs 51%); and time practicing as medical oncologist (31% 0-9 years; 33% 10-19 years; 36% 20+ years). All 39 physicians reported that they would enroll patients in optimization clinical trials. Oncologists reported the need for treatment optimization, with one oncologist noting “historically, we’ve given way too much treatment to patients.” Oncologists highlighted specific reasons to consider optimization trials. They included quality of life improvement by reducing toxicity; reduction in financial toxicity; fertility preservation; ability to avoid chemotherapy; minimization of overtreatment in patients with comorbid conditions; personalized treatment; opportunities to test novel therapies; and leveraging the availability of targeted therapies. At the same time, there was hesitancy amongst some oncologists with this approach, “All my life I’ve worked to try to improve things and so I am not totally philosophically comfortable with the notion that I’m going to be happy with a result that says, we haven’t improved it but we can get by with less.” In addition, oncologists also identified accrual barriers, like tumor-specific biology, individual (host) factors (e.g. disease characteristics, patient demographics, patient psychological state, patient preferences), prognostic markers of risk, access to therapies, provider experience, and system constraints. They voiced recommendations regarding preliminary data, trial design, and tools to support communication about and enrollment in optimization trials. **Conclusions:** While optimization clinical trials are generally accepted to be beneficial by oncologists, barriers impact their acceptance. Scientifically robust design and education to overcome barriers are needed to support future enrollment on trials tailoring therapy based on risk and potential benefit to allow true personalization of treatment.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-09-05

Using Mixed Methods to Examine Clinician and Patient Use of Terminology to Describe Trastuzumab Biosimilars

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Although the uptake of trastuzumab biosimilars to treat HER2-positive breast cancer is growing, knowledge gaps remain for both, patients and clinicians. In a mixed-methods study, inconsistencies in terminology used to describe trastuzumab biosimilars. We analyzed open-ended questions from surveys (n = 143 breast cancer patients, n = 33 medical oncologists) and interviews (n = 8 patients, n = 4 oncologist, nurse, pharmacists) identifying terminology as an a priori (top-down) category for qualitative thematic analysis. We specifically looked for examples of inconsistent or incorrect use of terminology in the interviews. Findings suggest that 1) terminology used to refer to trastuzumab biosimilars is variable across patients and some is not representative of the formal definition (e.g. generic, generic-like, interchangeable, Herceptin, generic Herceptin (as per how their oncologist refers to biosimilars) and 2) clinicians discussed the challenges of talking about biosimilars in a manner that is both understandable to patients and accurate. Specifically, one pharmacist highlighted concerns around this complexity and suggested that it should be part of clinician education to use the correct terminology, rather than using the term generic. A medical oncologist said that "Explaining biosimilars to a patient can be challenging" as part of their survey response. Lack of consistent terminology for trastuzumab biosimilars is a potential barrier to effective patient-clinician communication on this topic and may perpetuate lack of comprehension on the part of patients. Further, the intentional use (to make information more digestible to patients) of incorrect terminology by clinicians has the potential to negatively impact the patient-clinician relationship in cases where patients identify conflicting information on their own. The adoption of terminology that is consistent across clinicians and patient-facing resources on the introduction and description of trastuzumab biosimilars, may serve to facilitate common grounding among all roles.

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7:00 AM - 8:15 AM

P6-10-01

The Executioner Protein for Immunogenic Anticancer Drug-induced Necrosis in ER Positive Breast Cancer is Transient Receptor Potential Melastatin Member 4

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Immunotherapy has dramatically impacted cancer therapy, but it has been challenging to apply immunotherapy to estrogen receptor (ER) positive breast cancer and many other solid tumors that do not display neoantigens. One way to target these tumors is to induce necrosis, which robustly activates immune cells, inducing immunogenic cell death. However, anticancer therapy-induced necrosis was primarily characterized by morphological changes, and the molecular drivers of necrosis were largely obscure. To probe necrosis, we used our necrosis inducing anticancer agents, the small molecules BHPI and second-generation ErSO, which kill cancer cells by hyperactivating the anticipatory unfolded protein response (a-UPR). In orthotopic mouse xenografts, ErSO induces complete regression without recurrence of large, therapy-resistant primary ER positive breast tumors, of most lung, bone, and liver metastases, near complete regression of challenging breast cancer brain metastases and robust responses in PDX and patient derived organoids (PDOs) models. ErSO also induces complete or near complete regression in mouse xenograft models of ER positive ovarian and endometrial cancer. Using genome wide CRISPR-Cas9 screens with negative selection against our necrosis-inducing a-UPR hyperactivators, BHPI and ErSO, we identified the calcium-activated, ATP-

inhibited, plasma membrane sodium channel, Transient Receptor Potential Melastatin Member 4 (TRPM4) as critical for anticancer therapy induced necrosis. TRPM4 knockout in multiple models abolished ErSO-induced ATP depletion, sustained UPR activation, cell swelling, necrotic cell death and increased migration of immune cells. Notably, knockout of TRPM4 completely abolished the ability of ErSO to induce regression of ER positive breast tumors in mice. Supporting a broad role for the TRPM4 pathway in anticancer therapy induced necrosis, rapid cancer cell death induced by four necrosis-inducing cancer therapies unrelated to ErSO, that range from FDA-approved to preclinical, is strongly reversed by TRPM4 knockout. ErSO treatment induces migration of macrophage into regressing tumors. Medium from cancer cells killed by necrosis-inducing ErSO, but not by an apoptosis inducer, dramatically increases macrophage migration and activation, as shown by induction of pro-inflammatory cytokines. This work identifies a protein that plays a pivotal role in the action of diverse anticancer therapies inducing immunogenic necrosis. Since increasing levels of TRPM4 increase sensitivity of breast cancer cells to killing by ErSO, TRPM4 is a novel biomarker whose levels can be used to identify patients most likely to benefit from ErSO and other necrosis-inducing cancer therapies.

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P6-10-02

Self-assembled nano drugs of pyrotinib and indocyanine green based on photothermal photodynamic therapy

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Background: Photothermal and photodynamic therapy is a new tumor treatment strategy, which can kill tumor cells and reduce the damage to surrounding normal tissues, but the lack of targeting limits its efficacy. In this study, the targeted photothermal and photodynamic nanodrug P/ICG was synthesized by self-assembly of the targeted drug pyrotinib and photosensitizer indocyanine green (ICG), and its application in the photothermal and photodynamic therapy of HER2 positive breast cancer was explored. Method: In this study, the nano drug P/ICG was self-assembly synthesized of pyrotinib and ICG, and its physical parameters and stability were tested. We used 808nm near-infrared light and infrared thermal imager to verify the photothermal effect of nano drugs. Then we used DCFH-DA probe to detect the level of ROS in cells by laser confocal and flow cytometry to verify the photodynamic effect of the nano drug, and verified the antitumor effect of P/ICG combined with near-infrared light irradiation in vitro. We established a PDX mouse breast cancer model and verified the efficacy and safety of P/ICG in the treatment of HER2-positive breast cancer in vitro. Finally, the effect of P/ICG on ferroptosis was verified by MDA, CCK8 and WB experiments. Result: We mixed pyrotinib and ICG in a certain proportion, and purified them by high-speed centrifugation and ultrafiltration to synthesize nano drug P/ICG. P/ICG has good stability and can be effectively ingested by HER2-positive breast cancer cells. Subsequently, we proved through in vitro and in vivo experiments that P/ICG combined with near-infrared light irradiation can significantly inhibit the growth of tumor cells and improve the survival rate of mice. At the same time, P/ICG combined with near-infrared light irradiation increased the phosphorylation of Nrf2 protein, increased the level of free KEAP1 protein, and decreased the levels of SLC7A11, GPX4 and FTH1 protein, significantly increased the lipid peroxidation of tumor cells, and promoted the ferroptosis of tumor cells. Conclusion: Pyrotinib and ICG self-assembled nano drug P/ICG can significantly promote the ferroptosis of HER2-positive breast cancer cells and inhibit the growth of cancer cells, which can be used as a new strategy for the treatment of HER2-positive breast cancer. Key words: pyrotinib; HER2-positive breast cancer; Photothermal therapy; photodynamic therapy

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P6-10-03

Datopotamab Deruxtecan (Dato-DXd) in Advanced Triple-Negative Breast Cancer (TNBC): Updated Results From the Phase 1 TROPION-PanTumor01 Study

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Background: Datopotamab deruxtecan (Dato-DXd) is an antibody-drug conjugate (ADC) consisting of a humanized anti-TROP2 IgG1 mAb covalently linked to a highly potent topoisomerase I (Topo I) inhibitor payload via a stable, tumor selective, tetrapeptide-based cleavable linker. Dato-DXd has previously shown encouraging activity in heavily pretreated patients (pts) with metastatic TNBC (Krop, SABCS 2021). Here we report updated results from the TROPION-PanTumor01 study in pts with advanced/metastatic TNBC. Methods: TROPION-PanTumor01 (NCT03401385) is a phase 1, multicenter, open-label, 2-part dose-escalation/expansion study evaluating Dato-DXd in previously treated pts with solid tumors. Based on previous clinical and exposure-response results from pts with NSCLC, Dato-DXd 6 mg/kg IV Q3W is being evaluated in pts with advanced TNBC that relapsed/progressed on standard therapies; 2 pts received 8 mg/kg prior to selection of 6 mg/kg. The primary objectives were safety and tolerability. Tumor responses, including objective response rate (ORR; complete response [CR] + partial response [PR]) and disease control rate (DCR; CR + PR + stable disease [SD]), were assessed per RECIST v1.1 by blinded independent central review. Results: As of April 29, 2022, 44 pts received Dato-DXd (median follow-up, 16.6 mo [range, 13-22]) at the time of data cutoff. The primary cause of treatment discontinuation was disease progression (86%; PD or clinical progression), and 4 pts are still receiving therapy. Median age was 53 y (range, 32-82); 32% had de novo metastatic disease. Pts were heavily pretreated with a median of 3 (range, 1-10) prior regimens in the metastatic setting. Prior treatments included taxanes (91%), anthracyclines (75%), capecitabine (61%), platinum (52%), immunotherapy (43%), Topo I inhibitor-based ADC therapy (32%), and PARPi (18%). Treatment-emergent adverse events (TEAEs; all cause) occurred in 100% (any grade) and 50% (grade ≥ 3) of pts, respectively. Most common TEAEs (any grade, grade ≥ 3) were stomatitis (73%, 11%), nausea (66%, 2%), vomiting (39%, 5%), fatigue (34%, 7%), and alopecia (36%, 0%). One pt had grade 3 decreased neutrophil count; no cases of interstitial lung disease (ILD) or grade ≥ 3 diarrhea were observed. Serious TEAEs were reported in 9 pts (20%); no deaths associated with adverse events (AEs) were observed. Dose reductions occurred in 8 pts (18%) due to stomatitis (n=3), fatigue (n=2), dry eye (n=1), retinal exudates (n=1), and dysgeusia (n=1); 12 pts (27%) delayed treatment due to stomatitis (n=5), dry eye (n=1), keratitis (n=1), blurred vision (n=1), fatigue (n=1), bronchitis (n=1), skin infection (n=1), musculoskeletal chest pain (n=1), dysgeusia (n=1), chronic obstructive pulmonary disease (n=1), and dyspnea (n=1; >1 AE per pt). One pt (2%) discontinued treatment due to grade 1 pneumonitis (which was centrally adjudicated as not ILD). ORR in all pts was 32% (1 CR, 13 PRs), DCR was 80% (35/44), and clinical benefit rate (CR + PR + SD ≥ 6 mo) was 34% (15/44). Median duration of response was not yet reached; median progression-free survival (mPFS) was 4.3 mo (95% CI, 3.0-7.3), and

median overall survival (mOS) was 12.9 mo (95% CI, 10.1-14.7). In the subset of pts without prior Topo I inhibitor–based ADC therapy and with measurable disease at baseline, ORR was 44% (12/27). Among all pts without prior Topo I inhibitor–based ADC therapy (n=30), mPFS was 7.3 mo (95% CI, 3.0-NE), and mOS was 14.3 mo (95% CI, 10.5-NE). Conclusions: Dato-DXd continues to demonstrate encouraging and durable antitumor activity, along with a manageable safety profile, in heavily pretreated pts with metastatic TNBC. Based on these findings, the phase 3 randomized TROPION-Breast02 (NCT05374512) trial comparing Dato-DXd vs chemotherapy as 1L therapy for pts with metastatic TNBC is currently underway.

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Toshio Shimizu, MD, PhD: 3D-Medicine: Grants or contracts (Ongoing); AbbVie: Consulting Fees (e.g., advisory boards) (Ongoing), Grants or contracts (Ongoing); Astellas Pharma: Grants or contracts (Ongoing); AstraZeneca: Study sponsor (Ongoing); Bristol-Myers Squibb: Grants or contracts (Ongoing); Chordia Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing), Grants or contracts (Ongoing); Chugai: Consulting Fees (e.g., advisory boards) (Ongoing), Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Study sponsor; Medical writing support provided by Articulate Science, LLC and funded by Daiichi Sankyo (Ongoing); Eisai: Grants or contracts; support for attending meetings and/or travel (Ongoing); Eli Lilly: Grants or contracts; Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events (Ongoing); Five Prime: Grants or contracts (Ongoing); Incyte: Grants or contracts (Ongoing); MSD:

Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events (Ongoing); Novartis: Grants or contracts (Ongoing); Pfizer: Grants or contracts (Ongoing); PharmaMar: Grants or contracts (Ongoing); Symbio Pharmaceuticals: Grants or contracts (Ongoing); Takeda Oncology: Consulting Fees (e.g., advisory boards) (Ongoing), Grants or contracts (Ongoing)

Erika Hamilton, MD: Abbvie: Research Funding - Paid to Institution (Ongoing); Accutar Biotechnology: Research Funding - Paid to Institution (Ongoing); Acerta Pharma: Research Funding - Paid to Institution (Ongoing); ADC Therapeutics: Research Funding - Paid to Institution (Ongoing); AKESOBIO Australia: Research Funding - Paid to Institution (Ongoing); Amgen: Research Funding - Paid to Institution (Ongoing); Aravive: Research Funding - Paid to Institution (Ongoing); Arcus: Consulting Fees to Institution (Ongoing); ArQule: Research Funding - Paid to Institution (Ongoing); Artios: Research Funding - Paid to Institution (Ongoing); Arvinas: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); AstraZeneca: Study sponsor, consulting fees and research grant paid to institution (Ongoing); AtlasMedx: Research Funding - Paid to Institution (Ongoing); Black Diamond: Consulting and Research Funding - Paid to Institution (Ongoing); Bliss BioPharmaceuticals: Research Funding - Paid to Institution (Ongoing); Boehringer Ingelheim: Consulting and Research Funding - Paid to Institution (Ongoing); Cascadian Therapeutics: Research Funding to Institution (Ongoing); Clovis: Research Funding to Institution (Ongoing); Compugen: Research Funding to Institution (Ongoing); Cullen-Florentine: Research Funding to Institution (Ongoing); Curis: Research Funding to Institution (Ongoing); CytomX: Consulting Fees and Research Funding to Institution (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Dana Farber Cancer Inst: Research Funding to Institution (Ongoing); Dantari: Consulting Fees and Research Funding to Institution (Ongoing); Deciphera: Consulting Fees and Research Funding to Institution (Ongoing); Duality Biologics: Research Funding to Institution (Ongoing); eFFECTOR Therapeutics: Research Funding to Institution (Ongoing); Eisai: Consulting Fees to Institution (Ongoing); Ellipses Pharma: Research Funding to Institution (Ongoing); Elucida Oncology: Research Funding to Institution (Ongoing); EMD Serono: Research Funding to Institution (Ongoing); Fochon: Research Funding to Institution (Ongoing); FujiFilm: Research Funding to Institution (Ongoing); G1 Therapeutics: Research Funding to Institution (Ongoing); Greenwich Lifesciences: Consulting Fees to Institution (Ongoing); H3 Biomedicine: Consulting Fees and Research Funding to Institution (Ongoing); Harpoon: Research Funding to Institution (Ongoing); Hutchinson MediPharma: Research Funding to Institution (Ongoing); Immunogen: Research Funding to Institution (Ongoing); Immunomedics: Research Funding to Institution (Ongoing); Incyte: Research Funding to Institution (Ongoing); Infinity Pharmaceuticals: Research Funding to Institution (Ongoing); InvestisBio: Research Funding to Institution (Ongoing); iTeos: Consulting Fees to Institution (Ongoing); Jacobio: Research Funding to Institution (Ongoing); Janssen: Consulting Fees to Institution (Ongoing); Karyopharm: Research Funding to Institution (Ongoing); Leap Therapeutics: Research Funding to Institution (Ongoing); Lilly: Consulting Fees and Research Funding to Institution (Ongoing); Loxo: Consulting Fees to Institution (Ongoing); Lycera: Research Funding to Institution (Ongoing); Mabspace Biosciences: Research Funding to Institution (Ongoing); MacroGenics: Research Funding to Institution (Ongoing); MedImmune: Research Funding to Institution (Ongoing); Merck: Consulting Fees and Research Funding to Institution (Ongoing); Mersana: Consulting Fees and Research Funding to Institution (Ongoing); Merus: Research Funding to Institution (Ongoing); Millennium: Research Funding to Institution (Ongoing); Molecular Templates: Research Funding to Institution (Ongoing); Myraid Genetic Laboratories: Research Funding to Institution (Ongoing); Novartis: Consulting Fees and Research Funding to Institution (Ongoing); Nucana: Research Funding to Institution (Ongoing); Olema: Research Funding to Institution (Ongoing); OncoMed: Research Funding to Institution (Ongoing); Onconova Therapeutics: Research Funding to Institution (Ongoing); ORIC Pharmaceuticals: Research Funding to Institution (Ongoing); Orinove: Research Funding to

Institution (Ongoing); Orum Therapeutics: Consulting Fees to Institution (Ongoing); Pfizer: Consulting Fees and Research Funding to Institution (Ongoing); PharmaMar: Research Funding to Institution (Ongoing); Pieris Pharmaceuticals: Research Funding to Institution (Ongoing); Pionyr Immunotherapeutics: Research Funding to Institution (Ongoing); Plexikon: Research Funding to Institution (Ongoing); Propella Therapeutics: Consulting Fees to Institution (Ongoing); Puma Biotechnology: Consulting Fees to Institution (Ongoing); Radius Health: Research Funding to Institution (Ongoing); Regeneron: Research Funding to Institution (Ongoing); Relay Therapeutics: Consulting Fees and Research Funding to Institution (Ongoing); Repertoire Immune Medicine: Research Funding to Institution (Ongoing); Rgenix: Research Funding to Institution (Ongoing); Roche/Genentech: Consulting Fees and Research Funding to Institution (Ongoing); SeaGen: Consulting Fees and Research Funding to Institution (Ongoing); Sermonix Pharmaceuticals: Research Funding to Institution (Ongoing); Shattuck Labs: Research Funding to Institution (Ongoing); Silverback: Consulting Fees and Research Funding to Institution (Ongoing); StemCentRx: Research Funding to Institution (Ongoing); Sutro: Research Funding to Institution (Ongoing); Syndax: Research Funding to Institution (Ongoing); Syros: Research Funding to Institution (Ongoing); Taiho: Research Funding to Institution (Ongoing); TapImmune: Research Funding to Institution (Ongoing); Tesaro: Research Funding to Institution (Ongoing); Tolmar: Research Funding to Institution (Ongoing); Torque Therapeutics: Research Funding to Institution (Ongoing); Treadwell Therapeutics: Research Funding to Institution (Ongoing); Verastem: Research Funding to Institution (Ongoing); Vincerx Pharma: Research Funding to Institution (Ongoing); Zenith Epigenetics: Research Funding to Institution (Ongoing); Zymeworks: Research Funding to Institution (Ongoing)

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12/9/2022

7:00 AM - 8:15 AM

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Homologous recombination deficiency across subtypes of primary breast cancer

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Background: Homologous recombination deficiency (HRD) is highly prevalent in triple-negative breast cancer (TNBC) and predictive of response to PARP inhibition in the primary setting (Eikesdal et al, *Ann Oncol*, 2021). However, the prevalence of HRD across breast cancer subtypes has not been established. Methods: Pretreatment tumor biopsies from 201 patients (32 TNBC and 169 non-TNBC) with primary breast cancer in the phase II PETREMAC trial (ClinicalTrials #NCT02624973) were examined. These samples underwent targeted cancer gene panel sequencing and BRCA1 promoter methylation analysis to assess HRD status

defined by homologous recombination repair (HRR) gene mutations and/or BRCA1 promoter methylation. HRR genes included BRCA1, BRCA2, BRIP1, BARD1, and PALB2 by strict definition (HRR-S), and additionally ABL1, ATM, ATR, ATRX, BLM, CDK12, CHEK1, EMSY, ERCC4, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, MEN1, MRE11, NBN, PTEN, and SETD2 by wider definition (HRR-W). HRD strict (HRD-S) was defined as biallelic gene inactivation by HRR-S mutations or BRCA1 methylation. Finally, tumors underwent PAM50 gene expression subtyping and evaluation of functional HRD by RAD51 nuclear foci analysis, for which a low score has been associated with HRD. Results: HRD-S was present in 13% of the breast cancers (total: n= 27/201; TNBC: 15/32; 47%; non-TNBC: 12/169; 7%), whereas HRD-W (HRR-W or BRCA1 methylation) was observed in 29% (total: n=58/201; TNBC: 19/32; 59%; non-TNBC: 39/169; 23%). Among 190 tumors analyzed for PAM50 intrinsic subtype, HRD-S was detected in 3/60 and 4/48 (5% and 8%) of tumors classified as luminal A and B, respectively, 1/35 (3%) of HER2-enriched, 4/21 (19%) of normal-like, and 12/26 (46%) of basal-like tumors. Out of 58 non-TNBC biopsies examined by RAD51 staining, four (7%) were classified as HRD-S and all these were scored as RAD51 low. The remaining 54 non-TNBC samples were homologous recombination proficient, and none of these exhibited functional HRD by RAD51 low scores. All four HRD-S/RAD51 low tumors were hormone receptor-positive, HER2 negative, and belonged to the luminal A (n=1), luminal B (n=2), and basal-like (n=1) subtypes, with HRD caused by germline BRCA1 (gBRCA1), gBRCA2, somatic BRCA1 mutations and BRCA1 methylation, respectively. Conclusion: The prevalence of HRD across all breast cancer subtypes suggests that HRD analysis and therapy targeting such DNA repair defects should be tested in future clinical trials.

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12/9/2022

7:00 AM - 8:15 AM

P6-10-05

Mutations in the RNA Splicing Factor SF3B1 drive endocrine therapy resistance and confer a targetable replication stress response defect through PARP inhibition.

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Background:

Heterozygous hotspot mutations in the RNA splicing factor SF3B1, occur in 3% of unselected breast cancers and are associated with oestrogen receptor (ER+) breast cancer (BC) where they are enriched in metastatic disease and are associated with a poor clinical outcome. SF3B1 mutations drive distinct signatures of alternative splicing through cryptic 3' splice site selection leading to global transcriptomic and proteomic changes. The functional consequences of the mis-splicing events and resultant genetic vulnerabilities are poorly understood and precision medicine approaches that exploit these characteristics are not clinically available (Table 1).

Methods:

To understand the role of SF3B1 mutations in ER+ BC, we generated a series of SF3B1 mutant (SF3B1MUT) isogenic cell lines which were characterised using RNA-sequencing and high content mass-spectrometry proteomic profiling. SF3B1 interactome analysis was also performed using immunoprecipitation of SF3B1 followed by mass-spectrometry. The molecular consequences of aberrant splicing were investigated using a targeted screening approach of 280 genes predicted to be alternatively spliced in SF3B1MUT BC, while high-throughput drug screens were used to identify novel therapeutic options for patients with SF3B1MUT breast cancer using isogenic cells. Hits were validated in vitro and in vivo using cell line and patient derived xenografts.

Results:

Transcriptomic and proteomic profiling of SF3B1MUT cells identified global alternative 3' splice site selection and subsequent proteomic changes induced by the mutations. Investigation of the SF3B1K700E interactome identified an enrichment of SF3B1K700E binding with ER α , aberrant splicing of ER target genes, global rewiring of ER α chromatin binding and resistance to endocrine therapy. Silencing of the aberrantly spliced candidate genes PPIH, TRIM37, HIGD1A, BRD9, and PHKG2 significantly enhanced the growth of the SF3B1 mutant cells, suggestive of a dose dependent tumour suppressive effect.

Through synthetic-lethal drug screens we found that SF3B1MUT cells are selectively sensitive to PARP inhibitors. SF3B1MUT cells display a defective response to PARPi induced replication stress. Mechanistically, this occurs via defective ATR signalling in SF3B1MUT cells, which upon PARPi exposure leads to increased replication origin firing and loss of pChk1 (S317) induction. The resultant replication stress leads to failure to resolve DNA replication intermediates via the endonuclease MUS81 and cell cycle stalling at the G2/M checkpoint. These defects can be further targeted by ATM, CDK7 or FACT inhibition, when used in combination with PARPi treatment. This SF3B1MUT selective PARPi sensitivity is preserved across multiple cell lines and patient derived tumour models. In vivo, PARPi produce profound anti-tumour effects in multiple SF3B1MUT cancer models and eliminate distant metastases.

Conclusions:

Our integrative analysis reveals mechanistic insight into the role of SF3B1 mutations in endocrine therapy response in ER+ breast cancers, where altered SF3B1 induces ER-transcriptional re-programming. We further identified a robust synthetic-lethal relationship of mutant SF3B1 with PARP inhibition that is caused by a defective response to PARPi induced replication stress. Furthermore, we identified several potential selective combination strategies together with PARPi that are selective for SF3B1MUT cells. Together, these data provide the pre-clinical and mechanistic rationale for assessing already-approved PARPi in a biomarker-

defined subset of advanced ER+ BC.

Table.1

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Identified potential therapies for SF3B1 mutant cancers from this study and the literature

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12/9/2022

7:00 AM - 8:15 AM

P6-10-06

A preoperative window-of-opportunity study of imlunestrant in estrogen receptor-positive, HER2-negative early breast cancer: Results from the EMBER-2 study.

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Background: Imlunestrant is a novel, orally bioavailable selective estrogen receptor degrader (SERD) with pure antagonistic properties that result in sustained inhibition of estrogen receptor (ER)-dependent gene transcription and cell growth. In a phase 1 study, imlunestrant monotherapy showed favourable safety, pharmacokinetics (PK) and preliminary efficacy in heavily pre-treated ER-positive (ER+) advanced breast cancer patients (Jhaveri ASCO 2022). Here, we present pharmacodynamic (PD) data from the preoperative window of opportunity (WOO) study (EMBER-2, NCT04647487), evaluating the biological activity of imlunestrant

monotherapy in ER+, HER2-negative (HER2-) early breast cancer (EBC).
Methods: Post-menopausal women with stage I–III operable ER+ (>50%) or Allred score >5, HER2- untreated EBC ≥1 cm in diameter were randomized 1:1 to imlunestrant 400 mg once daily (QD) or imlunestrant 800 mg QD for 15 days (treatment window of -2 to +7 days) up to the surgery date. Pre- and on-treatment tumor samples were compared for changes in PD biomarkers. Primary study objective was change in ER expression (measured by IHC and quantified by H-score). Secondary objectives were change in progesterone receptor (PR) expression (measured by IHC and quantified by H-score) and Ki-67 (measured by IHC and expressed by percentage positive scoring) along with evaluation of safety and tolerability.
Results: From Apr 28, 2021, to Mar 11, 2022, 58 patients were enrolled of which 54 were biomarker-evaluable for ER expression (400 mg: n = 28; 800 mg: n = 26). Patient demographics and tumor characteristics for all enrolled patients were similar across cohorts, with a median age of 64 years (50-83), 72% invasive ductal carcinoma (IDC), 28% invasive lobular carcinoma (ILC), 59% stage I, 36% stage II and 5% stage III disease. 91% of the patients had a compliance rate higher than 80%. Among biomarker evaluable patients, relative reduction in PD biomarkers after a median of 15 days (range 13 to 23 days) of treatment are presented in Table 1. There was no significant difference in PD biomarker modulation noted between the two imlunestrant doses (400 mg vs 800 mg) or based on tumor histology (IDC, ILC). Imlunestrant was well tolerated. There were no discontinuations due to adverse events (AEs). Treatment-related AEs (TRAEs) were mainly grade 1, most commonly: fatigue (10%), diarrhea (9%), hot flushes (7%), and nausea (5%). There were no TRAEs of diarrhea and nausea observed at the 400 mg dose. No grade 3 or higher TRAEs were reported.
Conclusion: Imlunestrant demonstrated evidence of target engagement along with consistent biological activity across all evaluated dose levels and was well tolerated in an EBC population, further supporting continued adjuvant development in the ongoing EMBER-4 study. Additional biomarker analyses for the EMBER-2 study are also planned.

Table 1. Relative reduction in PD biomarkers from Baseline to Day 15

	400 mg cohort	800 mg cohort	Total
ER (N=54)			
n (%)	28 (52)	26 (48)	54 (100)
Geometric mean percent change ^a (90% CI)	-81 (-91, -61)	-70 (-78, -59)	-76 (-84, -65)
Geometric mean ratio ^b (90% CI)	2 (1, 4)		
PR (N=52)			
n (%)	26 (50)	26 (50)	52 (100)
Geometric mean percent change ^a (90% CI)	-76 (-90, -38)	-82 (-92, -60)	-79 (-88, -62)
Geometric mean ratio ^b (90% CI)	1 (0, 2)		
Ki67 (N=42)			
n (%)	22 (52)	20 (48)	42 (100)
Geometric mean percent change ^a (90% CI)	-71 (-80, -57)	-72 (-81, -59)	-71 (-78, -63)
Geometric mean ratio ^b (90% CI)	1 (1, 2)		
Ki-67 among patients with baseline Ki-67 ≥ 5% (N = 39)			
n (%)	22 (56)	17 (44)	39 (100)
Geometric mean percent change ^a (90% CI)	-71 (-80, -57)	-78 (-84, -70)	-74 (-80, -67)
Geometric mean ratio ^b (90% CI)	1 (0, 1)		

CI = confidence interval; N = number of biomarker evaluable patients in population; n = number of patients in the specified category.

^aGeometric mean percent changes for PR, ER, and Ki-67 are based on t-statistic assuming a normal distribution.

^bGeometric mean ratios are based on a linear model with treatment and histology as fixed effects.

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CDK2 inhibition with BLU-222 in combination with ribociclib demonstrates robust antitumor activity in pre-clinical models of CDK4/6 inhibitor-naïve and -resistant HR+/HER2- breast cancer

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Cyclin-dependent kinase 4/6 (CDK4/6) inhibitors are standard of care in combination with endocrine therapy in advanced hormone receptor-positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) breast cancer. Despite improved progression-free and overall survival, almost all patients develop CDK4/6 inhibitor resistance and experience disease progression on treatment. Aberrant activation of CDK2/cyclin E is a key resistance mechanism by which tumors can evade CDK4/6 blockade. Therefore, patients with HR+/HER2- breast cancer could benefit from treatment with a selective CDK2 inhibitor in combination with CDK4/6 inhibitors both in the resistant and first-line (1L) settings. BLU-222 is a novel, potent, and selective small-molecule inhibitor of CDK2 with favorable pharmacokinetic properties when administered orally, currently in early-stage clinical development. In pre-clinical studies using the MCF-7 xenograft model of HR+ CDK4/6-responsive breast cancer, treatment with BLU-222 combined with the CDK4/6 inhibitor ribociclib led to pronounced and durable tumor regression superior to ribociclib alone. In a derived palbociclib resistant MCF-7 xenograft model, ribociclib had no anti-tumor activity while BLU-222 led to a strong and durable anti-tumor response (83% tumor growth inhibition [TGI]) that was further improved when given in combination with ribociclib (110% TGI). To further explore the mechanism of aberrant CDK2 activation in CDK4/6 resistant, HR+ breast cancer, we engineered isogenic T47D cell lines to overexpress cyclin E1 (CCNE1) with or without p16, an endogenous inhibitor of CDK4/6 activity. In in vitro proliferation assays, co-expression of CCNE1 and p16 sensitized T47D cells to BLU-222 by approximately 10-fold compared to the parental control (110 nM vs 1078 nM, respectively). CDK4/6 inhibition with ribociclib had no anti-proliferative effect in the CCNE1 overexpressing cell lines regardless of p16 expression status. In vivo, treatment of the empty vector control T47D xenografts with ribociclib led to tumor stasis, while ribociclib in combination with BLU-222 led to tumor regression. T47D xenografts overexpressing both CCNE1 and p16 were resistant to ribociclib however CDK2 inhibition with BLU-222 single-agent treatment led to tumor regression. Finally, the activity of BLU-222 was evaluated in a patient-derived xenograft (PDX) model of CDK4/6 inhibitor-resistant HR+/HER2- breast cancer where the patient had progressed on 1L palbociclib/fulvestrant and 2L abemaciclib/fulvestrant therapy. In this PDX model, BLU-222 in combination with ribociclib led to tumor stasis, even in the absence of fulvestrant. In conclusion, these data support CDK2/cyclin E activation as a key vulnerability in CDK4/6 resistant, HR+/HER2- breast cancer and provide a rationale for the study of BLU-222 in patients with disease progression following CDK4/6 inhibitor treatment. Additionally, the improved durability of response when BLU-222 is combined with CDK4/6 inhibitors in the CDK4/6-naïve setting

supports the combination of these agents as 1L treatment. BLU-222 is currently under investigation in VELA (NCT05252416), a phase 1/2, first-in-human trial for patients with cyclin E aberrant cancers and HR+/HER2- breast cancer.

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12/9/2022

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P6-10-08

Evaluation of potent novel second-generation MELK-selective inhibitor in aggressive breast cancers

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Background Inflammatory breast cancer (IBC) and triple-negative breast cancer (TNBC) are aggressive breast cancer subtypes with poor clinical outcomes due to the lack of well-validated and actionable targets and the onset of chemo-resistant metastasis. TNBC and IBC account for 15-20% and 2-4% of all breast cancer diagnoses but result in 30% and 8%–10% of breast cancer-related deaths, respectively. MELK (maternal embryonic leucine zipper kinase) is a potential therapeutic target in both TNBC and triple-negative IBC (TN-IBC). We have shown that 1) MELK expression is higher in basal tumors (mostly TNBC) and in IBC than in non-IBC, 2) high MELK expression is an independent prognostic factor for poor overall survival

($P=0.0002$) and poor distant metastasis-free survival ($P=0.008$) in breast cancer, and 3) MELK knockout leads to significantly lower metastatic burden and prolonged survival in a xenograft model of TNBC (unpublished data). MELK inhibitor (MELKi) OTS167 is in clinical trials but it lacks specificity and cross-reacts with other essential kinases. It is critical to discover novel, selective inhibitors with good bioavailability that target MELK and minimize adverse effects. We have developed a second-generation small-molecule MELK inhibitor 30e that is a highly potent and slow-binding ATP-competitive inhibitor of MELK. 30e exhibits potent cellular inhibition of MELK ($IC_{50} < 10$ nM), as assessed using a live cell NanoBRET assay, and is highly selective as assessed by live-cell KiNativ profiling experiments in MDA-MB-231 TNBC cells. Methods We screened a panel of TNBC and IBC cell lines for MELK expression by western blot and qPCR analysis. We assessed the effects of MELK inhibition with the 30e on migration and invasion. The role of MELK in regulating cancer stem cell phenotypes was assessed using the mammosphere assay and flow cytometry (CD44+/CD24-/low surface marker). MELK's protumorigenic role was determined in vitro using a soft agar assay, and the anti-tumor activity of 30e was assessed in vivo using a TN-IBC orthotopic xenograft mouse model. Results We found that TNBC had high mRNA levels of MELK (62%) compared to non-TNBC cell lines (25%), which correlated with MELK protein levels. 30e inhibited cell viability in TNBC and IBC cells in a dose-dependent manner and with IC_{50} s ranging from 0.45 to 1.76 μ M ($P \leq 0.05$). However, no significant effect was observed when normal MCF-10A breast cells were treated with 30e ($IC_{50} > 20$ μ M). 30e also significantly reduced colony formation ability. Further, we observed that 30e reduced mammosphere formation efficiency and the CD44+/CD24-/low subpopulation in both TNBC and IBC cells in a dose-dependent manner ($P \leq 0.05$), suggesting the potential of 30e to inhibit the stem cell population in vitro. The soft agar assay also showed a significant decrease in colony formation in the TNBC and IBC cells after treatment with 30e, an indirect indicator of in vivo tumorigenicity. To assess the efficacy of 30e treatment on tumor growth, we evaluated this inhibitor as a single agent in a SUM-149 (TN-IBC) orthotopic mouse model. The mice were treated with intraperitoneal injections daily with 3 doses (2.5, 5, and 10 mg/kg) of 30e. Our data show that 30e suppressed tumor growth in a dose-dependent manner ($P < 0.007$). Conclusions and Future Directions Our data demonstrate that a novel, potent and specific MELK inhibitor inhibits tumor growth by suppressing the cancer stem cell phenotype. MELK is a promising target for aggressive cancers such as TNBC and IBC. We are evaluating how MELK inhibition modulates the tumor microenvironment, which is a critical component of breast cancer response to treatment. We performed a cytokine antibody array and are validating the top targets. Further, we will evaluate 30e in combination with standard-of-care treatment for toxicity and inhibition of metastasis.

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P6-10-09

Mutational landscape of breast cancer patients in ROME trial: preliminary results

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BACKGROUND: The Rome Trial is a randomized phase II trial (NCT04591431). The aim is to evaluate efficacy and safety of a tailored treatment (TT) compared to standard of care (SoC) in patients with solid tumors. Here we report the preliminary results of the molecular alterations, microsatellite status (MS) and tumor mutational burden (TMB) in metastatic breast cancer (mBC) cohort. **METHODS:** MBC patients who received at least 1 and no more than 2 systemic treatments were enrolled. Tissue samples were collected within 6 months from the screening. Centralized Next Generation Sequencing (NGS) was performed on both tissue and liquid biopsy. Molecular alterations were evaluated by the Molecular Tumor Board (MTB) using COSMIC, ClinVar, OncoKB and VarSome datasets. Genes with at least 10% frequency of mutation, MS and TMB are reported. **RESULTS:** From Oct 2020 to June 2022, 980 pts with solid tumors were enrolled. Complete screening mutational data are available for sixty-two pts from the mBC cohort (63% HR+/HER2-, 35% triple negative, 2% HR-/HER2+). NGS was available both on tissue and liquid biopsy in 48 (77%) pts, 14 had only liquid biopsy available due to tissue test failure. 328 genes resulted altered with a median of 7 alteration per pts (0-31). Some pathways were frequently altered: PIK3CA/AKT/MTOR (60%), TP53 (60%), Cell cycle/cyclin (35%), FGF/FGFR (26%), BRCA1/2 (17%). The most frequent altered genes were: TP53 (61%), PIK3CA (50%), ESR1 (27%), CCND1 (27%), FGF19 (24%), FGF3 (24%), FGF4 (22%), MYC (22%), FGFR1 (21%), PTEN (21%), EMSY (16%), RB1 (14%), RAD21 (14%), TET2 (13%), BRCA2 (11%), GATA3 (11%), KRAS (10%). No pts with MSI status were reported. Eight (13%) had a high TMB (>10) and the overall median TMB was 5.5 (0-24). Median TMB was similar in tissue and liquid samples (5 and 5.3 mut/mb, p= 0.8). Actionable mutations were detected in 34 pts (54%). Twenty-eight (45%) pts were assigned to a specific TT after the MTB discussion: ipatasertib (16), pemigatinib (5), ipilimumab plus nivolumab (4), lapatinib plus trastuzumab, TDM1 and everolimus (1). MTB requested a germline test for 6 pts: 4 were confirmed (66%; 2 BRCA, 1 PALB2, 1 BRIP1). **CONCLUSIONS:** The extensive NGS analysis performed in the ROME trial shown that several pathways are commonly mutated in mBC, with target drug potentially available. About 15% of pts had a high TMB but MSI is confirmed as a rare event in breast cancer. Germline mutations have been identified in patients with no prior indication for germline testing.

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12/9/2022

7:00 AM - 8:15 AM

P6-10-10

Genetic alterations in breast cancer associated with MDM2 dependency and sensitivity to the MDM2 inhibitor milademetan

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Background: Murine double minute 2 (MDM2), a potent negative regulator of p53, promotes tumorigenesis if dysregulated. MDM2 dysregulation occurs via different mechanisms, including MDM2 gene amplification, MDM2 overexpression, and loss of cyclin-dependent kinase inhibitor 2A (CDKN2A), which encodes the MDM2 regulator p14ARF. Combined inactivation of MDM2 and GATA3 in hormone receptor-positive (HR+) breast cancer is lethal to the cell.

Pharmacologic inhibition of MDM2 is a rational therapeutic strategy for MDM2-dependent, TP53 wildtype (WT) tumors, including tumors with MDM2 amplification or CDKN2A loss, and GATA3-mutant HR+ breast cancers. We determined the frequency and associated characteristics of genetic alterations of MDM2-dependent breast cancers, and evaluated sensitivity of these tumors to the small-molecule MDM2 inhibitor milademetan (RAIN-32).

Methods: Genomic data were obtained from three datasets: METABRIC; TCGA PanCancer Atlas, GDC v23.0 (April 2020); AACR Genie, v11. Among TP53 WT breast cancer samples from each dataset, the frequency of GATA3 frameshift mutations, MDM2 amplification (copy number [CN] ≥ 12), and CDKN2A homozygous loss was determined individually and as co-alterations. The antitumoral activity of milademetan was evaluated in a GATA3-mutant, TP53 WT HR+ breast cancer cell line (MCF7 GATA3 G336fs*17), a breast xenograft model (MCF7 GATA3 G335fs), and ex vivo in MDM2-amplified patient-derived breast cancer organoids (CTG-2810, ER+/PR+/HER2-, MDM2 CN 8).

Results: Genetic alteration frequencies in TP53 WT breast cancers by dataset are shown in the Table. GATA3 frameshift mutations (7.3–11.7%), MDM2 amplification (0.3–1.1%), and CDKN2A loss (0.2–1.2%) occurred across breast tumors, but were found with highest frequencies in HR+ tumors. Co-alteration frequencies in TP53 WT breast cancers across the aforementioned datasets were < 1%: GATA3 mutations/MDM2 CN ≥ 12 (0.2–0.3%); GATA3 mutations/CDKN2A loss (0.1–0.2%); MDM2 CN ≥ 12 /CDKN2A loss (0%). Mean MDM2

expression (log₂ (TPM+1)) in HR+ breast cancers (TCGA) were: GATA3 mutations, 5.12; CDKN2A loss, 5.88; MDM2 CN ≥12, 8.13, TP53 WT without these alterations, 4.78; mutant TP53, 4.35. A GATA3-mutant ER+ breast cancer cell line was sensitive to milademetan in vitro (IC₅₀ 126 nM). Milademetan 100 mg/kg displayed antitumor activity in GATA3-mutant HR+ breast xenograft and PDX models (p< 0.05 vs. vehicle). Milademetan also displayed activity in MDM2-amplified HR+ breast cancer organoids (IC₅₀ 0.2 μM). In a phase I study (NCT01877382), a patient with heavily pretreated MDM2-amplified breast cancer (MDM2 CN 16.8) had tumor shrinkage (18.2%) and PFS of 7.3 months with milademetan (orally 260 mg 3/14 days).

Conclusions: The frequency of genetic alterations potentially targetable by MDM2 inhibition among TP53 WT breast cancers (i.e., GATA3 mutations, MDM2 amplification, and CDKN2A loss) is greatest in the HR+ subset, and these genetic biomarkers are associated with higher MDM2 expression. Preclinical data show that the MDM2 inhibitor milademetan has antitumor activity in GATA3-mutant and MDM2-amplified HR+ breast cancers, and support the clinical evaluation of milademetan in these tumors. Two clinical trials of milademetan – MANTRA-2 (Phase 2 basket study in solid tumors with TP53 WT and MDM2 CN ≥12; NCT05012397) and MANTRA-4 (Phase 1 study of milademetan + atezolizumab in solid tumors with CDKN2A loss) – are enrolling patients or in planning.

Dataset	TP53 WT samples, N	Frequency of alterations in TP53 WT samples, %		
		GATA3 fs		
		mutations	MDM2 CN ≥12	CDKN2A loss
METABRIC	1246	7.3	1.1	1.2
HER2-/HR+	1107	7.6	0.8	1.0
HER2+	74	0.4	0.3	0.2
HR+	50	0.4	0.2	0.1
HR-	24	0	0.1	0.1
TNBC	61	0.1	0	0.1
TCGA PanCancer Atlas	616	11.2	0.2	0.5
HER2-/HR+	299	5.7	0.1	0.2
HER2+	68	0.8	0	0
HR+	61	0.8	0	0
HR-	7	0	0	0
TNBC	9	0	0	0
AACR Genie*	3590-7578	8.9	0.3	0.2

CN, copy number; fs, frameshift; HR, hormone receptor; TNBC, triple-negative breast cancer.

*No hormone receptor or molecular subgroup data available.

Disclosure(s):

Francois-Clement Bidard, MD PhD: Astra-Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Exact Science: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing); General Electric: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing); GSK: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME

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12/9/2022

7:00 AM - 8:15 AM

P6-10-11

Engineered neoantigen-specific T cell receptors to treat metastatic breast cancer

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T cell receptor engineered T cell (TCR T) therapy has emerged as a promising therapeutic modality for solid cancer following recent trials demonstrating the safety and efficacy of TCR T therapies against some types of metastatic solid cancers. However, the broader application of TCR T towards many solid tumors, including metastatic breast cancer (MBC), has been limited by several factors, chiefly among them the current scarcity of tumor selective target antigens. Neoantigens, which are expressed exclusively in cancer cells, are currently underrepresented in TCR T development, being targeted in only about 7% of trials conducted to date, and thus represent a relatively untapped source of potentially safe and effective novel targets. Driver

mutations in AKT1, ESR1, PIK3CA, and TP53 are common in patients with MBC, and could serve as ideal neoantigen targets for TCR T therapies. We hypothesized that we could generate MBC driver mutation-specific T cells from which we could isolate and clone neoantigen-specific TCRs to generate TCR T products for MBC. We identified 13 driver missense mutations that are among the most frequent in patients with MBC, which included AKT1 (E17K), ESR1 (K303R, Y537S, D538G), PIK3CA (E542K, E545K, H1047L, H1047R), and TP53 (R175H, R248Q, R248W, R273C, R273H), then designed peptide libraries consisting of 15-mer overlapping peptides that contain these mutations. To determine if these neopeptides could elicit T cell responses, we isolated T cells from 15 healthy donors and 11 MBC patients who expressed at least one of the targeted mutations and performed successive stimulations with neopeptide pulsed dendritic cells, then screened the resulting T cell lines for neoantigen specificity using an IFN- γ ELISpot assay. We observed neopeptide T cell responses in 8/16 lines generated from healthy donors and 7/11 lines generated from MBC patients, which were collectively directed against 11/13 of the targeted driver mutations. To isolate neoantigen-specific TCRs from one of these lines, we performed IFN- γ capture, limiting dilution, and 5' RACE, and isolated an HLA-B*35 restricted TP53 R248W-specific TCR. Gene transfer of this TCR conferred edited T cells with potent activity towards the TP53 R248W and not the TP53 WT peptide as assessed by ELISpot (1036 vs 46 SFU/1x10⁵ cells, respectively) and chromium release cytotoxicity assay targeting peptide pulsed autologous PHA blasts (37.5% vs 0% lysis at E:T 40:1, respectively). To increase the throughput of TCR discovery, we next used a single cell RNA sequencing based TCR discovery approach whereby we stimulated T cells from one of the generated lines with ESR1 WT or neopeptide and identified responsive T cell clones through upregulation of IFN- γ and/or TNF- α . This strategy has so far enabled us to identify and validate two ESR1 mutant-specific TCRs. This includes an HLA-C*01 restricted TCR that confers edited T cells with dual activity towards both ESR1 Y537S and D538G, but not WT peptide as determined by both ELISpot (2094, 3194, and 79 SFU, respectively) and chromium release cytotoxicity (31.3%, 77.8%, and 9.1% lysis, respectively), as well as an HLA-B*40 restricted TCR that confers high ESR1 Y537S specificity (5039 vs 138 SFU in response to ESR1 Y537S vs WT peptide, respectively). In summary, we have demonstrated responses of T cells derived from both healthy donors and MBC patients towards neopeptides derived from common MBC driver mutations. We have so far isolated neoantigen specific TCRs from two of the neoantigen-specific T cells lines, including TCRs specific towards TP53 R248W, ESR1 Y537S, dual ESR1 Y537S+D538G that are restricted to three different HLA alleles, and have successfully used these TCRs to generate TCR T products with high neoantigen activity. These results encourage further efforts to identify TCRs recognizing these MBC driver mutations, with our ultimate aim to translate neoantigen-targeted TCR T therapies to clinical trials of MBC.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-10-12

Discovery and Development of Next-Generation Estrogen Receptor Mutant Inhibitors using DNA-Encoded Chemical Library Screening

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Background: Activating somatic ESR1 mutations Y537S and D538G occur more frequently in endocrine therapy-resistant metastatic breast cancer, which is associated with an aggressive phenotype and poor survival in breast cancer patients. These gain of function mutant receptors are constitutively active and allow resistance to first-line endocrine therapies. Therefore, the development of next-generation small molecule drugs targeting mutant estrogen receptor (ER) is an important priority. Here, we searched the small molecule inhibitors for Y537S and D538D ER mutants using DNA-encoded chemical library screening. Methods: Wild type (WT) and mutant ER ligand binding domain (LBD) proteins were expressed in *E. coli*. The soluble proteins were purified by Ni-NTA chromatography followed by anion exchange and size exclusion chromatography. Homogeneous time-resolved fluorescence (HTRF) and fluorescent polarization (FP) assays were performed in these purified proteins. We employed a DNA-encoded chemical library affinity selection using our in-house collection of 6 billion compounds. Hit compounds were resynthesized and validated in biochemical assays. Finally, we have performed functional studies in CRISPR-Cas9 knock-in of Y537S and D538G mutant MCF-7 breast cancer cells. Results: We have successfully purified microgram amounts of ER α LBD of WT, Y537S, and D538G proteins. To test whether the purified WT and mutant proteins are active, HTRF and FP assays were performed in the presence and absence of estradiol and 4OH tamoxifen. Steroid receptor coactivator 3 (SRC3) peptide binding to the WT ER protein occurred only in the presence of estradiol. However, Y537S and D538G proteins are recruited by the SRC3 peptide in the absence of estradiol, indicating that these mutants are constitutively active and bind to SRC3. Furthermore, an *in vitro* biochemical FP assay was also established for WT and mutants in the presence of estradiol and 4OH tamoxifen. The screen of our multibillion small molecule collection of DNA-encoded chemical libraries identified several hits in WT and mutant ER. To confirm the selection output, we synthesized off-DNA compounds and validated these in biochemical and cell-based studies. We have identified that the compounds, CDD-1272 and CDD-1274, are active in HTRF and FP assays. Furthermore, these

compounds inhibit WT and mutant cell growth in the presence of estradiol. More importantly, CDD-1274 degrades ER mutant and cyclin D1 proteins. In addition, CDD-1274 induced p21 protein expression in WT and mutant cells. Conclusions: We have identified potent novel ER mutant binders by using our DNA-encoded chemical library platform. Our compounds are active in biochemical and ER mutant cell lines, suggesting these molecules are potential chemical probes to explore in in vivo models of breast cancer. Support: NIH/NCI R03 CA259664 and CPRIT RP220524 to MP.

Disclosure(s):

Murugesan Palaniappan, Ph.D: No financial relationships to disclose

Kurt M. Bohren, Ph.D: No financial relationships to disclose

Yong Wang, Ph.D: No financial relationships to disclose

Damian W. Young, Ph.D: No financial relationships to disclose

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7:00 AM - 8:15 AM

P6-10-13

An update to a Phase I trial of CFI-402257, an oral TTK inhibitor, in patients with advanced solid tumors with HER2-negative breast cancer expansion cohorts

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Background: TTK (also known as MPS1), a dual-specificity serine-threonine kinase, is critical for the spindle assembly checkpoint, chromosome alignment, and error correction in mitosis. Inhibition of TTK causes premature mitotic exit with unattached chromosomes, to result in chromosomal missegregation, aneuploidy, and cell death. CFI-402257 is a potent and highly selective inhibitor of TTK. Robust suppression of tumor growth was achieved upon oral dosing of single agent CFI-402257 in ER+/HER2- cell line and patient derived xenograft models. CFI-402257 demonstrated enhanced cytotoxicity in CDK4/6 inhibitor resistant ER+ breast cancer cell line models compared to parental cell lines, including those with RB1 loss. CFI-402257 has previously exhibited monotherapy and combination efficacy with a tolerable safety profile in ER+/Her2- Breast cancer patients in an ongoing clinical study which is updated here. Methods: This is an ongoing phase I, multi-center, dose escalation study (3+3 design) to determine the safety, tolerability, and maximum tolerated dose of CFI-402257 and to evaluate anti-tumor activity at the recommended phase 2 dose (RP2D). CFI-402257 was dosed once daily on a continuous schedule in 28-day cycles at a starting dose of 5 mg. Dose escalation included

patients (pts) with advanced solid tumors. Dose expansion at the RP2D included pts with advanced solid tumors (Cohort A), advanced Her2-negative (ER+ or TNBC) with 1-4 prior lines of chemotherapy for metastatic disease (Cohort B), and ER+/Her2- breast cancer in combination with Fulvestrant (500 mg IM Day 1, 15 and 29 and then every 28 days) who have had prior treatment with an aromatase inhibitor in combination with a CDK4/6 inhibitor (≥ 3 months) and ≤ 1 prior chemotherapy for metastatic disease (Cohort C). Results: At data cutoff of May 2, 2022, 87 pts were enrolled. 86 pts (66 pts receiving monotherapy and 20 patients receiving combination therapy) received ≥ 1 dose of study therapy and were analyzed for safety. One pt was not dosed due to elevated liver enzymes prior to first dose. The median age for mono was 61 years (range, 35-81) and for combo was 54 (range, 31-70). The median number of prior regimens mono and combo was 5 (range, 0-17; and 1-9, respectively). Tumor types in mono were breast cancer (27 pts), ovarian cancer (7 pts), GI cancer (3 pts), pancreatic cancer (3 pts), and other (30 pts). 20 breast cancer pts were enrolled in the combo. To date, 11 dose levels have been studied (range: 5 to 294 mg) in mono. There were 4 dose limiting toxicities (neutropenia >7 days at 168mg/day, febrile neutropenia at 210mg/day, and neutropenia and colitis at 294mg/day, all grade 3). The RP2D of 168 mg was established. 3 pts in mono (biliary obstruction, febrile neutropenia, and pancytopenia) and 0 pts in combo discontinued study due to adverse events (AEs). Treatment emergent adverse events (TEAE's) occurring in $\geq 30\%$ of pts were fatigue (31 pts; 47%), nausea (30 pts; 46%), decreased appetite (22 pts; 33%), and diarrhea (21 pts; 32%) in mono; and nausea (11 pts; 55%) and diarrhea (7 pts; 35%) in combo. 35% of mono and 39% of combo AEs were considered related to CFI-402257 by the investigators. Grade ≥ 3 AEs and serious AEs were reported in 25 pts (38%) and 17 pts (26%), respectively in mono; and 5 pts (25%) and 3 pts (15%) in combo. The investigator assessed best overall response rate (partial response [PR] or better within the efficacy population) of 6% (PR; hepatocellular carcinoma n=1, breast cancer n=2 from n=47) in mono and 18% (PR; n=2 breast cancer) in combo (n=11), with additional patients still to be assessed. Conclusion: CFI-402257 is well tolerated as mono and combination with fulvestrant. Efficacy signals are emerging with pts in the combo cohort demonstrating anti-tumor activity. Additional efficacy will be updated at the time of the presentation.

Disclosure(s):

John Hilton, MD, FRCPC: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing); BMS: Consulting Fees (e.g., advisory boards) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing)

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12/9/2022

7:00 AM - 8:15 AM

P6-10-14

Lysosomal acid lipase (LIPA) as a novel therapeutic vulnerability for treating TNBC

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Background: TNBCs have the highest mortality rate among all BC subtypes. There is thus an urgent and unmet need for effective targeted therapies in TNBC. Recently we, identified a novel agent ERX-41 that showed good efficacy in treating TNBC in preclinical mouse models, however, its molecular action remain unknown. In this study, we identified LIPA as novel molecular target of ERX-41. Methods: We have used CRISPR knockout pooled library and multiple TNBC models for identifying molecular target of ERX-41. Mechanistic studies were performed using LIPA mutants, RNA-seq, Turbo-ID mapping, Mass spectrometry, Immunoprecipitation, and Western blotting. The in vivo efficacy of ERX-41 was examined using four different patient-derived xenograft (PDX) models. We evaluated LIPA protein expression in TNBC using tissue microarray (TMA). Results: To identify the molecular target of ERX-41, we performed an unbiased CRISPR-Cas9 knockout (KO) screen in MDA-MB-231 cells and the results identified LIPA as a top hit. KO of LIPA alone (which encodes lysosomal acid lipase (LAL) abrogated cytotoxic response to ERX-41. Cellular thermal shift assays confirmed that ERX-41 binds to LAL. In silico modelling and mutational studies confirmed that ERX-41 interacts with LAL through residues in its LXXLL domain and that ERX-41 ability to induce ER stress and cell death in TNBC is independent of the lipase activity of LAL. Unbiased RNA-seq studies with and without ERX-41 in parental and LIPA KO SUM-159 cells revealed induction of genes involved in ER stress and UPR response by ERX-41 in parental SUM-159 cells but not in cells with LIPA KO. Ultrastructural studies using live-cell confocal microscopy show that LIPA KO abrogated ER morphological changes at 2 and 4 h after ERX-41 treatment. Further, subcellular localization studies showed LIPA localizes to endoplasmic reticulum (ER). Unbiased proteomic approaches (TurboID and DIA mass spec) identified a core set of proteins that were both LAL binders and affected by ERX-41 treatment. GO analyses of LAL binding proteins

confirmed their involvement in protein folding. Tumor micro array (TMA) analyses confirmed that >80% of primary TNBC tumors had significant and detectable LAL protein expression in contrast, normal breast tissue had lower LAL expression. ERX-41 (10 mg/kg body weight) decreased growth of four distinct TNBC patient-derived xenografts (PDXs) in vivo. Conclusions: Our results identified a new molecular target (LAL) for ERX-41 and novel mechanism of action (disruption of protein folding and induction of ER stress) that may have utility in treating patients with TNBC.

Disclosure(s):

Suryavathi Viswanadhapalli, PhD: No financial relationships to disclose

Xihui Liu, PhD: No financial relationships to disclose

Uday Pratap, PhD: No financial relationships to disclose

Gangadhara R. Sareddy, PhD: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-10-15

Targeting MARCKS in inflammatory breast cancer increased paclitaxel sensitivity

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Background. Because of its high metastatic potential, inflammatory breast cancer (IBC) is the most lethal and aggressive form of breast cancer. We previously demonstrated that Myristoylated Alanine-Rich C Kinase Substrate (MARCKS) protein overexpression was associated with shorter metastasis-free survival (MFS) in IBC patients, but not in non-IBC (nIBC) patients. However, the mechanism of action of MARCKS and its particular association to poorer outcome in IBC compared to nIBC are poorly understood. **Methods.** We evaluated in vitro the inhibitory effect of MPS (MARCKS phosphorylation site domain), a peptide targeting MARCKS phosphorylation site domain (PSD) in single and in combination with paclitaxel treatment, on cell proliferation and cell motility in two cell lines of different phenotype (SUM149 for IBC and MDA-MB-231 for nIBC), as well as its distinct molecular mechanisms of action. We also assessed the clinical relevance of the protein expression of MARCKS and phosphatase and tensin homolog (PTEN) in a large series of IBC vs. nIBC patients. **Results.** In vitro, the treatment with MPS peptide impaired cell proliferation, migration, and invasion in SUM149 compared to MDA-MB-231 cells. More important, MARCKS inhibition increased paclitaxel sensitivity when using combination therapy in SUM149 cells compared to MDA-MB-231 cells. Interestingly, we could partially explain this specific inhibitory effect in IBC cells using western blot: MARCKS inhibition in single and in combination induced up and downregulation of the PTEN/AKT signaling pathway respectively in IBC compared to nIBC cells. Importantly, a negative correlation of MARCKS and PTEN was only found in the clinical IBC samples (180 patients) compared to nIBC samples (355 patients). More importantly, the group of patients with negative MARCKS and positive PTEN protein expression was associated to better 5-year MFS only in IBC patients. **Conclusion.** These results indicate two major findings: first, the important prognostic value of the negative correlation of MARCKS and PTEN expression in IBC patients, and second the specific role of MARCKS in regulating different downstream pathways and increasing the paclitaxel response in combination treatment in IBC compared to non-IBC. They suggest a potential IBC-specific targetable biomarker, the inhibition of which might impair disease aggressiveness and perhaps enhance patients' survival.

Disclosure(s):

Maroua MANAI, Ph.D: No financial relationships to disclose

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or their Agents (e.g., speakers' bureaus) (Ongoing); Guardent: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Menarini: Consulting Fees (e.g., advisory boards) (Ongoing); Olaris: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Contracted Research (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Semonix: Consulting Fees (e.g., advisory boards) (Ongoing)

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12/9/2022

7:00 AM - 8:15 AM

P6-10-17

Pharmacological Strategies to Target Circadian Clock Genes in TNBC

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Pharmacological Strategies to Target Circadian Clock Genes in TNBC Yuanzhong Pan, Priya Jayachandran, Evanthia T. Roussos Torres, Steve A. Kay Background: Triple-negative breast cancer (TNBC) remains the most aggressive form of breast cancer and more targeted treatment options remain challenging. Our recent analysis of clinical data showed that circadian clock genes (including positive regulators BMAL1 and CLOCK, and negative regulators CRYs, PERs, and REV-ERBs) play important roles in breast cancer, and most prominently in TNBC. We have also shown in other cancer types that cells with a mesenchymal signature and stem-cell like state rely on BMAL1/CLOCK activity to support proliferation. BMAL1 and CLOCK are transcription factors that have remained “undruggable” to date. Alternatively, our lab developed small molecule compounds that target the negative regulators CRY, REV-ERB and CK2. We are therefore prompted to study if the clock genes can serve as a therapeutic target in TNBC using our small molecules that target clock regulators in TNBC. In addition, BMAL1 and CLOCK require ubiquitin E3 ligases and proteasomes for their transcriptional function, thus we hypothesize proteasome inhibitors may provide synergy to improve response to our novel clock-based therapeutics. Methods: We first used shRNA-mediated gene knockdown (KD) to disrupt the core circadian clock regulator BMAL1 and CLOCK in a panel of TNBC cell lines across different molecular subtypes (MDA-MB-231, MDA-MB-157 and MDA-MB-436, MDA-MB-453, HCC70, HCC1143, BT549, Hs578T). After KD, cell proliferation was quantified using CellTiter-Glo. We then tested our small molecule compounds SHP656—that stabilizes CRY, SR29065 and derivatives—that agonizes REV-ERB, and GO289—an inhibitor of CK2 that stabilizes PER. Based on our knowledge of the clock regulators, we tested drug synergy between SHP1705 and proteasome inhibitors MG132 and Carfilzomib across a range of concentrations. RNA-seq of cells treated with either single drug or drug combination were performed to study the mechanism of the synergistic effect. Results: A subset of the tested TNBC cell lines showed significantly impaired proliferation after BMAL1 or CLOCK KD. All cells in the mesenchymal-like molecular subtype responded to BMAL1/CLOCK KD, which is consistent with our previous data in other cancer types. It also confirmed BMAL1 and CLOCK have the potential to serve as therapeutic targets for mesenchymal-like TNBC. We then tested

the clock compounds in our TNBC panel. We found SR29065 and GO289 both inhibit cancer cell proliferation at a clinically relevant EC50. Combination of our novel small molecule SHP1705 with the proteasome inhibitor MG132 and carfilzomib, demonstrated significant synergistic effects in vitro. In order to understand the mechanism of the synergistic effect between clock compounds and proteasome inhibitors, we performed RNA-seq on single drug and combo-treated cells. Differential expression analysis revealed that over two-thousand genes are specifically changed in the combo group. GO analysis showed that these genes are enriched in MYC target genes. Because MYC is also, like BMAL1 and CLOCK, a E-box binding transcription factor, this result implies that the mechanism driving synergy may be due to a disruption of E-box-dependent transcription. Conclusions: Here we showed that the core circadian clock regulator BMAL1 and CLOCK are potential therapeutic targets in mesenchymal-like TNBCs. Using REV-ERB agonists and CK2 inhibitors to target BMAL1/CLOCK transcription activity, we can achieve compound EC50s in single-micromolar range. In vivo experiments in murine models of TNBC are underway to determine the efficacy of single agent and combination therapy with proteasome inhibitors. Given the recently established safety of CRY stabilizers there is great potential for translation of these findings to clinical trials in patients with TNBC.

Disclosure(s):

Yuanzhong Pan, n/a: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

P6-10-18

Developing novel lysyl oxidase (LOX) inhibitors to overcome chemotherapy resistance in triple negative breast cancer

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Triple negative breast cancer (TNBC) is the most aggressive breast cancer subtype. It accounts for ~15% of all breast cancer patients yet is responsible for 30% of breast cancer deaths. TNBC is treated primarily with conventional chemotherapy; however, resistance to therapy is common, leading to high mortality rates. Importantly, the benefit of current therapeutic strategies used in chemoresistant TNBC, i.e., immunotherapy and antibody-drug conjugates, is confined to only a fraction of patients, and survival benefit is limited. Therefore, there is an urgent need to identify novel and effective treatment strategies to overcome chemoresistance. Recently, we identified hypoxia-induced ECM re-modeler, lysyl oxidase (LOX), a member of LOX family, as a key mediator of chemoresistance in TNBC. However, currently available LOX inhibitors are either non-selective and/or show toxicity. Here, we performed a high-throughput cell-based LOX activity screen (HTS) with more than 5,000 molecules selected from a diversified compound library and identified the bi-thiazole derivatives as novel potent LOX inhibitors. Our structure activity relationship (SAR) analysis resulted in two lead compounds 6403, a relatively LOX-specific inhibitor, and 6415, a more LOX/LOXL2 inhibitor. Both compounds reduced collagen cross-linking (canonical function of LOX) and led to chemosensitization in TNBC cell lines and in chemoresistant TNBC PDX organoids. In addition, 6403 and 6415 reduced the TGF-beta induced fibrosis and inhibited migration capacity of the breast cancer cell lines. Importantly, 6403 showed excellent pharmacokinetic profile and did not lead to any observable toxicity in mice. Notably, 6403 overcame doxorubicin resistance in LOX-expressing 4T1 syngeneic model with no apparent toxicity. Furthermore, our novel LOX and LOX/LOXL2 dual inhibitors show superior inhibition of LOX activity compared to the recently developed and clinically tested LOX family or LOXL2/LOXL3 inhibitors. Overall, we identified novel potent LOX inhibitors with no observable toxicity for further preclinical development and future clinical testing to overcome chemoresistance in TNBC.

Disclosure(s):

Metin Cetin, PhD: No financial relationships to disclose

Ozge Saatci, MSc: No financial relationships to disclose

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P6-10-19

Screening of GPCR-targeting drugs for repositioning in breast cancer

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Drug repositioning can overcome both substantial costs and the long process of new drug discovery and development in cancer treatment. Some FDA-approved drugs have been found to have the potential to be repositioned as anti-cancer drugs. However, the progress is slow due to only a handful of strategies employed to identify drugs with repositioning potential. In this study, we evaluated GPCR-targeting drugs by high throughput screening (HTS) for their repositioning potential in triple-negative breast cancer (TNBC) and drug-resistant human epidermal growth factor receptor-2-positive (HER2+) breast cancer (BC), due to the dire need to discover novel targets and drugs in these subtypes. We assessed the efficacy and potency of drugs/compounds targeting different GPCRs for the growth rate inhibition in the following models: two TNBC cell lines (MDA-MB-231 and MDA-MB-468) and two HER2+ BC cell lines

(BT474 and SKBR3), sensitive or resistant to lapatinib + trastuzumab, an effective combination of anti-HER2 therapies. We identified 7 drugs/compounds as potential hits, out of which 4 were FDA-approved drugs. We focused on beta-adrenergic receptor-targeting nebivolol as a candidate, primarily because of the potential role of these receptors in BC and its excellent long-term safety profile. The effects of nebivolol were validated in an independent assay in all the cell line models. The effects of nebivolol were independent of its activation of β_3 receptors and nitric oxide (NO) production. Nebivolol reduced invasion and migration potentials which may suggest its inhibitory role in metastasis. Analysis of the Surveillance, Epidemiology, and End Results (SEER)-Medicare dataset found a reduced but not statistically significant risk of all-cause mortality in the nebivolol group. In-depth future analyses including detailed in vivo studies and real-world data analysis with more patients are needed to investigate further the potential of nebivolol as a repositioned therapy for BC.

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Scaffold attachment factor B1 modulates cholesterol pathways in triple-negative breast cancer

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Historically known as a tumor suppressor by estrogen receptor (ER) co-repression in breast cancer (BC), the matrix binding protein Scaffold Attachment Factor B1 (SAFB) binds scaffold or matrix attachment region DNA elements (S/MAR DNA) in eukaryotic DNA. SAFB1 plays a role in cellular stress response, DNA repair, differentiation, and apoptosis. SAFB loss in ER-independent BC and pancreatic cancer (PC) patients resulted in poor survival rates, hinting at the role of SAFB1 as a tumor suppressor. To understand the tumor suppressive mechanism of SAFB1, we performed shRNA-mediated knockdown (KD) of SAFB in PC cell lines and triple-negative breast cancer (TNBC) cells, an aggressive subgroup of BC. Analysis of onco-properties showed an increase in clonogenicity potential and cell proliferation in SAFB KDs in both PDACs and TNBCs cells. Further, RNA-Seq analysis of SAFB KDs in the TNBC cell line revealed activation of the mevalonate (MVA) pathway and the resulting cholesterol biosynthesis as the key metabolic change. Both pancreatic ductal adenocarcinoma (PDACs) and TNBC exhibited higher levels of MVA pathway gene expression upon loss of SAFB. Sterol regulatory element binding proteins (SREBP) 1 and 2 dictate cholesterol biosynthesis, and SREBP2 promotes tumor properties via the MVA pathway. Molecular and metabolic analysis of SAFB KD TNBC showed an increase in lipid droplets and SREBP2 maturation. Using Chromatin Immunoprecipitation and quantitative real-time PCR (ChIP-qPCR) in TNBC we demonstrate the direct binding of SAFB to the SREBP2 promoter region. In addition, byproducts of the MVA pathway have been shown to activate YAP/TAZ-dependent tissue homeostasis and tumorigenesis. We also observed increased YAP1 mRNA levels and decreased YAP1 (Ser127) phosphorylation with SAFB loss in TNBC, explaining the aggressive tumorigenicity gained with SAFB loss. Our study thus far suggests SAFB has overt control over the SREBP2-MVA-YAP1 pathway, and loss of SAFB results in an enhanced tumor phenotype.

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P6-11-02

Mitochondria-Nuclear Crosstalk Regulates the WNT Pathway in Triple-Negative Breast Cancer

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Compared to hormone receptor (HR) positive breast cancer (BC), basal or triple-negative BC (TNBC) suffers a poor prognosis caused by a limited understanding of its driver signaling pathways. We used the transmitochondrial cybrid approach to understand the metabolic reprogramming and mitochondria-nuclear crosstalk in metastatic TNBC. In cybrids, mitochondria from cancer and benign cells are compared under a commonly defined nuclear background. Using cybrid-based discovery and its validation in cell lines, patient-derived xenografts, and clinical data, we have previously reported the activation of fatty acid oxidation (FAO) in metastatic TNBC. Recently, we developed a unique gene (DEG) signature by integrating gene expression data from cybrids with different omnibus databases such as TCGA and METABRIC. Our DEG could effectively distinguish the PAM50 subtypes of BC. Further analyses nominated negative regulation of the canonical WNT signaling pathway as one of the major pathways altered by mitochondrial character. The WNT pathway is known to regulate cell signaling, metabolism, epithelial-mesenchymal transition (EMT), and cancer stemness. Cybrids with benign mitochondria showed transcriptional activation of negative WNT regulators, including DKK1, SOST, DAB2, and CAV1. Citrate is a key metabolite from the tricarboxylic acid cycle (TCA cycle) and is an intermediate of many other metabolic pathways. Analysis of TNBC cybrids, cell lines, and BC tissues suggest that in TNBC, citrate levels are increased with the activation of CPT1A, the rate-limiting enzyme of FAO. We confirmed the reduction of the beta-catenin protein in TNBC cells after pharmacological and genetic inhibition of CPT1A and mitochondrial citrate transporter (SLC25A1). We further analyzed the gene set enrichment analysis (GSEA) using gene expression data developed from short and long-term CPT1A inhibited TNBC cells and observed that the FAO alters polycomb repressive complex 2 (PRC2) activity. PRC2 is a critical modulator of the H3K27 methylation pattern as well as pathways related to cancer stemness, including WNT/beta-catenin and Hedgehog (SHH) pathways. These results suggest that the mitochondrial FAO transcriptionally inhibits WNT antagonist genes through repressive histone modification and consequently activates the canonical WNT pathway and cancer stemness. Overall, our current observations provide new insights into the regulation WNT pathway by mitochondria-nuclear crosstalk in TNBC.

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P6-11-03

Lipid-rich environment induces epigenetic reprogramming in non-transformed breast epithelial cells enhancing a mammary cell plasticity

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Introduction. The identification of women specifically at risk for estrogen receptor negative breast cancer (ER- BC) and the targeted treatment of this disease are significantly unmet clinical needs. We analyzed the gene expression profiles of epithelial cells from the contralateral unaffected breasts (CUBs) of BC patients and identified a lipid metabolism gene signature enriched in the CUBs of women with ER- BC (PMID: 28263391). Subsequently, we observed that exposure of non-transformed breast epithelial cells to lipids results in significant changes in gene expression and histone posttranslational modifications; and increased flux through multiple metabolic reactions, including those of serine and methionine (PMID: 35508495). Interestingly, the upregulated genes are involved in neural development, axon guidance, neural crest pathways and stemness. Neural genes are highly expressed in Triple Negative Breast Cancers (TNBCs) especially in the C2 cluster. Given that mammary stem/progenitor cells have distinct metabolic properties compared to other mammary cell subsets, we hypothesized that upon lipid exposure, stem-like cells have a survival advantage, and that lipid induces epigenetic reprogramming into neural-like cells which may foster a malignant transformation. Methods. To interrogate potential mechanisms linking lipids and epigenetic reprogramming, we performed CUT&RUN for H3K4me3 and H3K27me3 in non-transformed, estrogen and progesterone receptor negative MCF-10A cells exposed to vehicle or octanoic acid (OA) for 24 hrs. Peaks were called using MACS2 and differential peaks identified with DiffBind. Differentially expressed genes affected by OA (PMID: 28263391) were compared with target genes from the CUT&RUN. To determine the contribution in OA exposed cells of serine and methionine metabolism to S-adenosyl methionine (SAM), ¹³C-glucose tracing was performed. The Aldefluor assay was used to identify stem-like (ALDH+) cells in lipid-exposed MCF-10A cells. To determine if lipid-exposed cells adopt a neural-like phenotype, MCF-10A cells were grown on Poly-D-Lysine/Laminin (PDL/LM) coated plates. Results. A total of 661 differential peaks were identified for H3K4me3 (FDR < 0.05) encompassing TNBC C2 markers (NRTN, CHRM3) and genes involved in neuron differentiation, axonogenesis (NGFR, NGF, FOXA2), neural crest migration (NTRK2, MMP2) and EMT (DLL4, MMP15). Approximately 73% of H3K4me3 OA-associated peaks encompass regulatory regions of genes

that experienced a significant increase in gene expression with OA exposure (FDR < 0.01), including NGFR (log₂ FC = 11.7), FOXA2 (log₂ FC = 11.6), NGF (log₂ FC = 8). Twelve H3K27me₃ peaks were significantly enriched in vehicle (FDR < 0.05) and associated with increased gene expression in OA, among them were the stem cell markers LGR6 (log₂ FC = 1.9) and PLAG1 (log₂ FC = 2.8). ¹³C stable isotope tracing revealed that in presence of OA, glucose contributes to increased fractional abundance of the SAM M+1 isotopologue (adj p = 0.003) indicating that carbons derived from the serine synthesis pathway are used for re-methylation of homocysteine to methionine. Vehicle treated cells growing on PDL/LM plates assumed an epithelial phenotype while OA-treated cells adopted a neurite-like phenotype. Upon OA treatment the percentage of ALDH⁺ cells increased by a minimum of 10%. Conclusions. The increase of fractional abundance of SAM and the upregulation of neural genes regulated by H3K4me₃ as well as the enrichment of ALDH⁺ cells and the development of a neural-like phenotype in a rich lipid environment, suggests that lipid exposure affects the production of SAM, which results in epigenetic fostered plasticity, leading to reprogramming/selecting cells with a multi-potential embryonic or stem-like state and/or differentiation to a neural/neural crest-like state.

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Novel roles of Inosine Monophosphate Dehydrogenase 2 (IMPDH2) in TNBC doxorubicin resistance

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Triple negative breast cancer (TNBC) is one of the major subtypes of breast cancer, being associated with the lowest survival rate after metastasis occurs. TNBC patients face limited therapeutic options, relying mostly on a combination of chemotherapies (anthracycline, taxanes and cyclophosphamide). However, around 40% of patients treated with chemotherapy relapse due to onset of chemoresistance, contributing to the dismal survival of this aggressive subtype. Therefore, understanding the molecular mechanisms underlying chemoresistance is critical to identify better therapeutic target options. Guanosine triphosphate (GTP) is important for several biological processes, including cell proliferation. We and others have shown that inosine 5'-monophosphate dehydrogenase 2 (IMPDH2), the rate limiting enzyme in the de novo synthesis of GTP, is important in migration and invasion of cancer, including TNBC, however the role it plays in chemoresistance remains to be elucidated. Our preliminary data revealed that IMPDH2 expression levels modulate doxorubicin sensitivity in different TNBC cell lines. Moreover, we have generated MDA-MB-231 cells that are resistant to doxorubicin (referred to as DoxoR), and revealed IMPDH2 to be upregulated in DoxoR cells, at both protein and mRNA levels as well as having higher activity. Consistently, DoxoR cells have ~50% more GTP than their naïve counterpart and, interestingly, are twice more sensitive to treatment with Ribavirin, a well-tolerated FDA approved IMPDH inhibitor, suggesting that Ribavirin could be repurposed for the treatment of chemoresistant TNBC. As expected, RNA sequencing of DoxoR cells revealed increased stemness properties when compared to naïve cells, which we confirmed experimentally in tumor sphere formation assays. Importantly, knockdown of IMPDH2 reverted the ability of DoxoR cells to form bigger tumor spheres, as well as reduced the IC50 of doxorubicin to that of naïve cells. Therefore, our data suggests that increased IMPDH2 and GTP levels in resistant setting could be a potential new vulnerability to be leveraged therapeutically to suppress and/or prevent the growth of chemoresistant lesions.

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Carnitine palmitoyltransferase 1A (CPT1A) mediates therapeutic response to endocrine therapy in estrogen receptor positive breast cancer

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Breast cancer (BC) is the most commonly diagnosed cancer and second leading cause of cancer-related deaths in women in the United States, with more than 70% of the cases are hormone receptor positive (HR+) disease. Endocrine based therapies (ET) are successfully used, however, 30-50% will acquire ET resistance leading to tumor progression. Since the mechanism of acquired resistance remains unknown for ~60% of patients, identifying novel mechanisms of resistance is essential. We recently reported that carnitine palmitoyltransferase 1A (CPT1A), the rate limiting enzyme in fatty acid oxidation, is overexpressed in aggressive HR+ tumors, including ET resistant patients. We propose that CPT1A level and activity changes the tumor microenvironment to enhance tumorigenesis and contribute to ET resistance. To determine the mechanism by which CPT1A is promoting cell proliferation, tumor microenvironment, cellular signaling and ET resistance, we used a series of in vitro studies incorporating a panel of either endogenously or experimentally derived CPT1A-low and CPT1A-high controls, HR+ breast cancer cell lines as well as their ET resistant counterparts. We determined that CPT1A is upregulated in cell lines that acquire ET resistance. Our analyses demonstrated that levels of CPT1A can affect tumor formation ability in both CPT1A-high and adjacent CPT1A-low tumor cells with concurrent changes in both intra- and inter-cellular signaling which may be essential to promote tumor progression and mediate therapeutic response. This represents a promising step in understanding the mechanisms that promote tumorigenesis and ET resistance in HR+ breast cancer.

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P6-11-06

Capecitabine, eribulin and paclitaxel differentially impact the metabolite pool in metastatic breast cancer patients

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Introduction: Metabolic reprogramming is recognized as a hallmark of malignancy. Cancer growth, and progression has been associated with lipid and amino acid absorption by cancer cells. However, the differential impact of chemotherapeutic agents on energy balance and metabolism while on-treatment and at the time of clinical progression, in breast cancer patients, is largely unknown. We hypothesize that increases in lipid and other related metabolites, like amino acids, throughout chemotherapy treatment are therapy-specific, and associated with disease progression. Methods: Serum samples from 15 metastatic breast cancer patients (hormone-receptor positive and triple negative breast cancer), receiving different chemotherapy regimens (n=5 paclitaxel, n=5 eribulin, n=5 capecitabine), were collected at multiple time points (baseline, 3- week on-treatment and disease progression). Disease progression was determined by CT scans using RECIST v1.1 criteria. Samples were prepared for metabolomics and analyzed via mass spectrometry using the MxP Quant 500 kit (Biocrates Life Sciences AG, Innsbruck, Austria). Data was processed using MetIQ software (Biocrates Life Sciences AG). Limma was used to identify differential metabolites during treatment and at the time of disease progression as compared to metabolites at baseline. Results: With capecitabine treatment, there was a differential impact on many lipid metabolites, including ceramides, with an initial decrease on treatment: Cer(d18:2/18:1)(-1.95 log-fold change (logFC)); and arachidonic acid, (-1.32 logFC) (p < 0.05 for both). However, at the time of disease progression, there was a 1.8 to 2 log-fold increase in Cer (d18:0/20:0); Cer (d18:1/22:0); Cer (d18:2/22:0); Cer (d18:1/23:0); 1.7 log-fold increase in diacylglycerol (DG (16:0_20:0)) along with 1.6 log-fold increase in amino acid methionine (p < 0.05 for all). Conversely, in the eribulin group, while on treatment, there was a 1.2 to 1.3 log-fold increase in triglycerides (TG), i.e., TG(16:1_36:2); TG(16:0_36:2); TG(18:1_33:1); TG(16:1_36:1); TG(20:4_34:1) and 1.5 log-fold increase in amino acid kynurenine; while there was a 1.3 to 1.4 log-fold decrease in fatty acids (FA), such as FA(20:2); FA(18:2); FA(18:1) (p < 0.05 for all). At the time of disease progression, there was a 1.2 to 1.3 log-fold decrease in lipids like cholesteryl esters (CE) and phosphatidylcholines (PC), e.g. CE (18:2); CE (18:3); PC aa 36:3; PC aa 36:2 (p < 0.05 for all). Similarly, in the paclitaxel group, with treatment, there was a 1.2 to 1.8 log-fold increase in CE(22:0); Hex2Cer(d18:1/26:1) and

DG(18:3_20:2) ($p < 0.05$ for all), while, at the time of disease progression, there was a 2 log fold decrease in PC like lyso PC a C20:3; and lyso PC a C16:1, as well as 2 to 2.5 log-fold decrease in amino acids like glutamine, and sarcosine ($p < 0.05$ for all). Conclusion: Lipid and amino acid pool while on treatment and at disease progression were differentially impacted by the three classes of chemotherapies, some of which to the same functional extent. Although a decrease in lipid metabolites was observed while on capecitabine (prodrug of 5-fluorouracil) treatment, an increase in both lipid metabolites and amino acids was observed at disease progression. With both paclitaxel and eribulin treatment, which are microtubule inhibitors, a decrease in lipid metabolites and amino acids was observed at disease progression. An understanding of differential metabolic reprogramming with different chemotherapeutic agents may provide novel points of therapeutic intervention for anti-cancer treatment, such as combination of chemotherapy with inhibitors of ceramide metabolism or amino acid inhibitors and contribute towards efficacious personalized medicine.

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Role of insulin resistance in HR+ mammary carcinogenesis

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Hormone receptor (HR+) breast cancer (BC) is responsible for more than 80% BC cases and more than 60% BC-related deaths in the US. The incidence and severity of BC are influenced by a variety of modifiable risk factors, including (but not limited to) nutritional behaviors and obesity. Specifically, women with a body mass index (BMI) > 25 Kg/m² exhibit an approx. 1.4-fold increase in the risk of developing postmenopausal HR+ BC as compared to women with BMI < 25 Kg/m². Along similar lines, women with type 2 diabetes (T2D) – one of many consequences of obesity – are at 1.23-fold increased risk to develop postmenopausal HR+ BC as compared to women without T2D. Moreover, a BMI >30 Kg/m² has been associated with decreased progression-free survival and overall survival (OS) in women with HR+ BC. Thus, a high number of postmenopausal HR+ BC cases and BC-related deaths could be effectively avoided by modifying dietary habits, both in prophylactic and therapeutic settings.

Mechanistically, obesity provokes numerous alterations that have been linked to accrued postmenopausal HR+ carcinogenesis, encompassing (1) increased circulating levels of glucose and insulin – reflecting insulin resistance (IR) coupled to T2D, (2) increased levels of estrogen, produced locally and systematically by adipocytes, and (3) chronic inflammation of the breast adipose tissue (AT). However, the relative contribution of IR vs. other obesity-associated alterations to BC development and sensitivity to treatment has not been elucidated. At least in part, this reflects the two most common approaches employed to cause obesity in preclinical studies: the use of high-fat diets (HFDs) and/or mice genetically predisposed to develop obesity (e.g., ob/ob mice), neither of which is suitable to uncouple IR from all other metabolic, hormonal, and inflammatory effects of obesity. Here, we combined a unique model of HR+HER2- carcinogenesis that recapitulates key immunobiological features of human HR+ BC

(notably, a cold tumor microenvironment coupled to a scarce sensitivity to immunotherapy, and exquisite sensitivity to CDK4/6 inhibitors), as established in mice by medroxyprogesterone acetate (M) pellets combined with 7,12-dimethylbenz[a]anthracene (D) oral administration, with a novel model of pure IR originating from the AT-specific deletion of RAB10, member RAS oncogene family (Rab10), a transducer of insulin signaling in adipocytes. Importantly, these mice are neither hyperphagic nor overweight, have normal glucose level at baseline and do not exhibit inflammatory alterations in the AT, but nonetheless display IR. While a HFD shortens tumor-free survival (TFS) in immunocompetent mice subjected to M/D-driven oncogenesis, it does not alter the growth of detectable M/D-driven tumors. Conversely, IR as imposed by the loss of Rab10 in the AT failed to alter TFS but accelerated the growth of tumors, resulting in shortened OS. Moreover, the deletion of Rab10 from the mouse AT enabled the development of tumors displaying features of increased aggressiveness, including systematic loss of progesterone receptor (PR) expression. Finally, the growth of tumors emerging in the context of a Rab10 *-/-* AT could be efficiently controlled by the systemic administration of metformin. In line with this notion, orthotopically injected mouse triple negative BC AT-3 cells grew faster in mice bearing an AT-specific deletion of Rab10 as compared to their wild-type littermates. In conclusion, IR as imposed by the loss of Rab10 in the mouse AT converts HR+ mammary carcinomas as driven by M/D into HR- lesions with increased aggressiveness. These findings have major implications for ethnic groups that are at high risk for T2D at BMIs that are considered normal for Caucasians, such as women of African American and Asian descent, especially in view of the fact that women from these ethnic groups are known to be at increased risk for aggressive triple-negative BC as compared to their Caucasian counterparts.

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P6-11-08

Non-transformed breast epithelial cells show neural-like gene signature after lipid exposure

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Introduction: The identification of women specifically at risk for estrogen receptor negative breast cancer (ER-BC) and the targeted treatment of this disease are significantly unmet clinical needs. To that end, we analyzed the gene expression profiles of epithelial cells from the contralateral unaffected breasts (CUBs) of BC patients and identified a lipid metabolism gene signature, which was enriched in the CUBs of women with ER-negative BC (PMID: 28263391). Subsequent experiment revealed that exposure of non-transformed breast epithelial cells to lipid results in significant changes gene expression, chromatin accessibility and histone posttranslational modifications (PMID: 35508495). Several of the upregulated genes are hallmarks of the various fates of vagal neural crest: Neural, neurogenic and mesenchymal lineages. We hypothesize that lipid exposure imparts a survival advantage of stem-like cells, that lipid-induced epigenetic changes lead to a neural crest-like transcription signature and that these genes are not expressed normally in the breast. Methods: MCF10A cells were exposed to vehicle or octanoic acid (OA) for 24 hours. Gene expression was assayed by RNA-seq and OA responsive genes were identified (PMID: 35508495). Single-cell RNA sequencing (scRNA-seq) data from 14 human reduction mammoplasties (RM) was obtained from a publicly accessible data set (PMID: 34031589). The scRNA data was clustered and identified by unsupervised clustering (Seurat, v3.4.1) using cell-type markers curated using Supplementary table 2 from (PMID: 34031589). The bulk RNA-seq data from the OA treated cells was deconvoluted to cell-lineages using Bisque. The most significant upregulated VNC neural/neuronal/mesenchymal genes from the gene expression analysis were then plotted on the lineage clusters using FeaturePlot to determine if these markers are found in the normal breast epithelium, or other cell lineages. The plots were then filtered and re-clustered to look at basal-luminal cell types only. We utilized a second resource, a web-application for snATAC-seq data from various stages of mouse mammary development developed by the Wahl lab (https://wahl-lab-salk.shinyapps.io/Mammary_snATAC/), to query these same genes. Results:

Deconvolution of the bulk RNA-sequencing data revealed a transition to a pericyte transcription program following exposure to OA. Nerve growth factor (NGF) was found to be expressed in pericytes while nerve growth factor receptor (NGFR) was found within the basal epithelial cell lineage. Genes overexpressed in the VNC neural cluster and overexpressed in the OA-exposed MCF10 cells, PPP1R1C (2.39x, adj p=1.6E-5), FOXD3 (6.7x, adj p=6.7E-10), DIO3 (5.9x, adj p=3.9E-6) and MOXD3 (4.2x, adj p=1.5E-23) all evidence little to no expression in the normal breast but are observed in murine fetal mammary stem cells. Schwann cell precursor (SCP) markers, CDH19 and ROPN1, significantly upregulated in OA treated cells: 5.4x and 1.6x, respectively, exhibited low expression in luminal progenitors but in the mouse were observed in the mammary stroma. CDH19, a gene exclusive to SCPs, is expressed in stroma following murine birth. PRRX1, a key regulator of the VNC mesenchymal cell fate cluster, is 9.3-fold (p adj=4.9E-49) overexpressed in the OA treated cells, expressed strongly in pericytes and stroma and to a lesser extent in basal epithelial cells of the normal human breast and stroma of the murine mammary gland. Conclusions: Treatment of non-transformed mammary epithelial cells with lipid, specifically OA, shows significant upregulation of multiple VNC genes associated with both neural and mesenchymal fate. scRNA-seq from RM patients reveals that many of these same markers are either found in non-epithelial cell clusters or are found with low expression in luminal mammary lineages (both progenitors and mature).

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P6-11-09

Effects of a 12 Week Breast Cancer Exercise Program on the Mitochondrial Derived Peptide MOTS-c

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Background:

Breast cancer survivors have an increased risk for comorbid conditions such as cardiovascular disease, diabetes, and hypertension. In addition, cancer related treatments negatively affect bone health, muscular strength, and quality of life. Exercise is an effective strategy to combat cancer related symptoms (fatigue, anxiety) and common comorbid conditions.

MOTS-c is a Mitochondrial Derived Peptide (MDP) that has a number of beneficial effects on metabolism, insulin sensitivity, and exercise capacity. Previously published preclinical studies have shown that MOTS-c treatment improves physical performance in young, middle-age, and old mice. In humans, it has been implicated to promote metabolic homeostasis, stimulate glucose utilization, fat-oxidation, reduce inflammation, and protect against both cardiovascular and metabolic disease.

We implemented a 12-week exercise program in breast cancer survivors. We evaluated changes in baseline and post12-week MOTS-c levels and corresponding body composition

changes.

Methods:

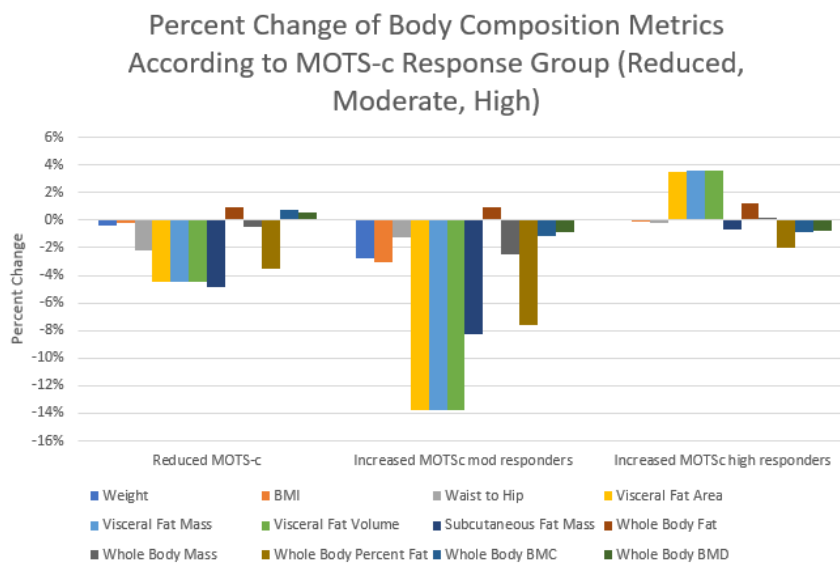
We evaluated 25 participant paired samples at baseline and post 12-weeks of exercise. Participants engaged in a 12-week exercise program, 3 times a week for 90 minutes/session. At baseline and post 12-weeks, participants underwent a DXA scan, body composition analysis, and a blood draw. The blood samples were analyzed using an in-house ELISA and compared to various clinical and body composition metrics.

Results:

The median age was lowest for the high responders (56.7 years) compared to moderate responders (57 years) and reduced MOTSc (61.5 years). We found 3 distinct groups: reduced MOTSc with exercise (n=8), increased MOTSc moderate responders (0-10pg/ml; n=2), and increased MOTSc high responders (>10 pg/ml; n=15). MOTSc had an inverse relationship with almost all tested metrics including: age, weight, BMI, waist to hip ratio, body composition—visceral (fat area, fat mass, fat volume), subcutaneous fat mass, whole body (body lean, body mass, body percent fat, bone mineral content (BMC), and bone mineral density (BMD). Although the majority of the metrics improved and had inverse relationships for MOTSc, the reduced MOTSc group had increased BMC and BMD. Interestingly, despite a higher MOTSc value, there was an increase in visceral fat as well as an increase in whole body fat across all groups. Of the 25 participants, 22 were Asian, two were Caucasian, and one was Native Hawaiian/Pacific Islander. Given the small number of participants, there does not appear to be any correlation between MOTSc and ethnicity in our study.

Summary:

We found significant changes in MOTSc according to clinical and body composition metrics after a 12-week exercise program. The findings in this study support previous findings on MOTSc metrics including MOTSc levels decreasing with age. However, there are few clinical trials evaluating MOTSc in cancer survivors. MOTSc is a potential biomarker related to exercise in cancer survivors. Our study was predominantly conducted in Asian women where there is limited data. This emphasizes the need for more clinical trials to be conducted with racially/ethnically diverse populations to better understand MOTSc's role in our varied cancer populations.



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Chloe Shen, n/a: No financial relationships to disclose

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P6-11-10

Investigating the role of mitochondrial protein translation in the metabolic adaptation of chemoresistant triple negative breast cancer

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BACKGROUND: Nearly 50% of patients with triple negative breast cancer (TNBC) treated with neoadjuvant chemotherapy (NACT) retain residual tumors resulting in high rates of metastatic relapse and poor overall survival. Residual tumors surviving NACT (Adriamycin plus cyclophosphamide; AC) were found to undergo a metabolic transition to heightened mitochondrial oxidative phosphorylation (oxphos; PMID: 30996079). Pharmacologic inhibition of mitochondrial electron transport chain (ETC) complex I with IACS-010759 (PMID: 29892070) had enhanced efficacy in residual, rather than treatment-naïve, tumors of orthotopic patient-derived xenograft (PDX) models. Our analyses of mitochondrial structure and function in human TNBC cell lines revealed differing adaptations in residual cells surviving treatment with conventional NACT agents. While DNA-damaging chemotherapies (e.g. Adriamycin, carboplatin) induced mitochondrial fusion and oxphos, taxanes (e.g. paclitaxel, docetaxel) induced mitochondrial fragmentation and reduced oxphos (Baek et al., Biorxiv Doi 10.1101/2022.02.25.481996). The mechanistic basis of these mitochondrial adaptations is not yet understood. The mitochondrial ETC consists of 92 proteins, 13 of which are encoded in the mitochondrial genome (mtDNA) and translated by the mitoribosome, while the remaining are encoded by the nuclear genome (nDNA), translated by the cytoribosome, and inserted into the inner mitochondrial membrane by accessory proteins, namely Oxidase (Cytochrome C) Assembly 1-Like (OXA1L). Disruption of OXA1L in mammalian cells has been shown to affect the levels and activity of ETC complexes I, III, IV, and V, and thus diminish oxphos. We aim to determine whether mitochondrial translation and OXA1L activity represent therapeutic vulnerabilities to overcome pro-survival metabolic adaptations in chemoresistant TNBC thereby augmenting treatment response. **METHODS:** We are evaluating the effects of conventional TNBC chemotherapies singly, and in standard combinations, on mitochondrial translation and ETC formation in human TNBC cells and PDX models (PIM001-P, WHIM14, BCM15116) using metabolomic and proteomic profiling. To perturb these processes genetically, we knocked down (KD) OXA1L with siRNA. We are complementing these studies pharmacologically using conventional antibiotics, such as tigecycline, as previous studies showed they inhibit mitochondrial translation in breast and other cancers (PMID: 25625193). These studies will reveal whether OXA1L and mitochondrial translation are required for metabolic adaptation and chemotherapy resistance of residual TNBC cells. PDX preclinical trials based on our published residual tumor testing schema (PMID: 30996079), will reveal whether the sequential combination of NACT followed by tigecycline can effectively perturb residual tumor relapse. **RESULTS:** Proteomic profiling of longitudinally harvested PDX tumors demonstrates substantial disruption of mitochondria- and nuclear-encoded ETC components in residual vs. treatment-naïve tumors. Interestingly, these patterns are distinct between different chemotherapy treatments, with an increase of ETC components in carboplatin-treated residual tumors compared to a decrease in docetaxel-treated residual tumors. Western blot analyses of human cell lines show OXA1LKD perturbs levels of both nuclear- and mitochondria-encoded ETC components. Preliminary findings suggest OXA1LKD increases sensitivity to chemotherapies in human TNBC cell lines. Finally, tigecycline effectively inhibits TNBC cell growth. We next will evaluate whether residual cells not killed by conventional chemotherapies have enhanced tigecycline susceptibility. **CONCLUSION:** These data suggest targeting mitochondrial translation may be a promising approach to overcome pro-survival metabolic adaptations in residual TNBC cells not killed by conventional chemotherapies.

Disclosure(s):

Mariah J. Berner, n/a: No financial relationships to disclose

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Michael T. Lewis, PhD: StemMed Ltd: Uncompensated limited partner (Ongoing); Tvardi Therapeutics Inc.: co-founder (Ongoing), Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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7:00 AM - 8:15 AM

P6-11-11

Breast cancer stem cell marker, CD24 regulates metabolic reprogramming in triple negative breast cancer

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Breast cancer stem cell (BCSC) is a subset of cancer cells that can dictate the tumor initiation, metastatic progression, and therapeutic resistance in BC. The eradication of this unusual population is emerging as a new paradigm in cancer treatment. Molecularly, CD24 negativity in conjunction with high expression of CD44 is considered a hallmark for the BCSCs. While extensive studies have been performed to delineate the role of CD44 in BCSCs, the regulation of CD24 and its functional role have not been fully understood. In this study, we investigated the regulatory mechanisms responsible for low CD24 expression in BCSCs and their functional relevance in BCSCs. Analysis of DNA from tumor tissues and blood from BC patients as well as BCSCs sorted from BC cell lines suggest that CD24 is epigenetically regulated via DNMT-1/HDAC1-dependent increased methylation of CpG islands in the CD24 proximal promoter region. To understand the role of CD24 in triple-negative BC (TNBC), an aggressive subgroup of BC, we knocked down (CD24-KD) and overexpressed (CD24-OE) CD24 in metastatic TNBC cells. While CD24-KD resulted in increased proliferation and stemness, CD24-OE diminished the proliferative and stem-like potential. To further identify the signaling cascade underpinning these effects, we performed phospho-proteome analysis using Reverse Phase Protein Array (RPPA). Remarkably, we observed an enhanced activation of AMPK and NF- κ B signaling cascades, and reduced PDGFR β signaling upon depletion of CD24. As signaling cascades are intricately linked to cellular metabolism, we performed a metabolomic analysis of CD24-KD and CD24-OE cells. Our comprehensive analysis revealed heightened activation of mitochondrial fatty acid β -oxidation (FAO) in CD24-KD and increased glutamine metabolism in CD24-OE cells. In coherence with these findings, we observed significant regulation of genes related to fatty acid metabolism in the TNBC patient cohort expressing low levels of CD24. Consistently, the CD24-KD cells demonstrated increased sensitivity towards FAO inhibitors while CD24-OE cells were more sensitive to glutamine metabolism inhibitors. In vivo studies to further understand the translational significance of this metabolic axis is underway. Taken together, our study demonstrates, for the first time, that CD24 presents a novel metabolic vulnerability that can target BCSCs to gain a therapeutic advantage in the treatment of drug-resistant TNBC patients.

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Divya Murthy, PhD: No financial relationships to disclose

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P6-11-13

Ferroptosis Heterogeneity in Triple-Negative Breast Cancer Reveals an Innovative Immunotherapy Combination Strategy

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Treatment of triple-negative breast cancer (TNBC) remains challenging. Deciphering the orchestration of metabolic pathways in regulating ferroptosis will provide new insights into TNBC therapeutic strategies. Here, we integrated the multiomics data of our large TNBC cohort (n=465) to develop the ferroptosis atlas. We discovered that TNBCs had heterogeneous phenotypes in ferroptosis-related metabolites and metabolic pathways. The luminal androgen receptor (LAR) subtype of TNBC was characterized by the upregulation of oxidized phosphatidylethanolamines and glutathione metabolism (especially GPX4), which allowed the utilization of GPX4 inhibitors to induce ferroptosis. Furthermore, we verified that GPX4 inhibition not only induced tumor ferroptosis but also enhanced antitumor immunity. The combination of GPX4 inhibitors and anti-PD1 possessed greater therapeutic efficacy than monotherapy. Clinically, higher GPX4 expression correlated with lower cytolytic scores and worse prognosis in immunotherapy cohorts. Collectively, this study demonstrated the ferroptosis landscape of TNBC and revealed an innovative immunotherapy combination strategy for refractory LAR tumors.

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Fan Yang, Yes: No financial relationships to disclose

Yi Xiao, M.D.: No financial relationships to disclose

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P6-11-14

Mitochondrial structure and function adaptation in residual triple negative breast cancer cells surviving chemotherapy treatment

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Background: Neoadjuvant chemotherapy (NACT) used for triple-negative breast cancer (TNBC) eradicates tumors in only 45% of patients. TNBC patients with substantial residual cancer burden have poor metastasis-free and overall survival rates. Our previous studies demonstrated mitochondrial oxidative phosphorylation (OXPHOS) was elevated, suggesting a unique therapeutic dependency of residual tumor cells that survived after NACT. However, mechanisms underlying this enhanced reliance on OXPHOS are yet unknown. Mitochondria are morphologically plastic organelles that cycle between fission and fusion to maintain mitochondrial integrity and metabolic homeostasis. Methods: We modeled residual disease in human TNBC cells by treating with chemotherapeutic agents at the IC50 of cell killing, then evaluating surviving cells after 48 hours of treatment. We modeled residual TNBC in orthotopic patient-derived xenograft (PDX) model (PIM001p) by treating with standard front-line NACT (Adriamycin + cyclophosphamide; AC), then longitudinally harvesting tumors prior to treatment, residual, and upon regrowth. We analyzed mitochondrial morphology, mtDNA content and integrity, mitochondrial oxygen consumption rate, and metabolomic flux. We developed a U-Net based deep learning model that automatically detects and quantifies mitochondrial features in transmission electron micrographs. To test the functional dependency of mitochondrial structure in TNBC, we perturbed mitochondrial fusion genetically (by knocking down the fusion-driving protein Optic Atrophy 1, OPA1) and pharmacologically (using the first-in-class small molecule OPA1 inhibitor, MYLS22). Results: Pharmacologic or genetic disruption of mitochondrial fusion and fission resulted in decreased or increased OXPHOS rate, respectively, in TNBC cells, revealing for the first time that mitochondria morphology regulates OXPHOS in TNBC. Upon comparing mitochondrial effects of conventional chemotherapies, we found that DNA-damaging agents (adriamycin, carboplatin) increased mitochondrial elongation, mitochondrial content, flux of glucose through the TCA cycle, and OXPHOS, whereas taxanes (paclitaxel, docetaxel) instead decreased mitochondrial elongation and OXPHOS rate. Increased levels of the short protein isoform of OPA1 were observed in residual cells that not killed by DNA-damaging chemotherapy treatment. Treatment of cells with adriamycin followed by MYLS22 or given concurrently with MYLS22 drastically decreased cell growth. Conversely, cells treated with adriamycin, inducing fusion, followed by the DRP1 inhibitor Mdivi-1, further inducing fusion, were less sensitive to adriamycin than were vehicle-treated cells. Further, we observed heightened OXPHOS, OPA1 protein levels, and mitochondrial elongation in residual tumors of the PDX model following AC treatment. We found that sequential treatment first with AC, thus inducing mitochondrial fusion and OXPHOS, followed by MYLS22 to inhibit OPA1 in residual tumors, was able to suppress mitochondrial fusion and OXPHOS and significantly inhibited residual tumor regrowth. Our deep-learning algorithm identified distinct changes in mitochondrial phenotypes in residual tumors of multiple PDX models. Treatment of non-chemotherapy-treated mice with the OPA1 inhibitor MYLS22 as a single agent had no effect on tumor growth, revealing that post-AC residual tumors have an enhanced dependency on mitochondrial fusion compared to treatment-naïve tumors. Taken together, our findings establish a functional role for mitochondrial structure in chemotherapeutic response and metabolic reprogramming, which may confer survival advantage to TNBC cells. These results suggest that pharmacologic perturbation of mitochondrial structure can overcome

chemoresistance in TNBC cells when administered rationally based on our understanding of chemotherapy-induced mitochondrial adaptations.

Disclosure(s):

Lily Baek, PhD: No financial relationships to disclose

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P6-11-15

Lipid accumulation in residual triple negative breast cancer cells surviving chemotherapy treatment

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Background: Triple negative breast cancer (TNBC) is an aggressive breast cancer subtype for which limited targeted therapies are available. Therefore, conventional chemotherapy remains the backbone of standard neoadjuvant treatment (NACT) for TNBC patients. Unfortunately, ~45% of patients will have substantial residual tumor burden post neoadjuvant chemotherapy, leading to poor prognoses (PMID: 28135148). Recently, it has been demonstrated that mitochondrial oxidative phosphorylation (oxphos) is upregulated and is a therapeutic vulnerability in chemoresistant TNBC (PMID: 30996079; Baek et al., doi.org/10.1101/2022.02.25.481996). However, mechanisms driving increased oxphos in chemoresistant TNBC are not understood. Upregulated fatty acid (FA) metabolism is a common adaptation in tumors, providing an energy source through fatty acid β -oxidation (FAO), and promoting lipid accumulation after fatty acid synthesis (FAS) when energy needs are met. Chemotherapy can induce oxidative stress through the generation of reactive oxygen species.

Cancer cells adapt to these damaging molecules by increasing de novo lipogenesis, resulting in the accumulation of lipid droplets (LDs) in the cytosol (PMID: 32782526, 20876798). We hypothesize that TNBC cells metabolically adapt to the stress of NACT by upregulating lipid metabolic pathways, providing highly energetic molecules that can be utilized to drive oxphos in chemoresistant TNBC. Methods: Using orthotopic patient-derived xenograft (PDX) models of TNBC (PIM001-P, PMID: 30996079, HCI-010, PMID: 22019887; WHIM14, PMID:24055055), we are measuring protein levels of fatty acid synthase (FASN) in vehicle tumors vs residual tumors surviving treatment with the standard front-line neoadjuvant chemotherapy regimens (Adriamycin plus cyclophosphamide (AC), docetaxel, carboplatin, or docetaxel+carboplatin) using immunohistochemistry (IHC). Vectra 3 microscopy (Akoya) is being used to quantify tumor cell-specific staining. We complemented our IHC analysis with reverse-phase protein array (RPPA). To assess LD accumulation in residual PDX tumors, we conducted transmission electron microscopy (TEM). To complement these PDX studies, we modeled the residual tumor metabolic state in cultured human TNBC cells. Following treatment with the IC50 of standard chemotherapeutic agents (AC, carboplatin, paclitaxel, docetaxel), we assessed oxphos by measuring oxygen consumption rate (OCR) using a Seahorse Bioanalyzer (Agilent). Further, we tested LD accumulation using LipidTOX staining. In ongoing studies, we are measuring incorporation of ¹³C palmitate into the tricarboxylic acid cycle (TCA) prior to and following chemotherapy treatments to assess if lipids fuel mitochondrial metabolism in residual TNBC cells. Results/Discussion: IHC in the PIM001-P PDX model after in vivo AC treatment revealed increased levels of FASN in post-AC residual tumors compared to the treatment-naïve tumors. Further, key proteins involved in fatty acid synthesis, FASN and Acetyl-CoA carboxylase, were significantly increased in residual PIM001-P cells that survived AC compared to vehicle by RPPA. TEM analysis of the HCI-010 PDX revealed significantly more LDs in carboplatin-treated tumors compared to vehicle. This finding was supported by increased LDs observed in TNBC cell lines treated with NACT compared to vehicle in our LipidTOX analyses. Taken together, these data indicate that NACT induces increased expression of key lipid metabolism proteins and accumulation of cytosolic LDs. Our future experiments will reveal if chemoresistant TNBC cells preferentially utilize and incorporate lipids into the tricarboxylic acid cycle, in turn driving oxphos. These data have the potential to provide rationale for the incorporation of FAO/LD inhibitors in sequential combinations with conventional chemotherapies to more effectively kill TNBC cells that are chemo-refractory.

Disclosure(s):

Katherine E. Pendleton, BS: No financial relationships to disclose

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Michael T. Lewis, PhD: StemMed Ltd: Uncompensated limited partner (Ongoing); Tvardi Therapeutics Inc.: co-founder (Ongoing), Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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Withaferin A induces metabolic crisis in breast cancer cell lines via decreasing c-myc expression: potential therapeutic implication

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Background: Breast cancer is the most diagnosed cancer and the leading cause of mortality among women in India and worldwide. Reprogrammed glucose metabolism is considered as the hallmark of the cancer with immense therapeutic relevance. Withaferin A (WA), a phytochemical isolated from the plant *Withania somnifera*, commonly known as Ashwagandha has the remarkable anticancer role. However, the mechanism of action of WA in breast cancer metabolism is still unelucidated. Breast cancer cells have metabolic vulnerability and high glucose dependency. Thus targeting glycolysis could be the better therapeutic approach. Chemotherapy and radiotherapy have the side effects, to overcome this natural products can be used to treat cancer. The potential of natural compounds in targeting metabolic vulnerabilities of cancer and highlighting prospective therapeutic benefits that can be determined by improving our understanding of this field. Aims and Objective: To explore the therapeutic effect of WA in breast cancer cell lines and to identify the role of WA in targeting Warburg effect via c-myc. Cancer cells exhibit upregulated Warburg effect, to fulfill the bioenergetics and biosynthetic demands of the rapidly growing cancer cells. Thus targeting the Warburg effect could be the better therapeutic approach. Materials and methods: Breast cancer cell lines (MBA-MB-231, MBA-MB-468, MBA-MB-453 and MCF-7) were procured from NCCS Pune and maintained in DMEM media supplemented with 10% FBS. SRB dye was used for cell viability as it binds to the protein of the cells. Further Colony formation assay (using crystal violet dye) was done to evaluate the effect of WA on colony formation. Metabolic assays \ (lactate production, glucose uptake and ATP generation) were performed using kits (Eton Bioscience). Transient silencing using si-RNA of c-myc was done with lipofectamine 3000.

Silencing of c-myc was done for Warburg effect and protein expression. RNA was isolated from breast cancer cells using Qiagen kit and RT-PCR was performed to evaluate the glycolytic gene expression before and after the treatment of the WA in breast cancer cell lines. To check the expression of glycolytic genes at protein level we had done the western blot. Protein isolation was done in RIPA lysis buffer and western blot was performed using primary antibodies of GLUT1, HK2, PKM2, c-myc. Statistical analysis was analyzed in graph pad prism. Breast cancer patient METABRIC data was analyzed and pathway deregulation score was calculated from Pathifier algorithm. Results: Withaferin A decreased the glucose uptake, lactate production and ATP production in different breast cancer cell lines. Further, WA induced suppression of key glycolytic enzymes via c-myc, decreased cell proliferation, biomass and colony formation ability of the breast cancer cells. Silencing of c-myc gene also showed the similar results to WA such as decrease in Warburg effect and reduction in glycolytic proteins expression. Through the LC-MS analysis WA decreases the key glycolytic metabolites and other pathway metabolites, induce metabolic catastrophe in breast cancer cells. Clinical relevance of our experiments was validated in dataset of ~2000 breast tumors (METABRIC) using Pathifier algorithm wherein we calculated deregulation score of glycolysis pathways in each of the tumor and normal sample. Importantly, higher deregulation of glycolysis was observed in breast tumor compared to normal tissues and found to be associated with poor prognosis. Conclusion: Our results highlight the anti- carcinogenic effect of Withaferin A in modulating breast cancer metabolism and the clinical significance of glycolysis in general. WA decreases the glucose metabolism and its flux through key metabolic pathways associated with the glycolytic intermediates. Therefore it could be argued that therapeutic targeting of breast cancer metabolism by WA may improve clinical outcome.

Disclosure(s):

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P6-12-01

ALCAM (Activated Leukocyte Cell Adhesion Molecule) is associated with HGF/MET signalling pathway in different subtypes of breast cancer

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Introduction. ALCAM (Activated Leukocyte Cell Adhesion Molecule), also known as CD166, is a cell adhesion molecule which belongs to the immunoglobulin superfamily and is widely expressed in various human tissues. It has been demonstrated that ALCAM plays an important role in the progression of malignant diseases and tumour metastasis in multiple cancer types including breast cancer. However, the molecular mechanism of ALCAM and cancer progression is currently unclear. The present study performed protein array analyses using ALCAM genetically manipulated cell models to select potential protein partners of ALCAM. The study focused on MET (Hepatocyte Growth Factor (HGF) Receptor), a prominent ALCAM interacting protein kinase and a protooncogene contributing to cancer progression and spread. Method. Human breast cancer cell lines MCF-7 and MDA-MB-231 were selected to create ALCAM knockdown cell models. A range of other breast cancer cell line with differing hormone receptor status were also used. Protein samples of transfected cells were used to perform Kinexus protein kinase microarray analysis. The protein interaction between ALCAM and other prospective protein kinases including MET was verified by the method of immunoprecipitation. Additionally, the ALCAM knockdown model was also assessed for the impact of ALCAM and HGF/MET on the biological functions by Electric Cell-substrate Impedance Sensing (ECIS). Results. MCF-7 and MDA MB-231 cells both were strongly expressed ALCAM. Cells models with ALCAM knocking down were successfully created by way of anti-ALCAM shRNA. We have shown on the protein kinase microarray analysis that the hepatocyte growth factor (HGF) receptor, MET was one of the kinases significantly affected following ALCAM knocking down. It was also found that the alteration of protein interaction between the MET protein kinase and ALCAM protein showed an opposite pattern between ER positive and ER negative ALCAM knocking down cells. This protein interaction was observed by immunoprecipitation in MDA-MB-361 and MDA-MB-231 cell lines, but not in MCF-7 cells. The biological analyses using the ECIS technologies showed that MET kinase inhibitors and exogenous recombinant HGF affected the ALCAM-mediated cell adhesion in different breast cancer subtypes. Conclusion. ALCAM is associated with HGF/MET signalling and the interaction between ALCAM and MET is different amongst subtypes of breast cancer which have different hormone receptor status.

Disclosure(s):

Yiming Yang, n/a: No financial relationships to disclose

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P6-12-02

Connecting Fluctuations in Estrogen Production, Release, and Action with Hormone-Dependent Gene Expression in Breast Cancers

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Estrogens are steroid hormones that play a key role in a wide range of physiological and pathological processes. Estrogen receptor-alpha, ER α , functions primarily as a nuclear transcription factor (TF) through ligand-dependent activation by 17 β -estradiol (E2), the predominant naturally-occurring estrogen. This results in dimerization, DNA binding to cis-regulatory elements called enhancers, and gene regulatory function of ER α . In vivo, E2 production and action fluctuates during reproductive cycles and possibly even in a circadian manner. In tissues and cells, E2-regulated gene expression is dynamic, with rapid induction of enhancer formation and target gene expression (or repression), followed by enhancer “decommissioning” and cessation of the gene regulatory effects. The effects of sustained E2 production and signaling, fluctuations in E2 levels, and removal of E2 on estrogen-regulated gene expression are unknown. Classical experiments exploring the gene regulatory effects of E2 involve stimulation of cultured cells throughout the duration of the experiment with a continuous and typically high dose of hormone, with the cells harvested at the end of the stimulation period. While this has allowed us to understand the molecular underpinnings of signal-dependent transcription, it has not allowed analysis of physiological fluctuations in estrogen signaling involving periods of stimulation (i.e., the presence of hormone) and non-stimulation (i.e., the absence of hormone). In our studies, we are applying a combination of next generation sequencing techniques and fluorescence microscopy to investigate signal-dependent responses to fluctuating and short duration E2 exposures using ER α -positive MCF-7 human breast cancer cells after E2 treatment and removal. Our initial results suggest that different E2 target genes respond differently to low dose E2 treatment and E2 withdrawal. Moreover, for some E2 target genes, sustained E2 treatment may not be required for a complete E2 transcriptional response. With these studies, we hope to connect physiological aspects of E2 production, release, and action with the molecular mechanisms of E2-dependent gene expression - an aspect of our understanding of estrogen signaling that has been lacking.

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Hyung Bum Kim, n/a: No financial relationships to disclose

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P6-12-03

Proinflammatory and estrogen signaling modulates the chemoresistance and metastasis of breast cancer cells through post-translational modifications of pioneering factor FOXA1

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ER-positive breast cancers compose most breast cancers at the time of diagnosis and are primarily driven by mitogenic estrogen signaling. In ER-positive breast cancers, the pioneer transcription factor FOXA1 plays a critical role in the estrogen receptor (ER) function. It binds to condensed chromatin and promotes chromatin accessibility for subsequent ER binding upon estrogen stimulation. We have reported that TNF α -stimulated proinflammatory signaling relocates FOXA1 to a new set of latent enhancers, which initiates the binding of estrogen liganded ER and subsequent expression of a unique transcriptome with clinical significance. The redistribution of FOXA1 occurs within 40 mins of the TNF α treatment, which implies a rapid signaling cascade that arises from changes to either FOXA1's post-translational modifications (PTMs) or its binding partners. To understand this genomic redistribution of FOXA1, we compared the post-translational modifications (PTMs) of FOXA1 from Vehicle, E2, TNF α , and E2+TNF α treated MCF-7 breast cancer cells. More than five acetylation and phosphorylation events have been identified around the DNA binding domain of FOXA1 by semi-quantitative and quantitative mass spectrometry approaches, and their abundance varies across

treatments. To study these PTMs of FOXA1, we used CRISPR/Cas9 to create specific knock-in mutations to mimic or prevent acetylation events in MCF-7 cells. Specifically, we engineered MCF-7 cell lines where K270 was mutated to glutamine (K270Q) to mimic acetylation. And for comparison, we also created cell lines where K270 was mutated to arginine (K270R) to prevent acetylation of FOXA1. Our data, including FOXA1 ChIP-seq and RNA-seq, revealed the genomic redistribution of FOXA1 with these PTMs, which subsequently alters gene expression programs and promotes cell growth, migration, or chemoresistance. These results were confirmed in other ER+ cell lines (such as T47D cells) providing evidence for the generalizability of our findings. Taken together, our data suggest that inflammatory signaling can reshape the enhancer landscape of FOXA1 through post-translational modifications, resulting in changes to estrogen signaling that have profound effects on breast cancer biology.

Disclosure(s):

Shen Li, Ph.D: No financial relationships to disclose

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Rosemary N. Plagens, PhD: No financial relationships to disclose

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P6-12-04

An Inducible Lineage Tracing System for the Identification of Tumor-Initiating Cells

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Background: Metastasis and therapeutic resistance are a major clinical challenge, responsible for the vast majority of cancer deaths. A subpopulation of tumor cells known to have intrinsic resistance to standard therapies and contribute to metastasis function as “cancer stem”, or tumor-initiating, cells (TICs). Enriched populations of TICs are typically identified by markers such as aldehyde dehydrogenase activity, the cell surface marker combination of CD44+/CD24-, or fluorescent reporters for signaling pathways that regulate TIC function such as STAT3. Despite their utility, TIC markers and reporters have limitations. Marker expression can be unstable and there is no established method to lineage trace long-lived TICs or to follow them as they undergo cell state changes. Methods: To augment existing TIC reporters, we developed a two component TAM-inducible, Cre recombinase-dependent, STAT3 signaling-specific lentiviral LT system. The first component is a vector that labels cells with active STAT3 signaling (EGFP+), followed by a self-cleaving peptide and TAM-inducible Cre-recombinase (4M67-EGFP-P2A-CreERT2). The second component is a constitutively expressed dual-color switching Cre-dependent reporter vector (EFS-loxPdsRedloxP-mNeptune2). Addition of TAM drives color switching from dsRed to mNeptune2 via CreERT2 recombination in STAT3 signaling cells. Both lentiviral vectors were constructed using Gateway® Cloning. Sum159 cells were transduced with the LT system and reporter activity was validated both in vitro and in vivo using confocal microscopy and flow cytometry. Four LT cell populations (EGFP+/mNeptune2+, EGFP+/dsRed+, EGFP-/mNeptune2+, and EGFP-/dsRed+) were enriched using fluorescence activated cell sorting, then analyzed by single cell RNA sequencing (scRNA seq). Results: Our results confirm the STAT3 LT reporter identifies STAT3 signaling cells (EGFP+), which can be labelled (mNeptune2+) upon addition of TAM. We conducted a TAM dose response curve to identify the optimal TAM dose for complete and partial labeling of STAT3 signaling cells. scRNA seq uncovered gene expression patterns within the TIC compartment and revealed similarities and differences in gene expression between the TIC compartment and the remaining LT reporter populations. Conclusion: These data demonstrate our LT system is a powerful tool that can be applied to uncover the role of TICs in metastasis and therapeutic resistance, as well as identify genetic vulnerabilities to specifically target TICs.

Disclosure(s):

Eric P. Souto, BS: No financial relationships to disclose

Michael T. Lewis, PhD: StemMed Ltd: Uncompensated limited partner (Ongoing); Tvardi Therapeutics Inc.: co-founder (Ongoing), Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

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The role of endothelial-specific AXL and its associated signaling pathways in the tumor microenvironment

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Most breast cancer deaths result from the development of metastases. The complex tumor microenvironment provides signals that can instruct both breast cancer cells to invade and tumor blood vessels to be leaky, hence supporting metastasis. We identified the receptor tyrosine kinase (RTK) AXL to be essential for metastasis. Genetic ablation of Axl in mouse models of HER2+ breast cancer, either globally or specifically in mammary epithelial cells, blunts metastasis but not primary tumor growth. We found that Axl expressed in tumor cells contributes to the remodeling of the tumor microenvironment, including immune cell recruitment and abnormal blood vessels. Hence, AXL in epithelial cells promotes cell invasion and shapes a pro-metastatic microenvironment that would be poorly responding to treatments such as immunotherapy. While AXL is known to be expressed on endothelial cells, its endothelial function has yet to be clearly defined. This project aims to address the hypothesis that AXL expressed on endothelial cells promotes processes that lead to abnormal blood vessel formation to promote metastasis. To address this hypothesis, we first studied the specific intracellular interactions between two RTKs, AXL and the known pro-angiogenic receptor VEGFR. Our preliminary analyses indicates that GAS6 can not only induce the phosphorylation of the permeability marker eNOS on its own but can also potentiate the VEGF's response. The index of linearity of the endothelial tight junctions upon GAS6 stimulation show increased permeability of the endothelial cells. To further characterize the signaling pathways controlled by these receptors, we plan to perform a phosphoproteomics screen. We will focus on studying the AXL+VEGFR phosphoproteome and define the signaling pathways that impact vascular permeability. The most interesting candidate(s) will be studied in the context of mouse tumor models. In parallel, we are generating a conditional deletion of Axl in endothelial cells by crossing *Axlfx/fx* mice with *Pdgfb:iCreER* animals. With this, we will study the specific endothelial effects of Axl in vivo, specifically with vessel permeability and retinal angiogenesis assays. Multiple anti-angiogenic therapies for cancer failed in the clinic highlighting the need for new strategies to target endothelial cells in cancer. This project will provide essential information on the role of endothelial specific AXL, in the context of the HER2 breast cancer, and of its downstream effectors. With more specific targets, anti-angiogenic therapies could decrease their off-target effects and increase their efficacy in the clinic. This project has the potential to uncover therapeutic targets that could reduce the metastatic burden in breast cancer patients, and therefore better the prognostic for the HER2 cancer subtype.

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Andréane Lalonde, n/a: No financial relationships to disclose

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P6-12-06

Neratinib vs. Trastuzumab plus Ribociclib in ERBB2-positive breast cancer: Preclinical mechanistic efficacy study

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Background: Despite the wide-ranging clinical success of human epidermal growth factor receptor 2 (HER2)-directed therapies, many HER2-positive breast cancer patients eventually progress because of the development of primary or acquired resistance. PIK3CA is found often mutated in breast cancer (>30%, TCGA dataset) and responsible for HER2-directed treatment failure. Purpose: Inhibition of pan-tyrosine kinases of HER-receptors along with the blockade of estrogen receptor (ER) prevents the activation of downstream effectors and crosstalk between HER2 and ER, leading to tumor cell death. Similarly, the combined inhibition of HER2-receptor signaling with cell cycle arrest leads to efficient tumor cell apoptosis. Here, we evaluate the mechanistic efficacy and comparability of neratinib (N) (an irreversible pan-ERBB tyrosine kinase inhibitor) in combination with fulvestrant (F) against ribociclib (R) plus trastuzumab (T) in HER2-amplified breast cancer cells. Methods: HER2+ breast cancer cell lines with Rb- wild-type- BT474 (ER+), SKBR3 (ER-), and MDA-MB453 (ER-, PIK3CA mutated [H1047R]) were used for the study. Cells were treated with N+F (F added in ER+ cell line only) or R or T as a single-agent or combination and assessed for real-time proliferation, 3D ON-TOP assay, changes in mitochondrial potential, and apoptosis. Cells treated with R and/or T were additionally examined for cell cycle arrest and changes in CDK4 mRNA transcription. Baseline CCND1 mRNA transcripts were quantified by RT-qPCR. Immunohistochemistry was used to assess baseline BCL2 expression in HER2+ tumor microarrays (TMA). Western blot was used to evaluate the effects on key downstream signaling proteins in response to the above treatment or combination. Results: High CCND1 expression was found in HER2+ cell lines that show promise for CDK4/6 inhibition. High BCL2 expression was found in HER2+ TMA that confirmed the natural resistance to programmed cell death. BT474 and MDA-MB453 were highly sensitive to N (+F), and high growth inhibition was evident at lower doses (< 20 nM). SKBR3 was comparatively less sensitive to N monotherapy and required dosing >160 nM to induce marked cell death. BT474 and MDA-MB453 had pronounced cytostatic responses to R or T+R, while a moderate response was observed in SKBR3. Substantial reduction in CDK4 transcription was noted following R or R+T treatment in MDA-MB453/BT474 but not in SKBR3. Apoptosis assays confirmed enhanced cell death with the R+T combination in BT474 and MDA-MB453 but not in SKBR3. Inhibition of key downstream oncogenic signaling (p-AKT/p-S6RP/p-ERK) was more evident with N compared to R, T, or R+T combination. Attenuated p-Rb expression (Ser 780 & Ser 807/811) was detected in all cell lines from R administration,

indicating interruption in cell cycle progression. Conclusion: Mechanistically, N+F was superior to T+R in terms of inhibition of HER2 and its downstream signaling in the HER2+/ER+ BC model. N+F induced significantly more apoptosis and inhibited cell proliferation compared to T+R. Additionally, N monotherapy was highly effective in HER2-amplified/ER-negative breast cancer cells with PIK3CA mutation.

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P6-12-08

Identifying FOXA1 Binding Partners using Proximity Labeling

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Approximately 75% of breast cancers are driven by the estrogen receptor alpha (ER), and despite the advent of endocrine therapy to block ER signaling pathways, a significant portion of women develop resistance to these drugs. The pioneer factor FOXA1 has been shown to facilitate nearly all DNA-binding events of ER in response to estrogen in ER+ breast cancer (ER+BC). Notably, up-regulation of FOXA1 is a hallmark of endocrine-resistant phenotypes and has been shown to reprogram enhancer elements, leading to an altered transcriptome. However, FOXA1 is a critical pioneer factor for multiple nuclear hormone receptors, aside from ER, and is implicated in regulation of important factors such as HER2 and the androgen receptor (AR). With the diverse array of breast cancer molecular subtypes displaying complex interplay between ER, HER2, AR, PR, and other hormone receptors, describing the complete ensemble of FOXA1 binding partners in various contexts, such as endocrine-resistant tumors, is of increasing importance. To define a comprehensive catalog of FOXA1 binding partners under basal conditions, we generated MCF-7 cell lines stably expressing constructs of FOXA1 fused at its N- or C-terminus to the biotin ligase miniTurbo. Using proximity labeling coupled with mass-spectrometry, we have comprehensively cataloged binding partners of FOXA1, including many expected proteins such as ER, AR, MLL3, YAP1, and GATA-3. Moreover, we have discovered more than 150 previously unidentified binding partners of FOXA1, which may exert profound effects on FOXA1 function. Importantly, high hazard ratios and significant dependencies are associated with several of these new binding partners, such as subunits of a previously described histone deacetylase (HDAC) complex containing genetic suppressor element 1 (GSE1) and lysine-specific histone demethylase 1A (KDM1A). Genomic approaches are currently underway to characterize where in the genome FOXA1 is interacting with these novel proteins and to guide future exploration into the physiological significance of these interactions. Integrating biochemical, molecular, and genomic approaches, we have potentially highlighted new mechanisms of FOXA1, which could have significant clinical impact in the future.

Disclosure(s):

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P6-12-09

Retinoic acid receptor (RAR) signalling plays a role in neratinib (NER) resistance in HER2+ breast cancer (BC) cell lines

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Introduction: NER is a pan-HER tyrosine kinase inhibitor (TKI) approved for the treatment of HER2+ BC in the adjuvant setting following trastuzumab and in combination with capecitabine for advanced disease. Resistance to small molecule TKIs like NER can develop in the clinic. Pre-clinical studies have highlighted that retinoic acid can inhibit BC growth and modulate HER2 signalling pathways. The RAR family of nuclear transcription factors consists of RAR α , RAR β and RAR γ . The synthetic retinoic acid fenretinide (FN) acts as a pan-RAR agonist, while AGN194310 (AG) acts as a pan-RAR antagonist. In order to investigate the anti-proliferative potential of co-targeting RAR and HER2 pathways in sensitive and resistant BC cell line models, we examined the effect of FN and AG in combination with NER in two HER2+, estrogen receptor-negative, trastuzumab-resistant cell lines HCC1569 and HCC1954, and their NER-resistant (NR) sub-lines HCC1569-NR and HCC1954-NR. Methods: HCC1569 and HCC1954 cell lines were cultured in RPMI/10% FCS at 37°C/5% CO₂. NR cell lines were generated by continuous exposure to 150nM NER for 6 months. 10 mM stock solutions of FN (H7779-Sigma), AG (SML2665-Sigma) and NER (supplied by Puma Biotechnology, Inc) were made in DMSO. Proliferation was measured as percentage growth versus DMSO control using

an acid phosphatase based assay after 5 days drug exposure. The half-maximal inhibitory concentration (IC50) was calculated for each drug using CalcuSyn. The combination assays were performed using fixed ratios. The combination index (CI) values were calculated at the effective dose that inhibits 50% growth (ED50) using CalcuSyn. Values < 1 represent a synergistic effect, a value of 1 is additive and values > 1 represent an antagonistic effect. All data presented as the mean of biological triplicate experiments \pm standard deviation. Results: This research found that the NR cell lines were >10-fold resistant to NER (HCC1569-NR IC50 $0.44 \pm 0.1 \mu\text{M}$, HCC1954-NR IC50 $0.198 \pm 0.019 \mu\text{M}$) compared to the parental HCC1569 (IC50 $0.018 \pm 0.015 \mu\text{M}$) and HCC1954 (IC50 $0.017 \pm 0.001 \mu\text{M}$) cell lines. Pan-RAR agonism by FN had a potent anti-proliferative effect in the HCC1569 (FN IC50 $0.22 \pm 0.02 \mu\text{M}$) and the HCC1569-NR cell lines (FN IC50 $0.28 \pm 0.13 \mu\text{M}$), with the HCC1954 and HCC1954-NR cell lines proving less sensitive (IC50 $6.47 \pm 1.3 \mu\text{M}$ and $1.9 \pm 0.2 \mu\text{M}$, respectively). When combined with NER, FN produced a strong antagonistic effect in the HCC1569 cell line (CI value: 15.63 ± 9.5) and a strong synergistic effect in the HCC1954 cell line (CI value: 0.42 ± 0.06). For the NR cell line models, the NER/FN combination proved synergistic (HCC1569-NR, CI value: 0.84 ± 0.46) or additive (HCC1954-NR, CI value: 0.97 ± 0.15). Next, we wanted to assess the impact of antagonising rather than activating RAR activity in our cell line models. All four cell lines were less sensitive to antagonist AG (IC50 >8 μM for all cell lines) compared to FN. The addition of AG to NER resulted in responses diametrically opposed to the FN/NER combination. The AG/NER combination produced a strong synergistic effect in the HCC1569 cell line (CI value: 0.52 ± 0.17), an antagonistic effect in the HCC1954 cell line (CI value: 2.1 ± 0.4) and an antagonistic effect in both NR cell lines (HCC1954-NR, CI value: 2.69 ± 0.6 and HCC1569-NR, CI value: 1.58 ± 0.12). Conclusions: This pre-clinical study suggests involvement of the RAR signalling pathway in response to NER and the development of NR. Results also suggest pan-RAR agonism, rather than pan-RAR antagonism, as a potential therapeutic strategy to overcome NR. Further investigation is warranted to determine how targeting the RAR signalling pathway may assist in the treatment of HER2+ BC.

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EPITHELIAL-MESENCHYMAL TRANSITION AND TUMOR STEM CELLS NETWORK IDENTIFICATION IN BREAST CARCINOMAS: IN SILICO STUDY.

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INTRODUCTION: Breast cancer (BC) is the most prevalent malignant tumor in the female population, except for skin tumors. Despite therapeutic advances, over 20% of patients with localized disease will relapse. The research of epithelial-mesenchymal transition (EMT), tumor stem cells (TSC), and the biological mechanisms related to refractoriness and metastasis development is, therefore, an opportunity for new therapeutic strategies and better results. **OBJECTIVES:** To identify breast cancer cellular markers related to EMT and TSC according to their histological subtypes, stage and to analyze their relationship with clinical outcomes. **METHODS:** After selecting a public breast cancer patients database with interactome, we identified differentially expressed genes, their associated processes, coexpression networks and interactions with pathways related to the stem phenotype and epithelial-mesenchymal transition. The characterization of key genes and the correlation with histological subtypes and clinical outcome allowed us to determine a group of genes as potential breast cancer EMT/TSC prognostic markers. **RESULTS:** In the 989 patients studied, 1033 differentially expressed genes

(DEGs) were found, categorized according to histological subtype (hormone receptor positive, HER2 positive, triple negative) and stage IV. Seven communities of gene coexpression were found, with the gray community showing greater interaction with hormone positive tumors, the green community with HER2 positive, and the turquoise community with the triple negative one. The hormone positive disease was related to extracellular matrix processes and neuronal communication, the HER2 positive to the extracellular matrix interaction and the triple negative tumors to mitotic processes. Investigation networks with EMT and TSC related genes demonstrated a strong correlation with HER2-positive and triple-negative tumors; being eight genes in HER2 positive subtypes correlated with survival (SYNDIG1, COL10A1, SLC24A2, LINC00922, KLKP1, MMP11 and ECM2); and one of the hormone positive subtype (ITIH5). ECM2 was highlighted in terms of EMT/TSC connectivity and survival. CONCLUSION: The EMT/TSC processes are significant in the various subtypes of breast cancer and impact on survival, especially in the HER2 positive subtype.

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Invasively distinct subpopulations cooperate via a laminin-332/Rac1 axis in triple-negative breast cancer

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Intratumoral heterogeneity poses a significant hurdle for cancer treatment, yet is under-characterized in the context of tumor invasion. Cancer cells from solid tumors can invade through two predominant modes: collective invasion, whereby cancer cells invade in multi-cellular packs or streams marked by intact cell-cell junctions; and single-cell invasion, whereby cells invade independently without intercellular adhesion. We have observed that collective and single-cell invasion co-occur within the same tumor microenvironment in triple-negative breast cancer, suggesting that invasive heterogeneity supports cooperative behavior between tumor subpopulations. To test this, we used a novel, published technique developed by the lab (SaGA) to isolate pure subpopulations of 4T1 cells that collectively invade (collectives) or single cells that invade alone (singles). 3-D spheroids of SaGA-purified collectives and singles exhibited almost exclusively collective and single-cell invasion, respectively, and these invasive phenotypes were retained over multiple passages. Integration of RNA sequencing and methylation array data obtained from RNA and DNA isolates, respectively, of collectives and singles revealed that collectives exhibit drastic overexpression and promoter hypomethylation of two laminin genes that form the laminin-332 complex, Lama3 and Lamc2. Additionally, an unbiased proteomic analysis of secreted proteins also revealed an overabundance of these laminins in collectives media. We found that singles have increased expression of integrin $\alpha 6$ and $\beta 4$, which together have been found to specifically bind to laminin-332 to activate the Rac1 GTPase. Interestingly, our RNA sequencing data revealed a binary overexpression of a Rac1 GTPase, Prex1 in singles, suggesting that singles have enhanced Rac1 activation when compared to collectives with the potential for hyperactivation upon laminin-332 binding. Indeed, laminin-332 resulted in higher GTP-bound Rac1 in singles and subsequently increased invasion of singles in 3-D models. Additionally, laminin-332 induced cell elongation at the leading edge of singles spheroids, which was reversible by treatment with a Rac1 inhibitor. Together, our data suggests that distinct subpopulations amidst a heterogeneous tumor cooperate via laminin-332 and Rac1 to facilitate tumor invasion in metastatic triple-negative breast cancer.

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Hope for OTHERS – An organ donation program for metastatic breast cancer research

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Background: Previous studies have shown that rapid autopsies (RA) provide a unique opportunity for tissue collection from patients who succumb to the disease. Because cancer patients are unable to donate their organs to other people, this program provides the patient an opportunity to leave a legacy by donating their body to research. These donations are vital for advancing breast cancer research. The UPMC/Pitt RA group revamped an existing program in 2018 through the formation of a larger multidisciplinary team that includes breast cancer laboratory and clinical researchers, pathologists, nurses, bioinformaticians, and tissue bankers. Because recruitment to the RA program was a challenge, we recently added patient advocates to the team to provide their essential perspective, and a dedicated research coordinator who serves as an ambassador for the program. Methods: Autopsy is performed by the Autopsy and Forensic Pathology Center of Excellence/Decedent Affairs Service of UPMC. Samples are banked in the Pitt Biospecimen Core (PBC), in addition to immediate processing including preparing of samples for sequencing and growing of organoids in the laboratory. Immunohistochemical (IHC) analysis is performed by UPMC/Magee Pathology. Results: The research coordinator quickly became an integral part of the program and closely interacts with care providers, patients and their families, pathologists on call, and manages interactions with transport services. Five breast cancer advocates have been instrumental in advising on additional changes to the program. The advocates attend regular team meetings and have formulated patient considerations for the the RA program, including appropriate and sensitive recruitment of patients, the role of physicians in decision making by the patient, registration for more than one RA program, potential issues with transporting a body across state lines and more. The advocates also developed the name for the program - "Hope for OTHERS" with Others standing for "Our Tissue Helping Enhance Research & Science". As of June 2022, the team has completed 26 autopsies, and an additional 20 patients have consented to the program. The completed autopsies include patients with breast tumors representing different molecular and histological classes, ethnicities, and genders. The average disease-free survival and overall survival of patients that underwent autopsy was 81.6 and 127.8 months, respectively. Most patients passed outside the hospital (86%), with 62% in home hospice and 24% in inpatient hospice. Average time between death and start and end of autopsy was 4.56 hrs and 7.09 hours, respectively. The most common metastatic sites from which specimens are collected are liver, lung and lymph nodes. Per patient we collect on average specimens from 4

different organs. In addition to the metastatic lesions, we have access to primary tumor tissue and liquid biopsies obtained during the breast cancer disease progression for 44% and 73% of the patients, respectively. For a subset of the patients, tissue has been grown as patient-derived organoids or xenograft models. Preliminary IHC and sequencing analysis has provided insight into inter- and intra-patient and intra-tumor heterogeneity. Further molecular studies are ongoing. Conclusion In summary, over the last 5+ years, we have established a successful post-mortem tissue collection program, by addressing a series of barriers through the formation and work of a multi-disciplinary well-coordinated team. We are currently expanding our omics studies using state-of-the-art technologies to improve understanding how intra- and inter-tumor heterogeneity play a role in the clinical course of advanced breast cancer, to increase diversity of the patients enrolled in the RA program, and to support the successful implementation of other RA programs nationwide and worldwide.

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P6-14-03

Oestrogen represses Noggin expression by interfering BMP/Smad signalling in ER positive breast cancer cells

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Background Bone morphogenetic proteins (BMPs) are members of Transforming Growth Factor β (TGF- β) superfamily. BMPs are actively involved in the disease progression and bone metastasis of breast cancer. As a natural antagonist of BMP, Noggin plays important roles in the regulation of BMP signalling. It can facilitate spread of breast cancer cells to bone and subsequent colonisation and formation of osteolytic bone lesions. The present study aimed to investigate the regulatory mechanism for Noggin expression in oestrogen receptor (ER) positive breast cancer cells. Method Noggin expression was analysed in The Cancer Genome Atlas (TCGA ER (+) n=763, ER (-) n=216) and E-MTAB-6703 (ER (+) n=733, ER (-) n=421) cohorts. Correlation between Noggin and ER was evaluated using Spearman test. The expression of Noggin in an ER positive breast cancer cell line MCF-7 was determined by depriving the cells from oestrogen using phenol red-free DMEM supplemented with 10% charcoal stripped foetal calf serum or adding 10-10M 17- β -oestradiol. Activation of Smad-1/5/8 and involvement of BMP receptors in the oestrogen repressed Noggin expression were further examined using recombinant human BMP7 and a BMP receptor inhibitor (LDN-193189). Influence of Noggin on cellular functions was evaluated in MCF-7 cells with Noggin overexpression using a lentiviral Noggin expression vector. Results Noggin expression was negatively correlated with ER α in both TCGA BRCA (r=-0.162, p<0.01, n=1093) and E-MTAB-6703 (r=-0.078, p<0.01, n=2302) cohorts. The expression of Noggin was increased in the MCF-7 cells upon a deprivation from oestrogen which was further validated by adding 17- β -oestradiol. This is in line with the increased expression of Noggin observed in the MCF-7 cells with ER silencing (GSE27473). Furthermore, an increased level of phosphorylated Smad1/5/8 was seen in the MCF-7 being hungered from oestrogen which was prevented by adding 17- β -oestradiol and LDN-193189, respectively. As a result, the oestrogen hunger induced Noggin expression was also decreased by adding with 17- β -oestradiol and LDN-193189. To further investigate the influence of oestrogen on BMP-Smad signalling regulated Noggin expression, Noggin expression and phosphorylation of Smad1/5/8 and Smad3 were determined in MCF-7 cells which were treated with rhBMP7 and in combination with 17- β -oestradiol and LDN-193189, respectively. BMP7 induced Noggin expression and activation of Smad1/5/8 can be diminished by 17- β -oestradiol and LDN-193189. Noggin overexpression in MCF-7 cells resulted in an increase of proliferation. Conclusion Noggin expression can be repressed by oestrogen through an inference of the BMP- Smad signalling. Overexpression of Noggin promoted proliferation of MCF-7 cells. Further investigation is required to clarify the exact role of Noggin in ER positive breast cancer and its implication in the disease progression and current therapies.

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P6-14-04

HIF1's Promotion of FASN-Dependent Palmitoylation of Sonic Hedgehog

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BACKGROUND Breast Cancer metastases develop via a series of complex steps that are often initiated through a cellular reprogramming called the epithelial-mesenchymal transition (EMT). One protein involved in the promotion of the EMT is Hypoxia-Inducible Factor-1 (HIF-1). The mechanisms by which HIF-1 initiates this process is unclear. Previous studies have demonstrated hypoxia to induce lipid metabolic reprogramming through HIF-1 α -induced regulation of the fatty acid synthase (FASN). FASN produces palmitate which has been shown to post-translationally modify and stabilize oncoproteins like Sonic Hedgehog (Shh). I hypothesize that the mechanism by which HIF-1 α fosters an EMT phenotype in breast cancer is through FASN-induced palmitoylation of Shh, which leads to activation of the Shh signaling pathway and its downstream targets. **MATERIALS AND METHODS** HIF1 protein was stabilized in MDA-MB-231 triple negative breast cancer cells by exposing the cells to Dimethylloxallyl Glycine (DMOG). Stabilization confirmed via a Western Blot analysis. Cells were then exposed to a combination of DMOG and TVB-2640, FASN activity inhibitor, DMOG only, and a vehicle treatment. mRNA expression of HIF1, FASN, and SHH of these treatment groups were analyzed with qt-PCR. **RESULTS** When MDA-MB-231 breast cancer cells were exposed to DMOG, mRNA expression of HIF-1, FASN, and SHH simultaneously increased. The DMOG-induced increase in SHH mRNA was prevented when FASN activity was inhibited. **CONCLUSION** Increases in SHH mRNA expression levels are dependent on HIF1 stabilization and FASN activity. These result points to a potential mechanism connection between these proteins that could elucidate how the EMT is initiated.

Disclosure(s):

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P6-14-05

Regulation of cellular identity and spatial organization during collective breast cancer invasion.

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An early step in breast cancer progression is invasion of tumor cells into surrounding tissues. In many breast cancers, particularly ductal carcinomas, this invasion is accomplished by tumor cells migrating as a cohesive group. This often involves cells that take on heterogeneous roles as either leader or follower cells. While studies in common mouse and human breast cancer models have established that leader cells express high levels of keratin-14 (K14) and other basal epithelial markers, the molecular mechanisms regulating K14+ leader cell identity remain obscure. Here we performed time-sampled single cell RNA-sequencing in 3D type I collagen-embedded tumor organoids isolated from the MMTV-PyMT luminal B model of breast cancer. 11 distinct cellular transcriptional states were identified and correlated with K14 expression and invasive strand formation. Having identified the leader cell state we next asked what transcription factors were enriched, reasoning that transcription factors could be master regulators of leader cell fate. 30 different shRNAs targeting 10 genes were systematically evaluated for their effects on collective invasion. From this screen, suppression of Hes1, the downstream target of Notch signaling, yielded a marked switch from collective to single cell invasion. Disseminating single tumor cells maintained high expression of K14 in Hes1 knockdown organoids which was phenocopied by gamma-secretase inhibition in a human TNBC PDX model. Because K14+ tumor cells highly express the Notch ligand Jag1, these results support a model in which Notch signaling, specifically through activation of Hes1, dictates leader cell identity and spatial organization during collective invasion. Studies are ongoing investigating the impact of Hes1 dynamics on leader cell adhesion, hybrid EMT state, and preference for single versus collective metastasis. Because Notch suppression induces leader cell dissemination, we propose that Notch targeted therapy should be combined with therapies eradicating leader cells.

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Kevin J. Cheung, M.D.: No financial relationships to disclose

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Histopathological and immune characterization of liver metastases from patients with breast cancer

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Background: Liver metastases (LM) are ultimately present in ~50% of all patients with metastatic breast cancer (BC). Metastatic seeding to the liver relies on the interaction between cancer cells and the host microenvironment, resulting into two main histopathological growth patterns (HGPs): the replacement HGP (metastasis mimics the liver architecture and exploits liver vasculature) and the desmoplastic HGP (presence of a fibrotic rim separating the hepatocytes from the tumor cells). While the prognostic value of these HGPs is established for colorectal cancer, with the desmoplastic HGP being associated with better prognosis, investigation is needed for BC. It has also been reported that patients with LM have a poorer response to immune checkpoints inhibitors. A systematic evaluation of the HGP and LM-associated immune infiltrates (stromal tumor infiltrating lymphocytes, sTIL) is currently lacking. In this study, we aimed at: (i) investigating HGPs and sTIL in LM from patients with BC, and, (ii) evaluating the association of these HGPs and sTIL with standard variables and outcome.

Patients and methods: The study currently includes clinical data and samples from: 1) a retrospective cohort of 122 patients from 7 hospitals with surgically resected LMs (represented by 548 hematoxylin and eosin (H&E)-sections), further referred to as 'surgical cohort' and, 2) LMs from 2 institutional post-mortem tissue donation studies for a total of 23 patients (97 H&E-sections). All available H&E-sections were used to assess HGP and sTIL. HGPs were scored according to a standardized method (PMIDs: 35650276) and categorized per patient as pure-replacement (rHGP, i.e. 100% of the tumor-liver interface is replacement) or any-desmoplastic (dHGP, i.e. at least 1% of the tumor-liver interface is desmoplastic). sTIL are expressed as the percentage of stromal area covered by mononuclear immune cells at the metastasis-liver interface. Associations were assessed using Fisher exact and Wilcoxon tests. Univariable and multivariable Cox regression analyses stratified by center were used to evaluate the role of HGP on progression-free (PFS) and overall survival (OS).

Results: In the surgical cohort, 54 (44%) of patients displayed a rHGP and 68 (56%) a dHGP. Intra-patient, meaning inter-slide, heterogeneity of the HGP was observed in 24/122 (20%) of the patients suggesting that scoring multiple slides is needed for accurate assessment of the HGPs. We did not find any statistically significant association between HGP and clinico-pathological data. Higher sTIL were associated with dHGP ($p=.003$), as well as with a higher

histological grade ($p = .087$), estrogen receptor-positivity ($p = 0.062$) and ductal histology ($p = .08$) of the primary tumor. rHGP was associated with worse PFS and OS, both at the univariable and multivariable level (Table).

In the post-mortem cohort, we observed a higher frequency of rHGP patients (19/23 patients, 83 %) and significantly lower levels of sTIL in the rHGP patients as compared to the rHGP patients from the surgical cohort ($p = .009$).

Conclusion: This study represents the largest study evaluating HGPs and immune infiltrates of LMs from patients with BC. Approximately half of the surgically resected LMs have a dHGP, which is associated with higher sTIL and a better prognosis. The results from the LMs from the post-mortem cohort suggest that a more advanced stage of the disease is associated with an increase in rHGP and with a more immunosuppressed environment.

Table

	PFS (HR : 95% CI; p-value)		OS (HR : 95% CI; p-value)	
	Univariable	Multivariable	Univariable	Multivariable
HGP (rHGP vs dHGP)	3.09 (1.78-5.38); $p < .001$	2.86 (1.58-5.18); $p = .05$	2.53 (1.23-5.18); $p = .01$	2.27 (1.09-4.73); $p = .03$
Menopausal status (pre vs post)	0.90 (0.53-1.52); $p = .69$	1.13 (0.61-2.07); $p = .69$	1.30 (0.61-4.71); $p = .31$	1.60 (0.66-3.90); $p = .30$
Extra Hepatic Met (yes vs no)	2.07 (0.98-4.37); $p = .05$	1.38 (0.57-3.32); $p = .47$	1.69 (0.61-4.70); $p = .31$	1.65 (0.50-5.42); $p = .41$
Time between BC and LM diagnosis (>1year vs ≤1year)	1.26 (0.72-2.22); $p = .41$	1.08 (0.58-2.00); $p = .81$	1.01 (0.05-2.01); $p = .98$	0.90 (0.44-1.85); $p = .78$

Univariable and multivariable analyses

Disclosure(s):

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Genetic ablation of ACF7, a member of the +TIP family of microtubule-binding proteins, impairs metastasis of HER2-positive breast cancer

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Breast cancer is the leading cause of cancer death in women worldwide. Among the different subtypes of this disease, HER2-positive breast cancer is known to be one of the most aggressive and is linked to poor prognosis. This subtype is prone to develop metastases, reflecting a significant cellular plasticity. While the molecular machinery controlling actin dynamics is well implicated in cell invasion, the contribution of the microtubules is ill-defined. We recently conducted a functional screen to identify such regulators, and characterized ACF7, a microtubule plus-end binding protein (+TIP), as a new promoter of invasion. Here, we aim to determine the *in vivo* contribution of ACF7 to tumor progression and to reveal the cellular and molecular mechanisms allowing this +TIP to promote metastasis. We analyzed the expression of ACF7 at the protein level across a panel of tumor microarrays and found that it is detectable in all breast cancer subtypes with the highest levels seen in HER2-positive. To study the role of ACF7 during tumor progression, we generated an ACF7 genetically engineered mouse model of breast cancer. We exploited a HER2-positive breast cancer mouse model (MMTV-NIC) that we bred with ACF7Flox mice. This approach allows for conditional deletion of ACF7 in mammary glands and represents a powerful model to define the roles of ACF7 in HER2-driven breast cancer. Our results show that ACF7 is not involved in tumor initiation and tumor growth as no difference between number of nodules per mouse, tumor mass or number of mammary intraepithelial neoplastic lesions was shown. However, our results show a significant decrease in lung metastasis in the ACF7cKO mice. To gain mechanistic insights into the roles of ACF7 in this specific process, we derived primary cell lines from tumors isolated from MMTV-NIC-ACF7WT and MMTV-NIC-ACF7cKO mice. We explored if ACF7 contributes to migration and invasion in a HER2 context. By using live-cell imaging, we demonstrated that ACF7-null cells display defects in both random and directed cell migration, as they show a delay in wound closure. We determined that ACF7KO cells show an increase in focal adhesions size, and exhibit defects in reorienting their actin and microtubules cytoskeletons parallel to the direction of migration. ACF7 was also found to promote cell invasion since ACF7KO cells were less efficient to cross a Matrigel membrane. To investigate the metastatic potential of ACF7-null tumors, we performed RNA-sequencing using RNA isolated from MMTV-NIC-ACF7WT and MMTV-NIC-ACF7cKO tumors. We identified a striking change in expression of genes involved in epithelial to mesenchymal transition (EMT), such as for example E-cadherin, Vimentin or the transcription factor Twist. These results suggest that ACF7 promotes metastasis through maintaining an EMT state in HER2 breast cancer cells. Collectively, our work demonstrates ACF7 as an important player in HER2 positive breast cancer progression via its functions in both cell migration and cell invasion. This work also suggests that developing approaches to

therapeutically target regulators of microtubule dynamics may reveal new opportunities to decrease tumor progression and metastatic expansion.

Disclosure(s):

Rebecca Cusseddu, n/a: No financial relationships to disclose

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P6-14-08

Epithelial/stromal cross talks that induce malignant transition of human ductal carcinoma in situ.

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Background: A large fraction of human DCIS (>50%) may not need the multimodality treatment options currently offered to all patients. More importantly, while we may be overtreating many, we cannot identify those most at risk for invasion/metastasis. Revealing the cellular and molecular mechanisms by which some DCIS remain indolent while others advance to invasive and metastatic breast cancers is currently a clinical unmet need. Methods: To address this gap, we developed the Mouse-INtraDuctal (MIND) model, by which patient-derived (PDX) DCIS epithelial cells are injected intraductally and allowed to progress naturally in mice. Single cell RNA-sequencing (scRNA-seq) was utilized to profile the DCIS epithelial and stroma cells in progressors vs. non-progressors. To distinguish between stromal (diploid) cells and tumor (aneuploid) cells, we calculated Copy Number Aberration (CNA) profiles from RNA using CopyKAT. Cell-type specific differential gene expression analysis of DCIS epithelial cells and microenvironment cell types in progressors and non-progressors was performed. We also predicted putative ligand:receptor interactions between the tumor cells and cell types in the microenvironment by CellPhoneDB. Results: Among 37 PDX DCIS MIND models followed for a

median of 9 months, 20 (54%) grafted into 95 glands, showed in vivo invasive progression (progressed) while 17 (46%), injected into 107 glands, remained non-invasive (non-progressed). ScRNA-seq was performed on 13 DCIS samples including 10 progressors and 3 non-progressors. Aneuploid cells were further analyzed to identify differentially expressed genes that were upregulated in progressors compared to non-progressors (log₂ fold=1, FDR p< 0.05). . Notable genes included NEAT1, EIF4EBP1, SCGB2A2, TFF1 and TFF3 that were upregulated in the progressors. NEAT1, the core structural component of the paraspeckles, is frequently overexpressed in human cancers and its expression is correlated with worse survival in cancer patients. NEAT1 drives tumor progression by regulating genes involved in cellular growth, migration, invasion, metastasis, EMT, stemness, radio- and chemoresistance, supporting its role as a potential biomarker and therapeutic target. TFF1/TFF3 mRNAs show increased expression in metastatic breast cancers. EIF4EBP1 is located on chrom 8p11-p12 which is frequently amplified in breast cancer and is associated with poor clinical prognosis. Further analysis using Cancer Hallmarks identified mitotic spindle, interferon signaling, DNA repair, oxidative phosphorylation and P53 pathway among the top signatures that were upregulated in the progressors. CellPhoneDB identified expression of several receptor/ligand interactions including CD74/MIF involved in epithelial/stromal and stromal/stromal cross talks that may play a role in DCIS invasive progression. Conclusions: Future studies will validate our findings using patient DCIS samples with known long-term outcome and in vivo MIND models to further refine risk associated biomarkers for invasion/metastasis and to identify more effective treatments.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

P6-14-09

Non-canonical Wnt/Ror2 signaling regulates tumor cell invasion and dissemination in breast cancer through cell-matrix crosstalk

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BACKGROUND: Metastasis is the main cause of mortality for breast cancer patients. The early steps of cancer metastasis require that tumor cells actively invade and disseminate from the primary tumor to distant organs. Cell-extracellular matrix (ECM) interactions represent fundamental interactions during tumor invasion and metastasis, yet how particular signal-transduction factors prompt the conversion of tumor cells into migratory populations capable of systemic dissemination remains elusive. OBJECTIVES: Wnt signaling is a known regulator of cell fate, migration, and polarity during various key biological processes. We previously discovered an inverse correlation between the canonical Wnt signature and a non-canonical Wnt receptor, Ror2, across breast cancers in TCGA. The objective of this study is to investigate how canonical and non-canonical Wnt signaling orchestrate tumor cell behavior during cancer invasion and metastasis. METHODS: We used clinically relevant syngeneic TP53-null Genetically Engineered Mouse Model (GEMM) tumors that molecularly reflect the different breast cancer intrinsic subtypes. In vivo transplantation of GEMM models and in vitro 3D tumor organoids were employed to elucidate the molecular mechanism underlying the migration, invasion, and metastasis of tumor cells upon genetic perturbation of Wnt/Ror2 signaling. RESULTS/DISCUSSION: From 3-dimensional (3D) tumor organoid models, we identified novel transcriptional alterations encompassing cell-cell adhesion, cytoskeletal remodeling, and ECM organization upon Ror2 loss. At protein levels, we discovered a significant increase in collagen fibril organization and integrin- α 5 and integrin- β 3 expression following Ror2 depletion. In addition, the matrisomal protein fibronectin (FN) was concomitantly upregulated and assembled in Ror2-deficient tumor cells at sites of invasion. Consequently, we observed FAK activation

and actin cytoskeleton alterations in Ror2-deficient tumor cells, leading to a promigratory tumor cell behavior. The altered cytoskeleton and cell-ECM interaction enhanced the rigidity of the Ror2-depleted cells. Furthermore, Inhibition of either integrin or FAK activation abrogated the increased invasion driven by Ror2-loss. Unexpectedly, these changes were distinct from processes regulated by Wnt/ β -catenin activation. From both spontaneous metastasis and experimental metastasis models, we discovered a shift from canonical to non-canonical Wnt signaling throughout the progression of lung metastasis, indicating that the balance of Wnt signaling may serve as a switch to dictate cell functions at different stages of metastatic development. Consistently, we found enhanced initial colonization in the lungs when Ror2 is depleted in these breast cancer cells. Together, these studies provide new insight into how canonical and alternative Wnt pathways coordinate cell-cell and cell-ECM exchanges during breast cancer progression and metastasis. Supported by grant NIH-CA016303

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Hongjiang Si, n/a: No financial relationships to disclose

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Jagged-1 promotes breast cancer metastasis through the lymphatic system

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While early detection of breast cancer (BC) has improved prognoses, there is an urgent need to improve outcomes for patients with distant metastatic disease. Higher expression of the Notch ligand JAG1 in primary BC tumors is strongly associated with lymph node metastasis and patient mortality, but causality is unclear. We show that JAG1 expression is higher in patients' metastatic BC cells colonizing lymph nodes than in primary tumors, suggesting that tumor cells with high JAG1 are preferentially able to metastasize to lymph nodes. JAG1 expression is higher in a derivative of BC line MDA-MB-231 selected for tropism to lymph nodes (MDA231-LN) than in the parental line or derivatives with other tropisms. To determine the mechanism(s) of JAG1-mediated metastasis, we generated clonal JAG1 knockout cell lines from MDA231-LN cells with corresponding JAG1 rescue lines. We investigated the role of JAG1 in spontaneous metastasis under clinically relevant conditions by orthotopically implanting JAG1 knockout and expressing cells, resecting the primary tumor, and following long-term metastatic spread in a mouse model. Quantification of tumor cells in blood showed that survival, metastatic burden, and JAG1 expression did not correlate with the number of circulating tumor cells. Conversely, JAG1 expression drove an increase in lymph node and body-wide metastatic burden and a trend toward decreased survival. In this model metastatic cells were abundant throughout lymph vessels, suggesting lymphatics are the primarily route of dissemination. Preliminary transcriptional analysis suggests that JAG1 alters interactions with lymphatic endothelial cells (LEC), potentially via VEGF signaling, leading us to examine downstream events in co-cultures of LEC with lymphatically invasive BC lines. Deciphering tumor-lymphatic endothelial signaling events may open new avenues to target BC metastasis.

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P6-14-11

Exosome-mediated Circ-CRSP1 promotes tumor proliferation and metastasis through stabilizing ELAVL1 protein and suppresses anti-tumor immune response in regulating the progression of Triple-Negative Breast Cancer.

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Background : Triple-negative breast cancer (TNBC) is one of the most malignant subtype of breast cancer. Lacking targetable molecular drivers, chemotherapy is almost the only effective systematic treatment for TNBC. Compared with other types of breast cancer, TNBC shows a higher long-term recurrence rate and worse prognostic outcome, and its main cause of death is tumor metastasis. Therefore, there is an urgent clinical need to explore underlying molecular mechanisms and find novel targets for therapeutic intervention, as well as biomarkers for early clinical diagnosis. **Materials & Methods:** To explore the signal pathways and target molecules related to tumor immunity by bioinformatics analysis of tissue samples [TNBC (n = 55), Her2 (n = 39), Luminal B (n = 30), Luminal A (n = 29), healthy (n = 11)]. Co-culture experiment was conducted to study the effect of TNBC-derived exosome-mediated molecules on the proliferation and migration of breast cancer. qRT-PCR assay was used to confirm the expression level of Circ-CRSP1 in tumor tissues, breast cancer cells, exosomes of breast cancer cells and serum exosomes of breast cancer patients. Overexpression and knockout experiments investigated the role of Circ-CRSP1 in promoting the proliferation and migration of TNBC cells. Protein molecular docking technique was used to predict the possible targeting binding protein ELAVL1, and molecular experiments and nude mice model were used to study the mechanism of Circ-CRSP1-ELAVL1 complex in tumor immunity. **Results:** TNBC-derived exosome-mediated molecular transmission promotes the proliferation and migration of breast cancer, and may promote distant metastasis of breast cancer by changing the tumor microenvironment (TME) before metastasis. Bioinformatics analysis of TNBC tumor samples confirmed that TNBC is strongly associated with tumor immune-related biological processes and signal pathways. Circ-CRSP1 is highly expressed in TNBC tumor tissues, TNBC cells, exosome derived from TNBC cells and serum exosomes of TNBC patients, and is related to the poor clinical prognosis of TNBC patients. Overexpression of Circ-CRSP1 enhanced the proliferation and migration ability of TNBC cells, and the expression levels of EMT and cell-cycle related genes altered. Circ-CRSP1 binds to protein ELAVL1 at the physical level. The target gene of Circ-CRSP1-ELAVL1 complex is involved in the immune response, and the overexpression of Circ-CRSP1 significantly down-regulates the expression level of immune-related genes. **Conclusion:** Exosome-mediated Circ-CRSP1 promotes the transport of ELAVL1 from nucleus to cytoplasm through targeted binding with ELAVL1, and then regulates cytoplasmic proliferation and metastasis and inhibits the stability and translation of anti-tumor immune-related gene mRNA, thus finally promotes the proliferation, invasion and metastasis of TNBC. This study can further understand the mechanism of circRNA in the growth and metastasis of TNBC from the theoretical level, further explore the feasibility of Circ-CRSP1 as a molecular target for gene therapy, and provide theoretical basis and pre-clinical data for Circ-CRSP1 in serum exosomes as a high risk screening index and prognostic marker for TNBC patients.

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Evaluation of changes in sequencing quality and transcriptomic profiles with increasing post-mortem interval: results from an optimization experiment within the UPTIDER tissue donation program

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Background. Postmortem tissue donation programs can importantly enhance sample access for translational research on metastatic disease. However, this post-mortem setting poses logistical and technical challenges in terms of preserving nucleic acid quality and in particular RNA. Here we present the results of an experiment within our breast cancer tissue donation program UPTIDER (NCT04531696), aiming at assessing RNA degradation rates and expression profile changes in function of tissue type and sample-specific postmortem interval (ssPMI). **Patients & Methods.** For 7 patients, bulk RNA sequencing was performed using the Lexogen protocol on fresh frozen samples from healthy or tumour tissues taken repeatedly (at 1.5h time intervals) during the autopsy. ssPMI was defined as the time between the death of the patient and the freezing of the sample. Quality threshold was set at 0.5 million (M) of assigned reads (AR). Other quality metrics included number of expressed genes, evolution of proliferation-, hypoxia-, stromal- and immune-related transcriptional signatures (PMID:18698033, 20087356) with increasing ssPMI. Associations between quality metrics and ssPMI were assessed by linear regressions for longitudinal data, with quality metrics as dependent variable, time as independent variable and accounting for the clustering of the data by patient and organ using the generalized estimating equation method. Three nested models - with constant, linear and non-linear relationship - were compared using ANOVA testing strategy. Non-linearity was rendered by a restrict cubic spline with three knots. All tests were performed by the Wald test on regression coefficients. **Results.** Ninety samples (67 healthy, 23 tumour) were analyzed. Median ssPMI was 7.50 hours (range: 3.07-11.12). Most (87%) samples passed quality thresholds, with median AR being 1.70M (interquartile range: [0.70M-3.57M]). No association was found between quality metrics and time in healthy samples. In tumor samples, regarding sequencing quality, negative associations with increasing time were found for AR and for number of expressed genes with an average decay of 242308 reads per hour (95 confidence interval (95CI): [94415.62-390200.50], p-value=.001) and 251 genes per hour (95CI: [17.30-485], p-value=.035), respectively. At the transcriptomic level, potential subtle changes were observed regarding immune (e.g. STAT1 signature: -0.02, 95CI: [-0.05;0.00]) and hypoxia-related signatures (e.g. PGAM1 signature: -0.03, 95CI [-0.05;-0.01]), while no effect of time was seen for the proliferation and stromal-related signatures. Sample size precluded organ specific analyses. **Conclusion.** A decrease in the number of AR and number of expressed genes with increasing ssPMI was found in tumor samples leading to subtle changes in few transcriptional programs. Healthy samples showed stable quality metrics over time possibly explained by a lower cell activity in healthy as compared to tumour cells. Knowledge derived from this study will be integrated in the upcoming transcriptomic analyses of the samples collected within UPTIDER.

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P6-14-13

Association of baseline tumor-infiltrating lymphocytes and cell-cycle regulation markers on prognosis and mortality in patients with advanced breast cancer according to tumor characteristics and treatment type

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We aimed to analyze the expression of cell-cycle regulation markers – minichromosome maintenance protein 2 (MCM2), Ki-67, Cyclin-A and phosphohistone-H3 (PHH3) and tumor-infiltrating lymphocytes (TILs) in pre-treatment core-biopsy samples of advanced breast carcinomas (ABC) in correlation with known predictive and prognostic factors. Consecutive breast cancer patients (n=398) treated during 2015-2019 were retrospectively analyzed. ABC was defined either as the first indication for locally recurrent, locally advanced or metastatic disease. TIL levels were evaluated of invasive tumor samples, and high expression was defined as TILs >15%. Immunohistochemistry was performed to analyze the expression of MCM2, Ki-67, Cyclin A and PHH3, which were correlated with the following clinicopathological parameters: clinical TNM, tumor grade, biological subtype, TILs, treatment type (chemotherapy-containing or non-chemotherapy). Univariate and multivariate analyses were used to assess factors associated with disease-free survival (DFS) and overall survival (OS). The multivariate analysis showed that patients with higher TIL levels had an improved 3-year DFS compared with those with low TIL levels, (79.5% vs. 63.7%, HR = 0.52, 95% CI = 0.32–0.78, p = 0.005), which may imply using the biomarkers to indicate initial treatment selection at the advanced stage. The effect was the most pronounced for triple-negative breast cancer (TNBC), and higher for HER2+ than hormone receptor positive breast cancer (HR+). Hormone receptor negative tumors showed significantly higher expression of the studied cell-cycle regulation markers Ki-67, MCM2 and Cyclin A compared with HR+ breast cancer, with TNBC showing the highest activity. Ki-67 and MCM2 were significantly associated with worse prognosis in HR+ breast cancer (p = 0.03; p = 0.04). Treatment type (chemotherapy vs. non-chemotherapy) as the initial treatment at the advanced stage influenced the 3-year DFS and OS in patients with high TIL levels in all molecular breast cancer subtypes. For those with low levels of TILs the difference was statistically non-significant. Our study showed that TIL and cell cycle marker testing could help to identify patients with more aggressive tumor types and the requirement of more aggressive treatment upfront. The proposed biomarker testing can help in selecting the appropriate treatment for increased disease-free survival.

Disclosure(s):

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P6-14-14

Advancing research on metastatic breast cancer: the UPTIDER post-mortem tissue donation program

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Background. Research in metastatic breast cancer is hampered by limited sample availability. Post-mortem tissue donation programs can help to overcome this problem but are logistically challenging and have thus far mainly focused on histopathological and genomic research. We here present the UPTIDER program (NCT04531696), aimed at the multilevel characterization of advanced breast cancer and generation of tumour models. Patients and Methods. Patients with stage IV breast cancer receiving their last line(s) of treatment are eligible for participation. Blood, urine and saliva samples are collected upon inclusion. Upon death, a post-mortem MRI (when possible) followed by a rapid autopsy is performed. Liquid biopsies from all body fluids and tissue samples from all macroscopically identified metastatic sites are collected. Samples are processed as mirrored biopsies in different conditions, such as fresh frozen for omics analyses, formalin fixed paraffin-embedded for histopathology, and slowly frozen in freezing medium or fresh for generation of xenograft and organoid models. Results. Since approval by the local Ethical Committee in November 2020, 22 patients have been enrolled and 15 autopsies have been performed. Mean interval between death and start of autopsy was 3h (range 2-6h), mean duration of the autopsies was 6h (4-9h). A post-mortem MRI was performed in 6 patients. Peripheral blood, central blood and bone marrow were collected from all patients; urine, ascites, cerebrospinal, pericardial and pleural fluid all in more than 2/3 of patients. On average, 232 (range 90-406) tissue samples of which 164 (45-303) pathological from 42 (15 – 79) metastases were collected for each patient. Most often sampled metastatic sites were lymph nodes, liver, bones, pleura and peritoneum. Samples from the primary tumour could be retrieved from all patients, either during the autopsy (n=6) or from historical archives. In total, 133 tumour samples were sent to collaborating partners for patient-derived xenograft creation. Already some have been successfully established and stored, including models derived from a patient with invasive lobular carcinoma (ILC) and one with metaplastic squamous cell carcinoma. When correlating microscopic and macroscopic findings, patients could largely be divided into three main categories. Eleven patients presented with overt and extensive disease burden, often characterized by diffuse visceral, pleural, peritoneal, bone and lymph node involvement. Two patients, both with ILC, presented with underestimated yet extensive disease

burden. While gross examination and cross sectioning of organs did not reveal clear involvement, microscopical invasion of stomach and liver, amongst others, was found. Lastly, limited disease burden was seen in two patients, both with leptomeningeal involvement. In those patients, massive tumoral infiltration in the subarachnoid space and along the blood-brain barrier was seen microscopically, with no grey matter invasion. Conclusion. We successfully launched a new and comprehensive post-mortem tissue donation program for patients with metastatic breast cancer, enrolling ~ 1 patient per month. Post-mortem tumour samples already resulted in successful establishment of some patient-derived xenografts. From a clinical point of view, vast underestimation of the disease extent on imaging during life as well as macroscopically during the autopsy was observed in some patients with metastatic ILC. For patients with leptomeningeal metastasis, we showed that the highly aggressive nature of their disease might be explained by extensive meningeal infiltration disrupting the blood-brain barrier. Further insights into disease progression and heterogeneity will be generated by the ongoing multi-omics analyses.

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7:00 AM - 8:15 AM

P6-14-15

PD-L1 expression regulated by JAK/STAT signaling pathway contributes to cell migration and invasion in breast cancer

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Background: Programmed death-ligand 1 (PD-L1) implicated in tumor immune evasion and predictive biomarker in immunotherapy is widely recognized, however, the role of PD-L1 in modulating tumor invasion remains largely unexplored. PD-L1 expression on tumor tissue is usually limited by the invasiveness, tumor heterogeneity as well as insufficient tumor tissue samples, while PD-L1 expression on circulating tumor cells (CTCs) might overcome the limitation. In the present study, we aimed to investigate the role and mechanism of PD-L1 in regulating the migration and invasion of breast cancer cells and to evaluate PD-L1 expression on CTCs in metastatic breast cancer patients. Methods: The expression level of PD-L1 in MCF-7 cells and MDA-MB-231 cells was assessed by quantitative real-time RT-PCR and Western Blot. Gain-of-function and loss-of-function study on cell migration and invasion abilities were carried out by overexpression of PD-L1 or silencing PD-L1. PD-L1 expression on CTCs in thirty-six metastatic breast cancer patients were detected. A novel staining procedure which included fluorescent glucose analog staining for CTC enumeration and immunostaining targeting CD45, vimentin and PD-L1 were analyzed. Survival curves were estimated by the Kaplan-Meier method and the log-rank test was used to compare between groups. All tests were two-sided, and p values were considered significant at the 0.05 level. Results: Compared with MCF-7 cells, PD-L1 mRNA and PD-L1 protein expression were significantly increased in MDA-MB-231 cells. Down-regulation of PD-L1 expression in MDA-MB-231 cells inhibited the migration and invasion of MDA-MB-231 cells, while overexpression of PD-L1 in MCF-7 cells increased the migration and invasion of MCF-7 cells. In addition, we found that PD-L1 expression was regulated by JAK/STAT signaling pathway. PD-L1 expression on CTCs in metastatic breast cancer patients was associated with triple negative breast cancers subtype ($P=0.013$). High expression of PD-L1 on CTCs in metastatic breast cancer patients was correlated to poor overall survival ($HR=3.165$, $95\%CI: 1.121-8.938$, $P=0.029$). Conclusion: Our results indicate that high expression of PD-L1 contributes to cell migration and invasion in breast cancer cell possibly partially through JAK/STAT signaling pathway. The PD-L1 expression on CTCs might serve as a promising non-invasive prognostic biomarker in patients with metastatic breast cancer.

Disclosure(s):

junqing chen, medical oncology: No financial relationships to disclose

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7:00 AM - 8:15 AM

P6-14-16

Claudin-9 and its subcoat anchorage proteins ZO-1 and ZO-3 in breast cancer, the clinical and therapeutic significance

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Introduction. Claudin-9 (CLDN9), a member of the claudin protein family, is thought to play a role in the control of tight junctions (TJ) in various cell types. CLDN9 protein needs intracellular subcoat proteins, primarily the Zonula Occluden (ZO)-1 and ZO-3 to anchor to the cytoskeleton in order to form TJ with other proteins, including occludin. In the body, CLDN9 is highly expressed in endocrine tissues but is relatively low in mammary tissues. The role of CLDN9 is not well understood in cancer. In the present study, we have for the first time examined the pattern of CLDN9 expression at protein and transcript levels in breast cancer and explored its clinical and therapeutic implications. Methods. CLDN9 protein and CLDN9 transcript in fresh frozen human mammary tissues were evaluated by immunohistochemistry and quantitative transcript analyses and, together with the ZO family members and occludin in our database, correlated with clinical indicators. Assessment of expression in a range of cell lines was also determined. The levels of CLDN9 transcript, was also assessed against the therapeutic responses of the patients to chemotherapies by using a dataset from TCGA database. Results. Breast tumour tissues had high levels of CLDN9 transcript in tumours versus normal tissues. However, high grade breast tumours had significantly lower levels than low grade ($p=0.02$ and $p=0.003$, grade-2 and 3 vs grade-1 respectively). Patients with metastasis also had significantly lower levels than those without ($p=0.0075$). Patients who died of breast cancer had higher levels of the transcript than those who survived, although this was not significant. CLDN9 expression was significantly correlated with ZO-1 ($r=0.20$, $p<0.001$) and ZO-3 ($r=0.179$, $p<0.01$), but not ZO-2 in our cohort. There was significant correlation with another key TJ molecule, occludin ($r=0.236$, $p=0.11$). CLDN9, together with ZO-1 and ZO-3 significantly linked to the survival of patients (144 \square 4.6 months for the low expressing group versus 113 \square 8.2 months for the high expression group, $p=0.013$). The expression profile of the CLDN9/ZO1/ZO3 complex also indicated potential as an independent prognostic indicator ($p=0.004$, HR=2.033). The prognostic value was highly applicable to non-triple negative breast cancer patients. CLDN9 transcript also appeared to have a significant impact on treatment responses; patients

who were sensitive to chemotherapies had a significantly lower levels of CLDN9 transcript than those who were resistant to treatment ($p < 0.000001$). In human cell lines, expression levels of CLDN-9 in ER (+) breast cancer cell lines, MDAMB361, MCF7 and BT474 were high; in a ER(-) breast cancer cell line MDAMB231, the expression level of CLDN-9 was lower. Conclusion. In conclusion, CLDN9 expression was differentially expressed in human breast cancer cells lines and appeared to reflect changes in ER status. It was apparent from levels of CLDN9 in a breast cancer cohort that expression was associated with grade and metastatic disease. Of significant notice was the finding that expression of CLDN9 in an expression profile with ZO1 and ZO3 has potential as a prognostic indicator, particularly in non-triple negative patients and in those who are chemotherapy resistant.

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7:00 AM - 8:15 AM

P6-14-17

Endomucins and their expression in breast cancer and the cellular and therapeutic impact

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Introduction. Endomucin-1 and endomucin-2 are two proteins structurally related, yet with low homology. The membrane bound sialoglycoproteins appear to play a key role in interfering with the formation of focal adhesion complexes (FAC) and matrix adhesiveness of cells, by mechanisms independent of the MUC1 repeat, which the endomucins do not possess. Endomucins are thought to be expressed at high levels in endothelium and haematopoietic cell lineages, although the levels in mammary tissues also seem high. Despite the seeming importance of endomucins in the adhesion and migration of cells, including cancer cells, the clinical value of endomucin in clinical cancer, including breast cancer, is largely unknown. The present study examined the expression profile of endomucins, together with the focal adhesion kinase FAK, in breast cancer and aimed to explore the cellular impact of endomucin on cancer cells. Methods. Human breast cancer cells MCF-7 and MDA MB-231 and a range of other cell types were used. An endomucin overexpression cell model was created and subsequently used to evaluate the function of the cells. The expression profile of the endomucin-1 and endomucin-2 transcripts and FAK, in an existing fresh frozen breast cancer tissue cohort, were quantified. Results. High levels of endomucins, particularly endomucin-1, are good indicators for the overall survival of the patient, $p=0.021$ for endomucin-1 and $p=0.15$ for endomucin-2. When expression levels of FAK were integrated into the survival analysis model, patients with high levels of both endomucins and low levels of FAK had the most favourable outcome, compared with those with most unfavourable outcome who had low level of endomucin and high FAK (survival during the follow up period respectively at 100% and 54%, $p=0.013$, Harzoud Ratio 0.298). Together with the Nottingham Prognostic Index, which independently predicts a poor

outcome ($p=0.009$, $HR=7.6$), the integrated expression profile of endomucin/FAK represents an independent prognostic indicator for favourable overall survival ($p=0.003$, $HR=0.13$), and indeed for a favourable disease free survival ($p=0.008$, $HR=0.17$). Mammary tissues, and indeed breast cancer cell lines, expressed high levels of endomucin-2 transcripts and low levels of endomucin-1 transcripts. High levels of endomucin-2 were also seen in fibroblasts and vascular endothelial cells. We created a breast cancer cell submodel with MCF-7, by overexpressing endomucin. It was shown that although endomucin over-expression had some marginal impact on the adhesiveness of breast cancer cells, the over-expression however, had significant impact on cells' sensitivity to FAK inhibitor, with a markedly reduced adhesiveness to matrix ($p < 0.001$ control versus endomucin overexpression cells). Discussion. Endomucins have a reduced expression in breast cancers and the reduction, together with low levels of focal adhesion kinase, facilitate a favourable outcome for the patients. Together with the findings of in vitro cell models, it would suggest that the expression profile of endomucins and FAK may be a good indicator, not only for evaluating clinical outcomes, but also for choice of target therapies.

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7:00 AM - 8:15 AM

P6-14-18

Effect of 3q oncogene SEC62 on migration and proliferation of triple-negative breast cancer cells

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Background Chromosome 3q26 amplifications represent a frequent alteration in various cancer entities including breast cancer. SEC62 – a 3q26 encoded gene – was identified as a potential onco- and tumor-driver gene for the pathogenesis of breast cancer. Although the precise physiological function of the respective protein Sec62 is not completely understood, Sec62 seems to induce an increased stress tolerance, enhanced cell migration and invasive potential in SEC62 overexpressing cells. SEC62 overexpressing breast cancer patients have been shown to have a higher rate of lymph node metastasis and poorer overall prognosis. Hence, we aimed to further evaluate the effect of Sec62 for triple-negative breast cancer by targeting cell migration and proliferation of triple-negative cell lines altered in their SEC62 expression. Objectives The aim of this study was to investigate the role of Sec62 for triple-negative breast

cancer in cell culture using functional analyzes comparing cell migration and cell proliferation in triple-negative cell lines using the effects of siRNA-mediated Sec62 depletion in vitro. **Material& Methods** In this study, three SEC62 gene silencing experiments each with two different siRNAs directed against the SEC62 mRNA were carried out in comparison to a control siRNA in combination with cell proliferation and cell migration tests plus Western blots for the triple-negative breast cancer cell line CAL120 in order to determine the suspected causal relationship between SEC62- overexpression and an increased cell migration and thus an enhanced invasion potential of the cancer cells. The cell proliferation was examined in real time in the 96 well xCELLigence system and the cell migration using Fluoroblock without matrigel using fluorescence microscopy. **Results** In cell migration assays, the median migrated cell number in the control siRNA group was 263 (241-279), the cell number in the groups of the two siRNAs directed against the Sec62 mRNA was 72 (70-149) and 178 (96-276) ($p < 0.01$). In cell proliferation assays, the median cell index in the control siRNA group was 7.5 (7.4-7.6), while it was 7.4 (7.3-7.5) and 7.6 (7.5-7.7) ($p=0.37$). In the first analyzes of the medians of the three gene silencing experiments of the cell line CAL120, the expected negative effect of the SEC62-siRNA on cell migration is confirmed, while, as expected, the effect on cell proliferation remains unchanged with decreasing Sec62 content. **Conclusion** In this in vitro study using cell migration and cell proliferation assays we found a correlation between SEC62 overexpression and increased cell migration. This implies a potential association between Sec62 and an increased tumor cell invasion in triple-negative breast cancer.

Disclosure(s):

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7:00 AM - 8:15 AM

Discussion 1 + Q&A: PD16-01 & PD16-02

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12/9/2022

7:00 AM - 8:15 AM

Discussion 2 + Q&A: PD16-03, PD16-04, PD16-05 & PD16-06

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7:00 AM - 8:15 AM

Discussion 3 + Q&A: PD16-07 & PD16-08

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12/9/2022

7:00 AM - 8:15 AM

Poster Spotlight Discussion 16: Imaging to Diagnose Breast Cancer and Direct Its Treatment: Who, When, and How?

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12/9/2022

7:00 AM - 8:15 AM

PD16-01

PD16-01 Racial Disparities in the Use of Preoperative Breast MRI after Breast Cancer Diagnosis

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Introduction: The use of magnetic resonance imaging (MRI) prior to surgical treatment for breast cancer has greatly increased over the past decade. As MRI more accurately defines disease extent vs mammography and sonography, it is frequently utilized for staging women at elevated risk of occult disease due to young age, dense breast tissue, and/or lobular histology. However, it is not known whether women from different racial backgrounds and socioeconomic statuses have equal access to preoperative breast MRI. The goal of this study was to assess whether the use of preoperative breast MRI varies by race and insurance type.

Methods: We identified adult women who were diagnosed with Stage 0-III breast cancer within our mixed academic/community health system between 2016-2019 and were subsequently treated with surgical resection. We limited our analysis to non-Hispanic Black and non-Hispanic White women, as they comprised 93% of the eligible cohort. Patients who underwent breast MRI between their date of diagnosis and date of surgery were considered to have had a "preoperative MRI." We used multivariable logistic regression to quantify the association between patient factors and receipt of preoperative MRI. Covariates included patient race, insurance type, age, year of diagnosis, clinical stage, histology, breast density, receptor subtype, and receipt of neoadjuvant systemic therapy.

Results: 1,268 women met inclusion criteria and had complete clinical information available for analysis. 362 (29%) were Black, and 906 (71%) were White. 718 (57%) had private insurance, 460 (36%) had Medicare, and 72 (6%) had Medicaid. Compared to White patients, a larger proportion of Black patients had Medicaid (15% vs. 2.0%), fatty or scattered density (i.e., level 1 or 2) breasts (69% vs 48%), and regional disease (26% vs 19%) (Table). Patients with Medicare had the highest proportion of fatty or scattered density breasts (67% vs private=46% vs Medicaid=56%), while patients with Medicaid had the highest proportion of regional disease

(35% vs private=23% vs Medicare=15%).

The proportion of patients who received preoperative MRI was higher for White (49%) vs Black women (37%, $p < 0.001$). After adjustment, Black patients were 52% less likely to undergo preoperative MRI compared to White patients (OR 0.48, 95% CI 0.35-0.66, $p < 0.001$). Compared to privately-insured patients, patients with Medicare had a similar likelihood of undergoing preoperative MRI (OR 0.81, 95% CI 0.54-1.22, $p = 0.309$), while patients with Medicaid may have had a lower likelihood of undergoing preoperative MRI (OR 0.55, 95% CI 0.30-1.00, $p = 0.053$).

Conclusions: Black patients with newly diagnosed breast cancer were less likely than White patients to undergo preoperative breast MRI, a disparity that persisted after controlling for insurance and clinical factors. Algorithmic use of preoperative MRI may mitigate provider- and system-level biases and promote more equitable resource utilization.

Characteristics of patients with non-metastatic breast cancer, diagnosed and treated at our institution (2016-2019)

Table. Characteristics of patients with non-metastatic breast cancer, diagnosed and treated at our institution (2016-2019).

	Black (n=362) n (%)	White (n=906) n (%)	All (n=1,268) n (%)	p-value
Mean age (SD)	61.2 (12.8)	60.9 (12.9)	61.0 (12.9)	0.756
Insurance				
Private	182 (50)	536 (59)	718 (57)	<0.001
Medicare	119 (33)	341 (38)	460 (36)	
Medicaid	54 (15)	18 (2)	72 (6)	
Other	7 (2)	11 (1)	18 (1)	
Histology				
Invasive ductal	211 (58)	504 (56)	715 (56)	0.389
Invasive lobular	73 (20)	235 (26)	308 (24)	
DCIS	57 (16)	111 (12)	168 (13)	
Other	21 (6)	56 (6)	77 (6)	
Receptor Status				
HR+, Her2-	95 (26)	277 (31)	372 (29)	0.006
Her2+	30 (8)	50 (6)	80 (6)	
HR-, Her2-	30 (8)	31 (3)	61 (5)	
Missing*	207 (57)	548 (61)	755 (60)	
Clinical Stage				
0	104 (29)	220 (24)	324 (26)	0.004
I	164 (45)	518 (57)	682 (54)	
II	72 (20)	143 (16)	215 (17)	
III	22 (6)	25 (3)	47 (4)	
Breast Density				
1 – fatty (least)	24 (7)	42 (5)	66 (5)	<0.001
2 – scattered	224 (62)	383 (43)	617 (49)	
3 – heterogeneous	101 (28)	394 (44)	496 (39)	
4 – extremely (most)	13 (4)	77 (9)	90 (7)	
Neoadjuvant Systemic Therapy				
Yes	46 (13)	87 (10)	113 (11)	0.265
No	316 (87)	819 (90)	1135 (90)	
Preoperative MRI				
Yes	133 (37)	445 (49)	578 (46)	<0.001
No	229 (63)	462 (51)	690 (54)	
Surgery				
Lumpectomy	255 (70)	552 (61)	807 (64)	0.006
Mastectomy	107 (30)	354 (39)	461 (36)	

*Biomarker data for 2019 cohort is pending.

*Biomarker data for 2019 cohort is pending

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Connor B. Grady, MPH: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

PD16-02

Factors Associated with Receipt of Digital Breast Tomosynthesis Among Racially/Ethnically Diverse Women Undergoing Screening Mammography

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Introduction: Digital breast tomosynthesis (DBT) is increasingly utilized in breast cancer screening, including among women at high risk for breast cancer. While there is a lack of rigorous data from randomized controlled trials demonstrating superior efficacy compared to two-dimensional (2D) digital mammography, observational studies suggest that DBT might have lower rates of false-positive results and increased detection of invasive cancer than 2D mammography. However, uptake of DBT might be lower among racial/ethnic minorities, which could contribute to breast cancer disparities. We evaluated whether sociodemographic and breast cancer risk factors were associated with receipt of DBT vs. 2D mammography among a racially/ethnically diverse population of women undergoing screening mammography.

Methods: We conducted a respective cohort study among women, age 40-74 years, who underwent screening mammography at Columbia University Irving Medical Center (CUIMC) in New York, NY, from February 2020 to January 2022. We extracted data from the electronic health record (EHR) on age, race/ethnicity, first-degree family history of breast cancer (yes/no), prior breast biopsies (yes/no), and mammographic breast density (high vs. low), and calculated individual 5-year risks of invasive breast cancer according to the Breast Cancer Surveillance Consortium (BCSC) model. High risk was defined as a 5-year invasive breast cancer risk $\geq 1.67\%$. Our primary outcome was receipt of at least one DBT screening examination from 2020-2022 (yes/no). We conducted multivariable logistic regression analyses to assess the association between demographic/clinical factors and receipt of DBT.

Results: Among 5617 evaluable women, mean age was 55.4 years (SD, 9.5 years) and 56%

identified as non-Hispanic White, 10% as non-Hispanic Black, 17% as Hispanic, 8% as Asian, and 9% other/unknown. Over 60% of women had high breast density, and 34% met high-risk criteria. Seventy percent of women had at least one DBT from 2020-2022. In multivariable analyses (Table 1), women with high vs. low breast density were 2.5 times more likely to receive DBT (odds ratio [OR]=2.51, 95% confidence interval [CI]=2.19-2.88), while first-degree family history of breast cancer, prior breast biopsy, and age were inversely associated with DBT. Racial/ethnic minorities were less than half as likely to undergo DBT compared to non-Hispanic Whites; for example, Hispanic women were over 85% less likely to receive DBT (OR=0.14, 95% CI=0.11-0.16). Overall, there was no association between breast cancer risk status (high vs. low/average) and receipt of DBT (OR=1.00, 95% CI 0.92-1.08).

Conclusion: We observed that the majority of women undergoing screening mammography at CUIMC from 2020-2022 received DBT for breast cancer screening. However, racial/ethnic minorities, including non-Hispanic Blacks and Hispanics, were significantly less likely than non-Hispanic Whites to have received DBT. Breast cancer risk according the BCSC model was also not associated with receipt of DBT. Future studies should determine which subsets of women are more likely to benefit from DBT.

Table 1

Characteristic	OR	95% CI	p-value
Age, years			
40-49		<i>Reference</i>	
50-59	0.86	0.73, 1.02	0.079
60-69	0.80	0.67, 0.95	0.012
70-74	0.54	0.43, 0.69	<0.001
Race/Ethnicity			
Non-Hispanic White		<i>Reference</i>	
Non-Hispanic Black	0.42	0.34, 0.51	<0.001
Hispanic	0.14	0.11, 0.16	<0.001
Asian	0.45	0.35, 0.58	<0.001
Unknown	0.17	0.14, 0.21	<0.001
First-degree Family History of Breast Cancer			
No		<i>Reference</i>	
Yes	0.67	0.51, 0.87	0.003
Mammographic Density			
Low/Average		<i>Reference</i>	
High	2.51	2.19, 2.88	<0.001
Prior Breast Biopsy			
No		<i>Reference</i>	
Yes	0.49	0.41, 0.58	<0.001

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7:00 AM - 8:15 AM

PD16-03

PD16-03 Use of post-neoadjuvant chemotherapy image-guided breast vacuum assisted biopsy to predict residual cancer in exceptional responders: A prospective cohort study

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Background: Post-neoadjuvant chemotherapy (NAC) image-guided biopsy of the residual imaging abnormality / tumor bed is increasingly used to assess residual disease in the breast and potentially identify exceptional responders who may not require surgical intervention. Previous studies have shown variable results on the diagnostic performance of this technique. The aim of this analysis was to assess the accuracy of post-NAC, image-guided vacuum assisted biopsy (VAB) to predict residual disease in the breast using a standardized assessment protocol. The findings could help further support the optimal design of trials omitting surgery in selected patients. Methods: Prospective cohort study (BR154b) of consecutive patients with HER2 positive and triple negative (TN) invasive ductal carcinoma (IDC), treated with NAC, who underwent post-NAC VAB to aid surgical planning between 02/2018 and 06/2022 at one institution. Patients with complete / near complete imaging response (residual imaging abnormality \leq 2cm) had a VAB to sample \geq 90% of the breast residuum / tumor bed previously marked by clip insertion. Biopsy samples were defined as representative if pathology features suggestive of tumor bed or residual cancer were identified. Pathologic complete response (pCR) was defined as no residual invasive or in situ disease in

the breast (ypT0). Diagnostic accuracy of VAB was calculated using final surgical pathology as the reference standard. Simple descriptive statistics were used. Results: A total of 54 women met the eligibility criteria and underwent post-NAC VAB. This was not representative in 3 cases and therefore 51 women were included in the analysis. Median age was 49 years [interquartile range (IQR): 43 – 61]. The majority of cancers were grade 3 (n=31) or grade 2 (n=19). Subtype distribution was 21 (41.2%) for hormone receptor (HR) positive / HER2 positive, 13 (25.5%) for HR negative / HER2 positive and 17 (33.3%) for TN IDC. There was associated DCIS at diagnosis in 37.3% of cases. The majority of the cancers at presentation were T2 (n=35, 68.6%) with a median tumor size on imaging of 28 mm (IQR: 28 – 43). There were associated microcalcifications in 29 cases (n=11 extending beyond the main tumor). Sixteen women presented with cN+ disease. On completion of NAC, 19 women had complete imaging response, while in the remaining the median size of the residual imaging abnormality was 12 mm (IQR: 9 – 16). A post-NAC VAB was performed with ultrasound or stereo-guidance in 48 and 3 cases respectively. The median size (gauge) of needle used was 10 (IQR: 10) and the median number of cores obtained was 8 (IQR: 6-8). In the surgical specimen, the overall breast pCR rate was 58.8% (52.4% for HR positive / HER2 positive, 76.9% for HR negative / HER2 positive and 52.9% for TN). The axillary pCR rate was 81.25%. The false negative rate (FNR) of post-NAC VAB was 4.76% (1/51, 95% CI: 0.12 – 23.82%). The sensitivity and specificity for residual disease were 95.24% (95% CI: 76.18 – 99.88) and 93.33% (95% CI: 77.93 – 99.18) respectively. The negative predictive value was 96.55% (95% CI 80.49 – 99.48) and the overall accuracy 94.12% (95% CI: 83.76 – 98.77). Conclusions: This analysis suggests that a standardized assessment protocol using image-guided VAB in patients with HER2 positive or TN IDC and exceptional response to NAC (residual imaging abnormality / tumor bed measuring ≤ 2 cm) aiming to sample $\geq 90\%$ of the breast residuum allows reliable prediction of residual disease and breast pCR with a FNR $< 5\%$. These results further support the optimal design of de-escalation trials in NAC exceptional responders testing the safety of omitting surgery.

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PD16-04

PD16-04 To monitor or not to monitor? MRI monitoring of neoadjuvant chemotherapy effect and its benefit on breast cancer patients' pathological complete response rate

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Introduction: Neoadjuvant chemotherapy (NACT) represents an essential tool for the treatment of selected breast cancer patients aimed to reduce the tumor size for a more conservative resection and to gain early information about the sensitivity to applied treatment. An effective early response assessment helps both to change the therapeutic strategy for patients nonresponding to the treatment used and to avoid the toxicity related to ineffective treatment. We assumed that changing the chemotherapy regimen might avoid the residual cancer burden (RCB) III outcome and lead to the highest possible rate of pathological complete response (pCR) achieved. We examined the benefit of MRI as a preferred method for interim response assessment to NACT with a primary focus on the relation between the pattern of responses to NACT within the MRI- monitored and non-monitored patients and the pattern of final outcomes on the RCB scale. Methods We present a real-life data-based retrospective analysis of 124 female patients with locally advanced breast carcinoma. All patients received NACT (anthracycline-based regimen followed by taxane-based regimen / early switch to taxanes after the 2nd cycle in nonresponders, and antiHER2 therapy if indicated) prior to surgery (mastectomy/breast-conserving surgery, sentinel lymph node biopsy/axillary dissection). Postoperative histopathological analysis of tumor specimens categorised 120 patients according to the RCB scale 0 – III. Four patients had surgery ex muros and were lost to follow-up. Patients were divided into two cohorts. Group A covered monitored patients with pre-treatment MRI and follow-up MRI after the 2nd cycle of NACT. If no response was detected, another follow-up MRI was indicated after the 2nd cycle of a new treatment. Group B comprised patients with no /incomplete MRI monitoring and patients without the change of therapy even though no response was detected by MRI after the 2nd cycle of NACT. Association between categorical variables was tested using chi-square tests. Statistical analysis was performed using StatsDirect® 3.3.5 (StatsDirect Ltd., Cheshire, UK). The data analysis was supported by a grant from the Cultural and Educational Grant Agency of the Ministry of Education, Science, Research, and Sport of the Slovak Republic (KEGA 041UK-4/2020). Results MRI-monitored patients had two times the odds of being RCB 0 (OR = 2.02, P = 0.122) and almost three times the odds of being RCB 0 or RCB I (OR = 2.83, P = 0.0206) than patients with no monitoring. Changing the NACT after the 2nd cycle in the cohort of monitored patients with no response to initial therapy was significantly associated with better outcomes on the RCB scale (P = 0.0042). This result was confirmed by comparing the pattern of results in patients with no response

within the group of incompletely monitored patients with known MRI results after the 2nd cycle ($P = 0.0257$). Changing the ineffective NACT after the 2nd cycle significantly increased the proportion of RCB 0-I by 23.4%, confirming the benefit of response monitoring by MRI. Conclusion Breast cancer constitutes a heterogeneity of tumor subtypes and it is acknowledged that their behaviour during NACT is highly variable and often unpredictable. MRI represents an effective tool for the assessment of tumor response to applied NACT. To achieve the most clinically meaningful impact of the selected treatment it is critical to monitor the tumor response within the first 3 cycles. Our data clearly confirmed that clinical decisions related to the detection of early response or no response (resulting in the change of NACT) lead to better treatment outcomes and less toxicity. The rate of pCR defines the applied treatment efficacy. Every single patient with results different from RCB III has a better prognosis, reduced need for further expensive treatment and also a more favourable quality of life. These key facts need to be carefully considered when discussing the cost and benefits of MRI monitoring.

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PD16-05

PD16-05 Systemic staging in breast cancer patients receiving neoadjuvant chemotherapy

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Introduction

Per NCCN guidelines, patients with stage I-III breast cancer should only have staging work up with CT chest, abdomen, and pelvis and bone scan if there are concerning symptoms, lab abnormalities, or physical exam findings. These patients do not require staging imaging because previous studies have documented the low incidence of metastatic disease found on systemic imaging, and the use of routine staging imaging has been shown to have a high false positive rate resulting in additional imaging and further work up with a low true positive rate. Despite the NCCN guidelines, extensive imaging is often performed prior to embarking on neoadjuvant therapy to look for evidence of metastatic spread of disease prior to surgery regardless of clinical stage and lack of symptoms.

Methods

We performed a retrospective analysis of patients at the University of Virginia diagnosed with invasive breast cancer who were recommended for neoadjuvant therapy and underwent systemic imaging to assess for the presence of distant metastatic breast cancer between 2012 and 2019. All receptor subtypes were included. Patients with signs/symptoms of metastatic disease at time of initial consultation were excluded. We evaluated the rate of metastatic breast cancer detected on systemic imaging. We also evaluated the rate of incidental findings on systemic imaging and how often this resulted in additional imaging or biopsy.

Results

328 patients met inclusion criteria and were recommended for neoadjuvant chemotherapy and underwent systemic staging. Of these, 8 patients had bilateral breast cancer at time of diagnosis. Included patients were 54.2% hormone receptor (HR) positive, 35.4% triple negative, and 23.2% HER2 positive; 74.1% were node positive (Table 1). Metastatic breast cancer was

identified in 9.1% (30 patients), which included 19 HR positive, 8 HER2 positive, and 7 triple negative patients. Of the patients found to have metastatic breast cancer, 80% had anatomic stage III disease at presentation and 93.3% were node positive. Two metastatic patients that were node negative had a cT2 or cT3 primary tumor. Systemic imaging identified incidental findings in 72.6% (238) patients. Most common incidental findings were pulmonary nodules (107), bone lesion or abnormality (71), hepatic lesions (55), and gynecologic lesions (50). Of the patients with incidental findings, 40.7% (98) underwent additional imaging for further work up or monitoring and 12.2% (29) underwent a biopsy or procedure for further work up. These biopsies identified benign or non-diagnostic results in 20 cases (69.0%) and identified an alternative malignancy in 9 cases (31%).

Conclusions

Within this study, asymptomatic metastatic disease was most commonly found in node positive stage III breast cancer, but was never or rarely found in stage I or II breast cancer patients. This validates NCCN recommendations that asymptomatic anatomic stage I or II breast cancer patients do not benefit from systemic staging. Yet, we did find a relatively high proportion of metastatic disease in asymptomatic patients with stage III breast cancer, indicating that systemic staging may be appropriate for this population. This must be balanced against the high probability of incidental findings with frequent additional imaging or biopsy, which has implications for patient anxiety, potential harm, and cost.

Table 1 Patient Characteristics

Table 1 Patient Characteristics		
	All Patients n = 328	Metastatic Breast Cancer Patients n = 30
	% (n)	% (n)
Bilateral Breast Cancer	2.4 % (8)	0
Age, mean (SD)	52.8 (12.9)	55.3 (12.8)
Histology		
IDC	84.8% (285)	70.0% (21)
ILC	6.5% (22)	13.3% (4)
Mixed Ductal/Lobular	6.0% (20)	13.3% (4)
Other	2.7% (9)	3.3% (1)
Receptor Status		
HR+	54.2% (182)	63.3% (19)
HER2+	23.2% (78)	26.7% (8)
TNBC	35.4% (119)	23.3% (7)
Grade		
1	7.1% (24)	10.0% (3)
2	42.3% (142)	50.0% (15)
3	50.6% (170)	40.0% (12)
Anatomic Stage Prior to Systemic Imaging		
1	4.8% (16)	0
2	56.3% (189)	20.0% (6)
3	39.0% (131)	80.0% (24)
T Stage		
cT1	15.8% (53)	0
cT2	49.4% (166)	30% (9)
cT3	23.8% (80)	40% (12)
cT4	10.1% (34)	30% (9)
N Stage		
Node positive	74.1% (249)	93.3% (28)

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7:00 AM - 8:15 AM

PD16-06

PD16-06 Early MRI and PET biomarkers for hormone receptor-positive/HER2-negative early-stage breast cancer in the setting of neoadjuvant endocrine therapy and neoadjuvant chemotherapy in the I-SPY 2 TRIAL

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Purpose

Neoadjuvant endocrine therapy (NET) is increasingly used for patients with hormone receptor-positive (HR+) breast cancer. Dynamic contrast-enhanced breast MRI is the most accurate modality to monitor tumor response during neoadjuvant chemotherapy (NAC)¹, but there is limited research on response to NET.

The Endocrine Optimization Protocol (EOP) is a sub-study of the ongoing I-SPY 2 TRIAL testing amcenestrant (an oral selective estrogen receptor degrader [SERD]), with or without addition of abemaciclib (a CDK4/6 inhibitor) or letrozole (an aromatase inhibitor) in patients with stage 2/3, MammaPrint (MP) low-risk (index 0 to 1) or high-risk 1 (index -0.57 to 0), HR+/HER2-negative breast cancer. All I-SPY2 (including EOP) patients undergo MRI at baseline (T0), 3 weeks (T1), 12 weeks (T2), and 6 months, prior to surgery (T3). Functional tumor volume (FTV)^{2,3} is derived as a quantitative measure of tumor burden from each MRI. A subset of EOP patients also have 3 dedicated breast PET (dbPET) exams with ¹⁸F-fluoroestradiol (an estrogen receptor-targeted tracer, FES) at T0, T1, and T3. FES uptake on dbPET indicates the presence of functional estrogen receptor.

This study evaluates changes in FTV and FES uptake in patients receiving NET in the ongoing EOP trial. FTV changes in EOP were compared with those in a cohort of patients who received NAC in I-SPY 2.

Methods

The breast MRI and FES-dbPET images from patients in the EOP trial as of June 2022 were evaluated by a blinded central radiology team at a single institution. FTV was measured using standard procedure in I-SPY 2. Percent FTV change (Δ FTV) at T_n (n = 1, 2, or 3) was calculated by $100 \times (\text{FTV}_{Tn} - \text{FTV}_{T0}) / \text{FTV}_{T0}$. FES uptake was quantified as standardized uptake value (SUV). Maximum SUV over the tumor volume (SUV_{max}) was measured using Osirix MD (Pixmeo SARL) and percent change (Δ SUV_{max}) was similarly defined. For comparison, FTV

was evaluated using curated imaging data of I-SPY 2 patients with stage 2/3, MP high-risk 1, HR+/HER2-negative cancer who completed standard NAC between 2010–2016.

Results

We included 55 EOP patients (NET cohort) and 68 I-SPY 2 patients (NAC cohort). At T0, median FTV was 9.8cc for the NET cohort and 10.1cc for the NAC cohort. Table 1 shows the longitudinal FTV change in the two cohorts. At T1, median FTV change was similar in the NET cohort (-33.8%) and NAC cohort (-33.9%). The NET cohort showed a dynamic range of FTV change from -65.4% (1st quartile) to -11.0% (3rd quartile), which covered the 1st to 3rd quartile ranges for the NAC cohort. At T2 and T3, FTV change was more gradual in the NET cohort compared to the NAC cohort.

Seven patients in the NET cohort underwent FES-dbPET. At T0, tumor FES uptake exceeded background uptake in all 7 patients with a median SUVmax of 8.2. At T1 and T3, tumor uptake decreased in all patients. Tumor uptake was indistinguishable from background for 3 patients (43%) at T1 and 5 patients (71%) at T3, despite evidence of residual tumor on MRI. The median change of SUVmax was -45.9% at T1 and -74.7% for T3 (Table 2).

Discussion

After 3 weeks of NET, we observed a large dynamic range of FTV change similar to that seen in NAC and a robust decrease in FES uptake. These results suggest the potential for combined use of early MRI change and FES-dbPET to provide scalable biomarkers to stratify response-based NET strategies.

Reference

1. Radiology 285: 358–375, 2017
2. Radiology 263:663–672, 2012
3. Radiology 279:44–55, 2016

Table 1: Longitudinal change of FTV (ΔFTV) in NET cohort and NAC cohort

Imaging marker	Time point	NET cohort		NAC cohort	
		No. of patients	Median [1st, 3rd quartiles]	No. of patients	Median [1st, 3rd quartiles]
ΔFTV _{T1}	T1	55	-33.8% [-65.4, -11.0]	68	-33.9% [-59.6, -11.2]
ΔFTV _{T2}	T2	42	-64.4% [-81.0, -45.3]	63	-83.8% [-95.0, -60.8]
ΔFTV _{T3}	T3	18	-66.0% [-83.6, -50.0]	64	-93.5% [-98.1, -82.4]

Table 2: Longitudinal change of SUV_{max} (ΔSUV_{max}) in NET cohort

Imaging marker	Time point	NET cohort	
		No. of patients	Median [1 st and 3 rd quartiles]
ΔSUV _{maxT1}	T1	7	-45.9% [-53.7, -43.0]
ΔSUV _{maxT3}	T3	7	-74.7% [-77.8, -64.2]

Disclosure(s):

Natsuko Onishi, MD, PhD: No financial relationships to disclose

Ella F. Jones, PhD: No financial relationships to disclose

Julia Carmona-Bozo, MD, PhD: No financial relationships to disclose

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Bonnie N. Joe, MD, PhD: Kheiron Medical Technology: research support to an institution outside the submitted work (Ongoing); UpToDate: Royalty (Ongoing)

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12/9/2022

7:00 AM - 8:15 AM

PD16-07

PD16-07 Association of MRI morphologic phenotype from unsupervised learning with breast cancer subtypes and treatment response

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Background

Breast cancer is a heterogeneous disease and can be categorized into clinically or biologically meaningful subtypes. Predictive models built by MRI biomarkers performed better when they are optimized by breast cancer subtype than models optimized in the full cohort [1]. Functional tumor volume (FTV) measured from breast MRI has been used to assess tumor response to neoadjuvant therapy longitudinally in the I-SPY 2 TRIAL. Tumors show distinct morphological patterns, or phenotypes, on MRI. Previous studies demonstrated that either qualitative or quantitative measurements characterizing these phenotypes may provide additional information about treatment response [2,3]. In this study, we investigated if MRI morphologic phenotypes defined by unsupervised clustering is associated with breast cancer subtype and pathologic complete response (pCR) after neoadjuvant chemotherapy (NAC).

Methods

A cohort of 990 patients enrolled in the I-SPY 2 TRIAL were included in this retrospective analysis. Patients were randomized to one of nine experimental drug arms or standard NAC, and pCR was assessed at surgery. DCE-MRI data acquired at pretreatment (T0) and early

treatment (T1) were analyzed. Four subtypes of breast cancer were defined by immunohistochemistry (IHC) based on hormone receptor (HR) and HER2 status.

Radiomic features were extracted by PyRadiomics [4] using FTV masks from DCE-MRI. MRI morphologic phenotypes were determined based on unsupervised hierarchical clustering approach on extracted radiomic shape features plus FTV using Pearson correlation with agglomerative ward linkage. The associations between the unsupervised clusters of radiomic features and FTV with four IHC subtypes and pCR were evaluated using χ^2 test of independence. Cramer's V [5] were computed to measure the strength of association (higher Cramer's V means stronger association). P-value < 0.05 was considered statistically significant.

Results

Three clusters were generated by unsupervised hierarchical clustering in a population of 910 patients included in our analysis (80 patients excluded due to missing pCR or DCE-MRIs). At T0, the unsupervised clusters showed statistically significant but weak association with pCR (Cramer's V = 0.088, $p = 0.029$), but the association between the clusters and HR/HER2 subtypes did not reach significance (Cramer's V = 0.055, $p = 0.48$). The unsupervised clusters based on T1 shape radiomic features showed statistically significant association with both pCR and HR/HER2 subtypes ($p < 0.001$ for both) with Cramer's V of 0.231 and 0.154, respectively. Our results showed stronger association between pCR and cancer subtypes with MRI shape radiomic features at T1 than at T0.

Various pCR rates were observed in MRI clusters at T1. They were 56%, 36%, and 23% in Cluster 1, 2, 3, respectively. Table 1 shows pCR rates by HR/HER2 subtype in each cluster. In all sub-cohorts, pCR rate was highest in Cluster 1 and lowest in Cluster 3. In HR+/HER2-, the pCR rate in Cluster 1 was 2-fold of the pCR rates in Clusters 2 and 3-fold of Cluster 3. pCR rate was statistically significantly different depending on the MRI clusters in the sub-cohorts except for the HR/HER2+ sub-cohort: HR+/HER2-, $p < 0.001$; HR+/HER2+, $p = 0.021$; HR-/HER2+, $p = 0.083$; HR-/HER2-, $p < 0.001$.

Conclusion

MRI phenotype generated by unsupervised clustering using radiomic shape features at both pretreatment and early-treatment time points was associated with pCR outcome. Stronger association was observed at early-treatment time point. The association differed by subtype, with the strongest observed in HR+/HER2- and triple negative subtypes. Our results suggest that radiomic shape features derived from DCE-MRI may be helpful for early prediction of tumor response to NAC.

Citations

1. npj Breast Cancer 6, (2020).
2. Tomography 6, (2020).
3. Annals of Surgical Oncology 20, 3823–3830 (2013).
4. Cancer Research 77, e104–e107 (2017).
5. Korean Stat Soc 42, 323–328 (2013).

Table 1. pCR rate by HR/HER2 subtype in each MRI cluster at T1

Cohort	MRI Cluster 1 (n = 146)	MRI Cluster 2 (n = 442)	MRI Cluster 3 (n = 322)	p-value (χ^2 test)
HR+/HER2- (n= 358)	38% (18/47)	17% (31/182)	12% (16/129)	< 0.001
HR+/HER2+ (n = 147)	55% (21/38)	39% (30/78)	23% (7/31)	0.021
HR-/HER2+ (n = 75)	76% (16/21)	71% (27/38)	44% (7/16)	0.083
HR-/HER2- (n = 330)	68% (27/40)	49% (70/144)	31% (45/146)	< 0.001

Disclosure(s):

Nu N. Le, n/a: No financial relationships to disclose

Natsuko Onishi, MD, PhD: No financial relationships to disclose

David C. Newitt, PhD: Kheiron Medical Technology: research support to an institution outside the submitted work (Ongoing)

Jessica E. Gibbs, BA: No financial relationships to disclose

Lisa J. Wilmes, PhD: No financial relationships to disclose

Efstathios Gennatas, n/a: No financial relationships to disclose

Barbara LeStage, n/a: Abbott Laboratories: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); AbbVie Inc: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Johnson & Johnson: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); Teleflex: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing)

Laura J. Esserman, M.D., M.B.A.: Blue Cross/Blue Shield: Consulting Fees (e.g., advisory boards) (Ongoing); Merck: Contracted Research (Ongoing)

Nola M. Hylton, PhD: GE Healthcare: research support to an institution outside the submitted work (Ongoing)

Wen Li, PhD: No financial relationships to disclose

12/9/2022

7:00 AM - 8:15 AM

PD16-08

PD16-08 Title: Characterizing Changes in Tumor Heterogeneity via Radiomic Phenotyping for Predicting Response to Neoadjuvant Chemotherapy for Locally Advanced Breast Cancer: Preliminary Results from the ACRIN 6698/I-SPY 2 trial

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Purpose: To predict pathologic complete response (pCR) in breast cancer patients undergoing neoadjuvant chemotherapy (NAC), from baseline and early-treatment DCE-MRI scans, in the context of the ACRIN 6698/I-SPY 2 BMMR2 challenge.

Materials and Methods: The BMMR2 dataset consists of 191 patients undergoing NAC for locally advanced breast cancer as part of the ACRIN 6698/I-SPY 2 trial. DCE-MRI was obtained at time points T0 (pre-NAC), T1 (3 weeks), and T2 (12 weeks). The BMMR2 challenge provided the MRI scans, tumor annotations, and limited clinical and demographic information. The data were split 60/40; using the 60% training data, the task was to develop models to predict pCR; the competition was for best area under the curve (AUC) when applied to the 40% unseen test data.

Using the publicly available CaPTk software we calculated 3 types of radiomic features within the segmented tumor volume: 1) texture of the signal enhancement ratio (SER) kinetic map of T0 images; 2) texture of the difference between the T1 kinetic maps (PE, WIS, WOS, and SER) and corresponding T0 maps; 3) texture of the difference between the T1 kinetic maps and the corresponding T0 maps, with T1 scans deformably registered to T0 scans. ComBat harmonization was applied to the extracted features to account for MRI acquisition differences. We computed the tumor longest diameter, functional tumor volume (FTV), and clinical tumor size each at T0 and T1.

We modeled pCR via logistic regression. Using the training data alone, with the criteria of performance in univariable modeling and low collinearity, we selected radiomic features and clinical, demographic, and size covariates. We then performed PCA on the combined set of selected radiomic features and size covariates. We evaluated multivariable models including the selected clinical covariates in combination with the first few PCs via cross-validated AUC (5-fold, 200 repetitions) on the training data. The best models were submitted for independent evaluation on the unseen test data of the BMMR2 challenge.

Results: Of the available clinical covariates, only hormone receptor (HR) \pm and human epidermal growth factor receptor 2 (HER2) \pm had any association with pCR. We retained these in all models, and performed PCA on the set combining the best-performing features and the size variables FTV at T0, FTV at T1, and longest diameter at T1. Models based on the first few PCs, HR, and HER2, had training AUCs in 0.78–0.81. Our best-performing model had an AUC on test data of 0.84, using the covariates PCs 1–5, HR, and HER2 (Table 1).

Conclusions: Our preliminary results suggest that radiomic phenotyping of changes in tumor heterogeneity can accurately predict pCR early in the course of NAC. Future analysis with larger samples from ISPY-2 could also examine the effect of different therapies, including targeted therapy and immunotherapy.

Table 1: Performance of candidate logistic regression models on training and test data.

predictors	AUC* on training data	AUC on testing data
PC1, HR±, HER2±	0.8108	0.8210
PC1, PC2, HR±, HER2±	0.8032	0.8218
PC1, PC2, PC3, HR±, HER2±	0.8034	0.8176
PC1, PC2, PC3, PC4, HR±, HER2±	0.7938	0.8269
PC1, PC2, PC3, PC4, PC5, HR±, HER2±	0.7787	0.8397†
PC1, PC2, PC3, PC4, PC5, PC6, HR±, HER2±	0.7777	0.8338
FTV ₀ , HR±, HER2±	0.7872	0.7562

Table 1: Performance of candidate logistic regression models on training and test data.
AUC: Area under receiver operating characteristic curve.

* Mean 5-fold cross-validated AUC across 200 replicates.
† Competition best-performing predictions.

AUC: Area under receiver operating characteristic curve.

* Mean 5-fold cross-validated AUC across 200 replicates.

† Competition best-performing predictions.

Disclosure(s):

Eric A. Cohen, MS: No financial relationships to disclose

Rhea D. Chitalia, PhD: No financial relationships to disclose

Snekha Thakran, Co-Author: No financial relationships to disclose

Walter C. Mankowski, n/a, Ph.D.: No financial relationships to disclose

Alex Anh-Tu Nguyen, M.S.: No financial relationships to disclose

Hannah Horng, B.S.: No financial relationships to disclose

Elizabeth S. McDonald, MD, PhD: No financial relationships to disclose

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Despina Kontos, PhD: iCAD Inc.: Research Grant made to the Academic Institution (Ongoing)

12/9/2022

7:00 AM - 8:15 AM

Discussion 1 + Q&A: PD17-01, PD17-02, PD17-03, PD17-04, PD17-11 & PD17-12

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12/9/2022

7:00 AM - 8:15 AM

Discussion 2 + Q&A: PD17-05, PD17-06, PD17-07, PD17-08 & PD17-10

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Disclosure(s):

Seth A. Wander, MD, PhD: Biovica: Consulting Fees (e.g., advisory boards) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Institutional Research Support (Ongoing); Foundation Medicine: Consulting Fees (e.g., advisory boards) (Ongoing); Genentech: Institutional Research Support (Ongoing); Hologic: Consulting Fees (e.g., advisory boards) (Ongoing); Nuvation Bio: Institutional Research Support (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing); Regor Therapeutics: Institutional Research Support (Ongoing); Veracyte: Consulting Fees (e.g., advisory boards) (Ongoing)

12/9/2022

7:00 AM - 8:15 AM

Poster Spotlight Discussion 17: Endocrine Therapy New Insights

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Lajos Pusztai, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria; Research Funding (Institution) (Ongoing); Bristol Myers Squibb: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria; Research Funding (Institution) (Ongoing); Clovis: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Daiichi: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Genentech: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); H3Bio: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Immunomedics: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria; Research Funding (Institution) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Personalis: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria; Research Funding (Institution) (Ongoing); Pieris: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Radius Health: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing); Seagen Inc: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria; Research Funding (Institution) (Ongoing); Syndax: Consulting Fees (e.g., advisory boards) (Ongoing), Honoraria (Ongoing)

12/9/2022

7:00 AM - 8:15 AM

PD17-01

PD17-01 Genomic analysis of circulating tumor DNA (ctDNA) from patients with HR+, HER2-mutant metastatic breast cancer (MBC) enrolled in SUMMIT: mechanisms of acquired resistance to neratinib + fulvestrant + trastuzumab (N+F+T)

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Background: In the SUMMIT trial, original cohorts of patients with HR+, HER2-negative (locally assessed), HER2-mutant MBC received N alone or N+F, with promising clinical response rates but abbreviated duration. Clinical progression coincided with emergence of additional HER2 mutations and/or amplification of the mutant allele [Smyth et al. *Cancer Discov* 2020;10:198–213]. Addition of T to the combination was postulated to prolong response; the combination of N+F+T in heavily pretreated patients with HR+, HER2-mutant MBC who had received CDK4/6 inhibitors (n=51) yielded a confirmed overall response rate (ORR) of 35.3%, median duration of response (DOR) of 14.3 months, clinical benefit rate (CBR) of 47.1%, and median progression-free survival (PFS) of 8.2 months [Jhaveri et al. *J Clin Oncol* 2022;40:1028]. Seven of these 51 patients were part of a randomized (1:1:1) cohort who received N+F+T, F+T, or F alone. Patients randomized to F+T or F could crossover to N+F+T upon progression. No patients responded to F or F+T; however, one of four patients who crossed over to N+F+T upon progression on F+T responded to the triplet, as did two of six who crossed over upon progression on F. We undertook ctDNA sequencing in patients who responded to N+F+T upfront and after crossover. Methods: Patients with HR+, HER2-negative MBC with activating HER2 mutation(s) and prior CDK4/6i received N+F+T (oral N 240 mg/d with loperamide prophylaxis, im F 500 mg d1, d15, and d29 of cycle 1 then q4w, iv T 8 mg/kg initially then 6 mg/kg q3w) or F+T or F alone. Efficacy endpoints included investigator-assessed ORR and CBR (RECIST v1.1), DOR, and best overall response. ctDNA was collected at baseline, every third cycle during treatment, and at the end of treatment and analyzed by next-generation sequencing. Samples were analyzed using the TEMPUS xF assay. Results: Sequencing results from ctDNA analysis are pending at the time of this abstract submission. Baseline HER2 mutations and co-alterations will be reported and compared with those found in tissue samples. Genomic spectrum and variant allele frequencies in samples taken at baseline, on treatment, and at the end of treatment from patients who experienced complete or partial response to N+F+T and then progressed (n=25) will be sequenced and mechanisms of acquired resistance will be posited. ctDNA genomic profiles of serial time points from patients randomized to F or F+T before and after crossover to N+F+T (n=10) will also be evaluated. Conclusions: Similarities and differences between the mechanisms of acquired resistance to N+F+T, and those previously reported to be associated with progression on N or N+F, will be discussed.

Disclosure(s):

Cynthia Ma, MD, PhD: Agendia: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Athenex: Consulting Fees (e.g., advisory boards) (Ongoing); Bayer Healthcare: Consulting Fees (e.g., advisory boards) (Ongoing); Biovica: Consulting Fees (e.g., advisory boards) (Ongoing); Eisai: Consulting Fees (e.g., advisory boards) (Ongoing); Eli Lilly: Consulting Fees (e.g., advisory boards) (Ongoing);

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12/9/2022

7:00 AM - 8:15 AM

PD17-02

PD17-02 ctDNA Molecular Response based on breast cancer driver mutations predicts progression in aromatase inhibitor-sensitive first line treatment of oestrogen receptor-positive (ER+) HER2-negative (HER2-) advanced breast cancer.

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Background: The combination of a CDK4/6 inhibitor and an aromatase inhibitor (AI) is the gold standard for AI-sensitive first line treatment of ER+ HER2- advanced breast cancer. Nevertheless, some patients progress rapidly and may benefit from alternative strategies. Early ctDNA dynamics have been shown to predict disease course in several clinical situations. Here, we use samples from the PADA-1 trial to assess this strategy for patients receiving AI and palbociclib as first line treatment. PADA-1 was designed to assess the clinical utility of sequential analysis of ctDNA for emerging ESR1 mutations to trigger an early switch from AI plus palbociclib to fulvestrant plus palbociclib treatment. The study included 1,017 patients and was positive on its primary end-point. The objective of this translational study was to analyze the predictive value of 4-week molecular response (MR) for patient progression. Material & Method: First, a CLIA-validated targeted next-generation sequencing-based test (Guardant360 Response) was used to characterize changes in ctDNA level via detection of somatic single-nucleotide variants (SNVs), insertion/deletion mutations (indels), and gene fusions in 74 genes

frequently mutated in cancer. A second analysis was restricted to cancer-associated mutations in 11 genes commonly mutated in breast cancer (PIK3CA, GATA3, TP53, AKT1, ERBB2, BRCA1, BRCA2, ATM, ESR1, PALB2 and RB1). The threshold for molecular response was defined as $\geq 50\%$ decrease in ctDNA (MR score < 0.5). Subjects with ctDNA levels below the test's limit of quantitation (ctDNA-low) were considered molecular responders. Results: 372 subjects with matched baseline and 4-weeks samples were available for analysis. Of these, 134 subjects (36%) were ctDNA-low, and 238 subjects (64%) quantifiable. Among the quantifiable subjects, 183 (77%) were molecular responders (MR+, MR < 0.5), and 55 (23%) were not (MR-, MR ≥ 0.5). PFS was moderately improved for both MR+ and ctDNA-low relative to MR- (HR=0.61 (95%CI 0.44-0.85), $p < 0.01$) over the full 29 months of follow up. Differential PFS event rate was observed only in the first 8 months following ctDNA assessment; during this time MR+ and ctDNA-low were associated with more significantly decreased risk of progression (HR 0.24, 95% CI 0.13 – 0.43, $p=0.0001$). Limiting ctDNA assessment to genes commonly mutated in breast cancer enhanced the predictive power of MR (HR=0.08, 95% CI 0.04 0.17, $p < 0.001$, for MR+ and ctDNA-low vs. MR- across 8 months post-assessment); however, fewer samples were quantifiable by this method (169 [45%] quantifiable; 203 [55%] ctDNA-low). Combining MR status with additional molecular features (e.g.tumor mutational burden and maximum mutation allele fraction) did not improve prediction of non-response. Conclusion: Changes in ctDNA fraction during the first weeks of treatment are predictive of long term clinical benefit on an individual patient basis, particularly during the first year of therapy. Adjusting the MR threshold and/or limiting to genes known to be relevant in the specific tumor can tailor the assessment of ctDNA change to specific clinical scenarios where greater sensitivity or specificity may be required. The identification of patients at high risk for early clinical failure at the onset of treatment may allow for therapy escalation and/or change to improve outcome in this population. Funding : Pfizer and Guardant Health

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12/9/2022

7:00 AM - 8:15 AM

PD17-03

PD17-03 Cell-free DNA monitoring in a phase II study of adjuvant endocrine therapy with CDK 4/6 inhibitor ribociclib for localized HR+/HER2- breast cancer (LEADER)

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Background: While adjuvant endocrine therapy (ET) reduces recurrence risk in hormone receptor-positive (HR+) breast cancer, many patients still experience disease recurrence. Adjuvant therapeutic advances are needed to improve outcomes. Meanwhile, monitoring for circulating tumor DNA (ctDNA) in the adjuvant setting may detect molecular residual disease and/or emergences of molecular recurrence from tumor dormancy. Cyclin-dependent kinase 4 and 6 (CDK 4/6) inhibitors have shown efficacy in HR+/HER2- metastatic breast cancer, and abemaciclib is now approved for adjuvant use in high-risk HR+/HER2- breast cancer. Adjuvant clinical trials have evaluated upfront use of adjuvant CDK 4/6 inhibition; however, the optimal timing of adding a CDK 4/6 inhibitor for HR+/HER2- breast cancer remains unknown. We conducted a prospective phase II clinical trial to evaluate the addition of the CDK 4/6 inhibitor ribociclib in patients with at least one remaining year of adjuvant ET regardless of duration of ET prior to trial enrollment, and we prospectively collected plasma for ctDNA analysis. **Methods:** Eligible patients had Stage I-III HR+/HER2- breast cancer and had been on adjuvant ET (any number of years) with at least one year of treatment remaining. Patients were randomized to one of two ribociclib schedules: continuous (400 mg daily, 28-day cycle) or intermittent (600 mg daily days 1-21, 28-day cycle) for one year. Patients were concurrently treated with an aromatase inhibitor (plus GnRH agonist, if premenopausal). Time to recurrence was calculated using the Kaplan-Meier method. ctDNA monitoring was performed using the Signatera™ platform, a tumor-informed assay based on whole exome sequencing of the primary tumor for multiplex PCR-NGS ctDNA assay design with targeting of up to 16 single nucleotide variants. Plasma samples were collected at the start of ribociclib/ET and serially during follow-up visits. **Results:** Among 81 patients treated with adjuvant endocrine therapy and the CDK4/6 inhibitor ribociclib, 42 patients had samples suitable for ctDNA analysis: 3 (7%) had a single ctDNA test, 17 (40%) had 2 serial ctDNA tests, and 22 (52%) had 3 serial ctDNA tests. After a median follow-up of 20 months, 2 patients who received ribociclib (intermittent dosing) experienced disease recurrence with recurrence-free survival of 100% at 1 year from study entry and 97% (95% CI 88-99%) at 2 years. ctDNA was detected exclusively in the only 2 patients that experienced recurrence, with lead times of 7 months and 8 months prior to clinical recurrence. Both patients had no detectable ctDNA at the start of ribociclib/ET. One patient had detectable ctDNA [mean tumor molecules/mL (MTM/mL) = 0.1] while on ribociclib/ET for 5 months, after which she completed a full 12 months of treatment. One month after completing ribociclib/ET (8 months after ctDNA detection), she presented with metastases in the liver and bones. The second patient had 2 negative ctDNA tests at days 0 and 147 while receiving ribociclib/ET and became ctDNA positive (MTM/mL = 0.1) at day 350. She developed CNS-only metastatic disease 7 months after completing ribociclib/ET. Among the other 40 patients who did not have detectable ctDNA, none have experienced recurrence. **Conclusions:** Overall, only 2 patients had detectable ctDNA, and both patients developed recurrent metastatic disease after completion of ribociclib with ET. Notably, one of these patients developed CNS-only disease.

While follow-up is early, the remaining patients did not have detectable ctDNA and have not developed recurrent disease. This study suggests monitoring for ctDNA may identify patients at increased risk for recurrence in the extended adjuvant period and potentially guide therapy escalation.

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12/9/2022

7:00 AM - 8:15 AM

PD17-05

PD17-05 Development and Validation of a Composite Biomarker Predictive of Palbociclib + Endocrine Treatment Benefit in Early Breast Cancer: PENELOPE-B and PALLAS Trials

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Background : The PENELOPE-B (NCT01864746) and PALLAS (NCT02513394) trials are large prospective, randomized, phase III trials that evaluated adjuvant palbociclib (PAL) + endocrine treatment (ET) vs ET in patients with hormone receptor–positive/human epidermal growth factor receptor 2–negative (HER2–) early breast cancer (EBC). Both studies did not meet the primary endpoint of improving invasive disease-free survival (iDFS). We conducted biomarker analyses to identify patients who might benefit from PAL + ET in EBC. Methods: Resected tumor tissue was collected from consenting patients . Gene expression analyses were conducted using the HTG EdgeSeq Oncology Biomarker Panel including 2549 genes . Based

on 91 genes from the HTG panel, the intrinsic molecular subtypes were calculated using Absolute Intrinsic Molecular Subtyping (AIMS) . Potential predictive treatment biomarkers were established in PENELOPE-B (n=906 with resected tissue) as the development set using an outcome-oriented approach based on iDFS with a selection procedure that maximized the log-rank statistic to estimate a standard Z score–based optimal cutoff. Independent validation was conducted on PALLAS (n=2085; PENELOPE-B-like with resected tissue and HTG data). Hazard ratios and corresponding 95% CIs were calculated using the Cox proportional hazards model, and iDFS distributions between treatment arms were compared using the log-rank test. Interaction between treatment and biomarker status was assessed. Results: Patient baseline characteristics were well balanced, with no differences in iDFS between the intent-to-treat set and the biomarker set for both trials. Approximately 73% of patients (PENELOPE-B [n=663] and PALLAS [n=1516]) had luminal A subtypes whereas only 7.1 % (PENELOPE-B [n=64]) and 8.3 % (PALLAS [n=172]) had a luminal B subtype. AIMS subtypes showed overall similar prognostic patterns for iDFS between PENELOPE-B and PALLAS. The biomarker-defined subgroup found in PENELOPE-B with optimal cutoff demonstrated a preferential benefit from PAL + ET (n=364 [96 events]; hazard ratio [95% CI], 0.63 [0.42, 0.95]; P=0.025). Independent validation of the PALLAS subgroup using the pre-defined optimal cutoff confirmed a significant benefit from PAL + ET (n=916 [70 events]; 0.55 [0.34–0.90]; P=0.015) while not in the rest of the patients (interaction p=0.0025). Significant treatment effects remained (0.55 [0.34–0.89]; P=0.015) after adjusting for the randomization stratification factors of PALLAS. Conclusions: The composite predictive biomarker defined from PENELOPE-B was independently validated in a prospectively defined retrospective analysis of a subset of patients selected from PALLAS. The composite biomarker identified a subset of EBC patients deriving benefit from the addition of PAL to ET. This patient stratification approach can potentially be applied to future adjuvant clinical trials for treatment of hormone receptor–positive/HER2– EBC.

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12/9/2022

7:00 AM - 8:15 AM

PD17-06

PD17-06 Immunohistochemical markers and determinants of clinical response in the Penelope-B trial

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Background: The Penelope-B trial did not show improvement in invasive disease-free survival (iDFS) with the addition of palbociclib to endocrine therapy (ET) in patients with high-risk early breast cancer (BC) after neoadjuvant chemotherapy (NACT). Biomarkers may be able to identify subgroups of patients deriving benefit from Palbociclib and guide future studies. Estrogen-receptor (ER), progesterone-receptor (PgR) and Ki-67 might be helpful in identifying patients benefiting from palbociclib. Concordantly, tumors with elevated expression of Cyclin D1 and phosphorylated retinoblastoma protein (phospho-RB) may harbor more dependency on CDK4/6 and thus higher sensitivity to palbociclib. Methods: The percentage of positive ER and PgR cells and Ki-67 assessed in surgical specimens after NACT were combined to obtain the immunohistochemical score 3 (IHC3, Cuzick et al JCO 2011, low vs high based on the median IHC3 value). Cyclin D1 and phospho-RB Ser 807/811 immunoreactive (phospho-RB) scores were analyzed in residual tumors after NACT (range 0-12 each). Proportional hazard regression model was used to assess the predictive and prognostic value of IHC3 and treatment on iDFS. Subgroup analysis was performed according to BC intrinsic subtypes (luminal-A/normal-like, luminal-B/HER2-enriched/basal) and HER2-status (HER2 0, HER2 low). Cox/Fine-Gray regression was used to define the predictive and prognostic value of CyclinD1

(≤ 1 , > 1), phospho-RB (≤ 2 , > 2) as dichotomized and continuous variables on iDFS, distant DFS (DDFS), locoregional invasive recurrence-free interval (LRRFI) and overall survival (OS). Multivariate analyses (MVA) were adjusted for age (≤ 50 vs > 50), Ki-67 (≤ 15 vs > 15), region (non-Asian vs Asian), ypN (ypN0-1 vs ypN2-3), risk status (CPS-EG=2 ypN+ vs ≥ 3), cT (cT1-2 vs cT3-4), ypT (ypT0-2 vs ypT3-4), and grade (G1-2 vs G3). The MVA for IHC3 includes all the covariates above except Ki-67. $p < 0.05$ was defined as statistically significant. Results: Data for ER, PgR, Ki-67, HER2, Cyclin D1 and phospho-RB were available for 1250 patients. Overall, 98.9% of the patients had ER+ tumors, 75.0% PgR+, 52.2% had HER2 low, 25.5% Ki-67 >15 , 50% had IHC3 score higher than median, 93.9% had Cyclin D1 > 1 , 57.8% had phospho-RB > 2 . Patients with IHC3 score high had a worse iDFS compared to patients with IHC3 score low (MVA HR 2.28 95%CI (1.78-2.91), $p < 0.0001$). Patients with luminal-A/normal-like tumors and IHC3 low had an improved iDFS with the addition of palbociclib to ET (MVA HR 0.35 95%CI (0.14-0.90), test for interaction $p = 0.01$). No difference was observed according to HER2 status. Cyclin D1 >1 has no predictive value but is prognostic for better iDFS (MVA HR 0.62 95%CI (0.41-0.94), $p = 0.023$), LRRFI (MVA HR 0.30 95%CI (0.15-0.63), $p = 0.001$) and OS (MVA HR 0.50 95%CI (0.28-0.89), $p = 0.019$). Similar results were obtained when Cyclin D1 was analysed as a continuous variable. Phospho-RB had neither predictive nor prognostic value. Phospho-RB highly correlates with Ki-67 ($p < 0.001$, Spearman correlation 0.248). Conclusions: Patients with high Cyclin D1 expression had a favorable prognosis independent of treatment arm, but patients with luminal-A/normal-like tumors and IHC3 low after NACT had an improved outcome when receiving palbociclib in addition to adjuvant ET. These exploratory studies suggest specific signatures/phenotypes could predict benefit from Palbociclib in high-risk early breast cancer.

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12/9/2022

7:00 AM - 8:15 AM

PD17-07

PD17-07 Cell-Cycle Inhibition and Immune Microenvironment in HR+/HER2- Breast Cancer During and After preoperative ribociclib and letrozole vesus chemotherapy: A correlative analysis of the 1402-SOLTI/CORALLEEN phase 2 trial

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Background Hormone receptor–positive/HER2-negative (HR+/HER2-) breast cancer (BC) is associated with low % of stromal tumor-infiltrating lymphocytes (sTIL) and immune gene expression and poor response to immune checkpoint inhibitors. Evaluating the effect of letrozole and ribociclib (L+R) on the immune microenvironment may suggest new opportunities for immunotherapy-based approaches for HR+/HER2- BCs. Here, we present an exploratory correlative analysis from CORALLEEN, a trial that evaluated the efficacy of L+R (vs. chemotherapy [CHT]) in patients with high-risk PAM50 Luminal B BC (Prat et al. *Lancet Oncology*. 2022). Methods CORALLEEN is a randomized exploratory study in postmenopausal women with operable stage I-III breast cancer, HR+/HER2- and Luminal B by Prosigna®. Patients were randomized 1:1 to receive either 6 cycles of ribociclib (600mg; 3-weeks-on/1-week-off) plus daily letrozole or CHT: 4 cycles of AC followed by 12 doses of weekly paclitaxel. The primary endpoint was the rate of PAM50 Risk of Relapse (ROR)-low score at surgery in each arm. Samples were prospectively collected at baseline, day 15, and surgery. sTILs score, ki67 IHC and gene expression analysis were determined in all available samples. Complete cell cycle arrest (CCCA) was defined as Ki67≤2.7%. Gene expression profiling by mRNA sequencing (RNAseq) was evaluated. We applied a collection of 194 immune- gene expression signatures (iGES), representing multiple biological pathways and cell types, including. Results 106 patients were randomly assigned to receive neoadjuvant L+R (n=52) or CTH (n=54).

Overall, Ki67, sTILs and RNA-seq was available in 95.4%, 96.7% and 83.1% of the samples across the 3 time-points. In terms of cell-cycle inhibition, L+R achieved a significant decrease in Ki67 protein expression and led to higher rates of CCCA at 2 weeks (89.6% vs. 43.2%, $p < 0.001$) and surgery (45.9% vs 25.5%, $P=0.054$) compared with CHT. Interestingly, the 11-gene PAM50 proliferative score was significantly lower in tumors with CCAA than in those with non-CCCA ($p < 0.001$) after L+R, but not after CTH ($p = 0.682$). In contrast, tumors with CCCA after CHT had a significantly lower rate of tumor cellularity compared to tumors with non-CCCA ($p = 0.002$). This was not observed in the L+R arm ($p=0.141$). Compared to baseline, no clear and significant patterns in % of sTILs were observed at week 2 and surgery. However, % of TILs at surgery in tumors with CCCA after CHT was higher than in tumors with non-CCCA (median 15% versus 1%, $p=0.017$). This was not observed in the L+R arm (median 1% and 5%, $p=0.584$). Interestingly, this inverse relationship between immune infiltration and CCAA was further confirmed by RNA- CHT compared to tumors with non-CCCA, whereas 174 (89.7%) of iGES were upregulated ($FDR < 5\%$) in tumors with non-CCCA after L+R compared to tumors with CCCA. Finally, L+R and CTH treatment at week 2 and surgery showed an increase in adaptive immune signatures indicative of activated T-cell and B-cell phenotypes; however, CTH was uniquely associated with increased cytokine signaling, enhanced antigen presentation, dendritic, granulocyte, macrophage and NK cells and decrease in Th17, Th2 and Treg cells. Conclusion In early-stage Luminal B breast cancer, L+R induce a potent anti-proliferative effect compared to CHT. Both treatments generally increased T- and B-cell immune infiltration; however, an inverse relationship between immune infiltration and anti-proliferative response at surgery exists according to treatment, where immune infiltration is increased in residual tumors with non-CCCA when treated with L+R, but the opposite is observed with CHT. The prognostic value of immune and anti-proliferative effects of L+R in residual tumors is currently being evaluated in the prospective RIBOLARIS phase II clinical trial (NCT05296746).

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

PD17-08

PD17-08 Pooled gene expression analysis and association with treatment response in patients with HR+/HER2- advanced breast cancer in the MONALEESA-2, -3, and -7 trials

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Background: The Phase III MONALEESA (ML)-2, -3, and -7 trials showed significant improvement in progression-free survival (PFS) and overall survival (OS) with ribociclib (RIB) + endocrine therapy (ET) over placebo (PBO) + ET in patients (pts) with HR+/HER2- advanced breast cancer (ABC); improvement in OS with cyclin-dependent kinase 4 and 6 inhibitors (CDK4/6i) has been observed in some, but not all clinical trials. Gene expression analyses for each separate ML study were reported previously. Given the differences in CDK4 vs CDK6 inhibition between RIB and other CDK4/6i, we evaluated the association between cell cycle (CC)-related genes and outcomes based on pooled analysis of gene expression using tumor samples from the ML-2, -3, and -7 trials.

Methods: Gene expression data were generated from pre-treatment archival tumor samples (primary, 73%; metastatic, 27%) with a customized NanoString nCounter panel (781 genes) including genes involved in CC, other signaling pathways, and breast cancer biology. Samples were pooled from 1139 pre- and postmenopausal pts with HR+/HER2- ABC across the 3 ML studies, which included pts on first- and second-line therapy. Data were categorized into training (80%) and test (20%) datasets. The training dataset was used to analyze each gene (modeled continuously) individually for an association with PFS, and genes with a gene x treatment (tx) interaction P value <.10 were evaluated in the test dataset. Genes or gene signatures were classified by tertiles based on expression level (low/medium/high). For each tertile, median (m) PFS was calculated by the Kaplan-Meier method, and hazard ratios (HRs) of tx benefit (RIB vs PBO) were estimated. A Cox proportional hazards model adjusting for clinical covariates was used. A machine learning approach (elastic net survival model with stability selection), which used available gene expression data and select clinical factors and their interactions with tx arms, was applied to predict PFS.

Results: This report focused on CC-related genes and signatures. Gene expression levels of CDKN2B and the expression ratio of CCND1/CDKN2A showed a predictive relationship with benefit from RIB in both training and test sets (Table). PFS benefit with RIB was consistent regardless of the CDK4/CDK6 expression ratio or level of expression of CCNE1, CDK2, RB1, combined CC-related genes, E2F gene signatures, RB gene signature, combined DNA-replication genes, or combined proliferation-related genes. A machine learning approach identified a clinico-genomic signature that was prognostic for PFS benefit with RIB. Selected

variables included gene expression levels of FXBO5, PGR, RBBP8, and STC2 and several clinical features (tx arm, de novo disease, prior ET, and visceral disease). Pts with a low signature score had a longer mPFS vs pts with a high signature score, in the RIB (HR, 0.37; 95% CI, 0.22-0.62) and PBO (HR, 0.30; 95% CI, 0.15-0.59) arms.

Conclusion: In the largest pooled analysis of the association of gene expression profile data with CDK4/6i tx response in pts with HR+/HER2- ABC, the PFS benefit with RIB + ET over ET alone was consistent irrespective of expression levels of most CC genes. Variation in magnitude of RIB benefit was observed, depending on CDKN2B expression levels, CCND1/CDKN2A expression ratio, and machine learning-derived signature scores. The clinico-genomic CDK4/6i signature requires validation in additional datasets.

Table. Progression-Free Survival by Gene Expression Subgroup

Gene expression		Low		Medium		High	
		PBO	RIB	PBO	RIB	PBO	RIB
CDKN2B (training) ^a	mPFS, mo	11	22.5	12.8	NR	18.5	22.1
	HR (95% CI)	0.46 (0.34-0.63)		0.43 (0.31-0.60)		0.73 (0.53-1.01)	
CDKN2B (testing) ^a	mPFS, mo	11	NR	16	19.3	16.7	19.2
	HR (95% CI)	0.37 (0.18-0.77)		0.59 (0.31-1.12)		0.88 (0.46-1.67)	
CCND1/CDKN2A (training) ^a	mPFS, mo	16.5	19.6	11.4	24.8	14.6	22.9
	HR (95% CI)	0.78 (0.56-1.08)		0.33 (0.24-0.46)		0.56 (0.41-0.78)	
CCND1/CDKN2A (testing) ^a	mPFS, mo	13.2	14.8	16	24.6	14.5	NR
	HR (95% CI)	0.72 (0.38-1.38)		0.62 (0.31-1.27)		0.46 (0.23-0.92)	
CCNE1	mPFS, mo	16.6	27.5	13.4	22.5	9.1	17.9
	HR (95% CI)	0.51 (0.36-0.72)		0.48 (0.35-0.67)		0.53 (0.39-0.71)	
CDK2	mPFS, mo	13.3	NR	14.9	22.2	11.2	22.5
	HR (95% CI)	0.5 (0.36-0.7)		0.64 (0.47-0.88)		0.44 (0.33-0.6)	
CDK4/CDK6	mPFS, mo	14.5	27.5	14.7	21.3	11.4	23.9
	HR (95% CI)	0.52 (0.38-0.72)		0.68 (0.49-0.94)		0.41 (0.3-0.56)	
RB1	mPFS, mo	11.1	19.2	14.5	22.9	13.6	27.5
	HR (95% CI)	0.56 (0.41-0.76)		0.6 (0.44-0.83)		0.43 (0.31-0.61)	
Cell cycle-related genes	mPFS, mo	18.2	NR	14.5	22.1	9	19.9
	HR (95% CI)	0.47 (0.33-0.68)		0.69 (0.5-0.95)		0.44 (0.33-0.59)	
E2F gene signature	mPFS, mo	17.3	24.9	12.8	24.8	10.8	19.9
	HR (95% CI)	0.62 (0.44-0.87)		0.44 (0.32-0.61)		0.49 (0.36-0.66)	
RB gene signature	mPFS, mo	17.3	NR	14.5	24.9	9.1	18.8
	HR (95% CI)	0.59 (0.42-0.83)		0.52 (0.37-0.73)		0.43 (0.32-0.58)	
DNA replication genes	mPFS, mo	16.5	27.5	13	24.8	11	19.6
	HR (95% CI)	0.58 (0.41-0.82)		0.47 (0.34-0.66)		0.5 (0.37-0.67)	
Proliferation-related genes	mPFS, mo	16.5	24.8	14.6	23.5	10.8	22.1
	HR (95% CI)	0.58 (0.41-0.81)		0.59 (0.43-0.81)		0.41 (0.31-0.56)	

NR, not reached; m, median; PFS, progression-free survival; PBO, placebo; RIB, ribociclib.
^a CDKN2B and CCND1/CDKN2A were evaluated in both training and testing sets and had a similar relationship with PFS.

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12/9/2022

7:00 AM - 8:15 AM

PD17-11

PD17-11 Circulating tumor DNA (ctDNA) reveals complex biological features with clinical relevance in metastatic breast cancer

12/9/2022

7:00 AM - 8:15 AM

PD17-12

PD17-12 Primary efficacy and safety results from the AMALEE trial evaluating 600 mg vs 400 mg starting doses of first-line ribociclib in patients with HR+/HER2- advanced breast cancer

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Background: In the Phase III MONALEESA (ML)-2, -3 and -7 trials, a 600 mg dose of ribociclib (RIB) demonstrated significant overall survival benefit in patients (pts) with HR+/HER2- advanced breast cancer (ABC) but was associated with QTcF (>480 ms, 3%-7%) and neutropenia (G3/4, 57%-64%) adverse events (AEs) which were managed by dose reductions. The Phase II AMALEE study was performed as a postmarketing commitment to assess whether reducing the starting dose of RIB from the recommended dose (3 wk on, 1 wk off) of

600 mg/day to 400 mg/day decreases QTcF prolongation without compromising the efficacy of first-line RIB in pts with HR+/HER2- ABC. Here, we present efficacy and safety results from the primary analysis of AMALEE. Methods: AMALEE is a randomized Phase II open-label study including pre- and postmenopausal pts with HR+/HER2- ABC with no prior therapy for ABC. Pts received RIB 400 mg + nonsteroidal aromatase inhibitor (NSAI) or RIB 600 mg + NSAI. The primary endpoint is to determine whether overall response rate (ORR) in the 400 mg arm is noninferior to the 600 mg arm. The key secondary endpoint is QTcF prolongation at cycle 1, day 15 (C1D15) 2 hours post dose. Additional endpoints included safety, progression-free survival (PFS), duration of response (DOR), time to response (TTR), and pharmacokinetics. Results: A total of 376 pts were randomized 1:1 to receive RIB at either 400 mg or 600 mg doses. Baseline (BL) characteristics and prior antineoplastic therapy were balanced across treatment (tx) arms. At the time of the data cutoff (June 11, 2021), median follow-up was 14.9 mo (min, 6.1; max, 23.8), and all pts had been treated for ≥6 months from randomization or had discontinued study tx. ORR for RIB was 41.5% (95% CI, 34.4-48.7) with 400 mg vs 45.3% (95% CI, 38.1-52.6) with 600 mg (ORR ratio for RIB 400 mg vs 600 mg, 0.921 [90% CI, 0.757-1.121]). The lower 90% CI boundary did not meet the prespecified noninferiority (NI) margin of 0.814. Results for ORR by subgroups were consistent with the overall analysis set. RIB plasma exposure was lower at 400 mg than 600 mg; the geometric mean Cmax and AUC0-24h at C1D15 were approximately 28% and 43% lower in the 400 mg than the 600 mg arm (Cmax 1080 vs 1500 ng/mL and AUC0-24h 16400 vs 28600 ngxh/mL). This study met the key secondary endpoint, change in QTcF at C1D15 in the RIB 400 mg group with a 90% CI upper boundary of < 20 ms. Mean change in QTcF from BL to C1D15 2 hours post dose was lower in the 400 mg (12.5 ms, 90% CI, 10.9-14.1) than the 600 mg arm (19.7 ms, 90% CI, 17.4-22.0). QTcF ≥501 ms occurred in 1.6% of pts in the 400 mg arm vs 0.5% in the 600 mg arm. Rates of G3/4 neutropenia were lower in the 400 mg (31.4%) than the 600 mg arm (46.3%). Other safety results were consistent with those previously reported for RIB in the ML trials. Median duration of exposure to RIB was 8.0 mo (min, 0.1; max, 23.7) in the 400 mg arm vs 8.8 mo (min, 0.5; max, 20.8) in the 600 mg arm. Dose reductions of RIB were more frequent in the 600 mg group with 30.5% vs 13.8% of pts requiring 1 dose reduction in the 600 mg and 400 mg groups, respectively. Dose reductions were primarily attributable to AEs, with neutropenia being the most frequently reported AE requiring a dose modification. Rates of discontinuation due to AEs were similar in the 400 mg vs 600 mg arms (8.5% vs 9.6%). PFS, DOR, and TTR data are currently immature. Conclusions: RIB at the 400 mg dose shows a better safety profile vs 600 mg in terms of key AEs that are RIB concentration dependent (neutropenia and QTcF prolongation). ORR was 3.8% lower with 400 mg than 600 mg. The lower 90% CI boundary of the ORR ratio did not meet the NI margin, thus this study was unable to demonstrate statistical NI of the 400 mg vs 600 mg dose of RIB using ORR as the endpoint. Updated results with additional follow-up and the clinically relevant endpoint PFS will be presented at the congress.

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12/9/2022

7:00 AM - 8:15 AM

Discussion 1 + Q&A: PD18-04, PD18-05, PD18-06 & PD18-07

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7:00 AM - 8:15 AM

Discussion 2 + Q&A: PD18-01, PD18-02 & PD18-03

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12/9/2022

7:00 AM - 8:15 AM

Discussion 3 + Q&A: PD18-08, PD18-09, PD18-10 & PD18-11

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7:00 AM - 8:15 AM

Poster Spotlight Discussion 18: Updates and New Therapies for HER2 Positive Disease

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12/9/2022

7:00 AM - 8:15 AM

PD18-01

PD18-01 Adjuvant Trastuzumab Emtansine Versus Paclitaxel plus Trastuzumab for Stage I HER2+ Breast Cancer: 5-year results and correlative analyses from ATEMPT (TBCRC033)

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Background: The ATEMPT trial primary analysis found that one year of adjuvant trastuzumab emtansine (T-DM1) achieved a 3-year iDFS of 97.8% for patients with stage I HER2+ breast cancer, but was not associated with fewer clinically relevant toxicities (CRTs) compared with paclitaxel and trastuzumab (TH). In this end-of-study analysis, we report 5-year survival outcomes and correlative analyses from the trial. Methods: Patients with stage I centrally confirmed HER2+ breast cancer were randomly assigned 3:1 to adjuvant T-DM1 for one year or TH and received T-DM1 3.6 mg/kg IV every 3 weeks for 17 cycles or paclitaxel 80 mg/m² IV with weekly trastuzumab IV followed by trastuzumab for 9 months. The co-primary objectives were to compare the incidence of CRTs between the 2 arms and to evaluate iDFS in patients receiving T-DM1. To investigate proteomic correlates of recurrence, spatial proteomic analyses were performed on samples from 13 patients experiencing iDFS events (cases) and 24 matched controls using the NanoString GeoMx Digital Spatial Profiler. The impact of HER2 heterogeneity on outcomes was investigated among 17 cases and 51 matched controls by fluorescence in-situ hybridization (FISH). HER2 genetic heterogeneity was assessed by scrutinizing the whole tumor area and defined as the occurrence of HER2 gene amplification in >5% but < 50% invasive tumor cells. The risk of recurrence was evaluated centrally with the HER2DX genomic assay from 225 primary tumor samples. Germline whole genome sequencing (WGS) was conducted among 55 patients experiencing T-DM1-induced thrombocytopenia and/or bleeding and 55 matched controls to identify genomic correlates for this side effect. Results: A total of 497 patients who initiated protocol therapy were included in this analysis (383 T-DM1 and 114 TH). After a median follow up 5.8 years, among patients receiving T-DM1 there were a total of 11 iDFS events, with 3 distant recurrences. The 5-year iDFS for T-DM1 was 97.0% (95% CI, 95.3-98.8%), the 5-year recurrence-free interval (RFI) was 98.6% (95% CI: 97.4-99.8%) and the 5-year overall survival (OS) for T-DM1 was 97.8 %

(95% CI, 96.3-99.3%). Although the study was not powered to evaluate the efficacy of TH, among the 114 patients receiving TH, a total of 9 iDFS events were observed, including 2 distant events; the 5-year iDFS with TH was 91.3% (95% CI: 86.0-96.9%), 5-year RFI was 93.3% (95% CI: 88.6-98.2%) and 5-year OS was 97.9% (95% CI: 95.2-100%). A total of 56 samples were evaluable for heterogeneity analyses, among which 14% (n=8) harbored HER2 genetic heterogeneity. Spatial proteomic analyses found that NF1 (adjusted $p=0.72 \times 10^{-6}$) and CTLA-4 (adjusted $p=0.15 \times 10^{-3}$) were significantly upregulated in primary samples from cases, while cleaved caspase 9, CD25, GTR, ICOS, p53 and PD-L2 were significantly upregulated in controls (all with adjusted $p < 0.05$). Germline WGS found that the top gene associations with thrombocytopenia and thrombocytopenia or bleeding were ALMS1 ($p=0.19 \times 10^{-3}$) and APBA3 ($p=0.23 \times 10^{-3}$), respectively, although none reaching the threshold for genome wide significance. rs62143195 and rs114169776 were the top single nucleotide polymorphisms associated with thrombocytopenia and thrombocytopenia or bleeding, respectively. Data on the impact of HER2 heterogeneity and of HER2DX score on survival outcomes will be presented. Conclusion: With longer follow-up, adjuvant T-DM1 confirmed outstanding long-term outcomes among patients with stage I HER2+ breast cancer, demonstrating a 5-year RFI of 98.6%. Spatial proteomic analyses identified a potential association between NF1 and CTLA-4 expression with recurrence. Details on the impact of HER2 heterogeneity and HER2DX assay on prognosis will be presented.

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7:00 AM - 8:15 AM

PD18-02

PD18-02 Adjuvant Paclitaxel and Trastuzumab Trial (APT) for Node-Negative, Human Epidermal Growth Factor Receptor 2–Positive (HER2+) Breast Cancer: final 10-year analysis

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Background: The APT trial evaluated the activity of adjuvant paclitaxel and trastuzumab (TH) among patients with small, node negative HER2+ breast cancer. This regimen showed a 7-year invasive disease-free survival (iDFS) of 93%, a recurrence-free interval (RFI) of 97.5% with only four (1.0%) distant recurrences, and a 7-year overall survival (OS) of 95%. In this end-of-study analysis, we report the survival outcomes at 10 years and assess the role of HER2DX testing in predicting long-term outcomes with adjuvant TH.

Methods: APT was a single-arm multicenter investigator-initiated phase II study in which patients with HER2+ breast cancer with tumors ≤3 cm and negative nodes (one single micrometastatic node allowed) received IV weekly paclitaxel (80 mg/m²) with IV weekly trastuzumab for 12 weeks, followed by IV trastuzumab for 9 months. The primary endpoint was 3-year iDFS. Here we report 10-year iDFS, RFI, breast cancer-specific survival (BCSS) and OS. In an exploratory analysis, the risk of recurrence was evaluated with the HER2DX genomic assay.

Results: A total of 410 patients were enrolled from October 2007 to September 2010, of which 406 started the study treatment and were included in the intent to treat analysis. Median age at enrollment was 55 years (range, 24 to 85 years), and most patients (67%) had hormone receptor (HR)-positive disease. Fifty percent of patients had tumors 1.0 cm or smaller and only 9% of patients had tumors between 2 cm to 3 cm. Mean tumor size was 1.1 cm. After a median follow-up of 10.2 years (122 months), 36 iDFS events were observed, consistent with a 10-year iDFS of 89.7% (95% CI, 86.3%-93.1%). Ten-year iDFS was 90.2% (95% CI, 86.3%-94.3%) and 88.5% (95% CI, 82.4%-95.1%) for patients with HR-positive and HR-negative tumors at baseline, respectively. 10-year RFI was 96.8% (95% CI, 95.0%-98.7%), 10-year OS was 94.2% (95% CI, 91.6%-96.8%) and 10-year BCSS was 99.1% (95% CI, 98.1%-100.0%). Of the iDFS events observed in the trial, 6 were non-breast cancer related deaths and 9 were contralateral tumors, all but one locally found to be HER2-negative upon biopsy (Table 1). Among patients experiencing an iDFS event, 7 patients (1.7%) had distant recurrences, including 1 with a T2 tumor, 3 with a T1c tumor and 3 with a T1b tumor. At baseline, 6 of them had HR-positive disease, 1 had HR-negative disease, and 6 had high-grade disease. Upon biopsy of metastatic lesions, 5 of the 7 distant recurrences were locally found to be HER2+, 1 was HER2-negative and 1 had unknown HER2 status. HER2DX testing was conducted on available baseline archival tumor tissue and analyses of patients' survival outcomes based on the HER2DX score will be presented.

Conclusion: After 10 years of follow-up, adjuvant TH confirmed excellent long-term outcomes for small, node-negative HER2+ breast cancer, with a 10-year RFI of 96.8% and a 10-year BCSS of 99.1%.

Table 1

DFS EVENT	ER-negative at baseline		ER-positive at baseline	
	N	Time to event (months)	N	Time to event (months)
Local/regional recurrence	3		2	
- ipsilateral axilla (HER2+*)	1	20	0	
- ipsilateral breast	2	12, 153	2	37, 65
HER2+*	1		1	
HER2-*	1		1	
Contralateral breast events	4	36**, 59**, 84, 90	5	12, 56, 88, 106, 130
- HER2+*	0		1	
- HER2-*	4		4	
Distant recurrence	1	63**	6	27, 46, 54, 59, 81, 86
Death	6	42, 45, 52, 62, 62, 119	9	14, 21, 48, 61, 62, 63
- Breast-cancer related	0		0	79, 106, 107
- Non-breast cancer related	6		9	
Any recurrence or death	13		23	

*HER2 status locally determined on a biopsy of the recurrent or contralateral tumor tissue
**Patient had subsequent breast cancer-related death, which was counted toward the calculation of breast cancer-specific survival

iDFS events with adjuvant paclitaxel plus trastuzumab after 10.2 years of follow up

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7:00 AM - 8:15 AM

PD18-03

PD18-03 Final analysis of the Phase III PEONY trial: long-term efficacy and safety of neoadjuvant–adjuvant pertuzumab or placebo, plus trastuzumab and docetaxel, in patients with HER2-positive early or locally advanced breast cancer

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BACKGROUND

In the Phase II NeoSphere study (NCT00545688), dual HER2 blockade with pertuzumab (P) + trastuzumab (H), + docetaxel (D) significantly increased pathologic complete response (pCR) vs. H+D in the neoadjuvant setting for HER2-positive early breast cancer (EBC), locally advanced (LA) BC, or inflammatory BC, with supportive progression- and disease-free survival (DFS) data. Consistently, the randomized, multicenter, double-blind, placebo (Pla)-controlled Phase III PEONY trial (NCT02586025) significantly improved total pCR (tpCR; primary endpoint) with P+H+D vs. H+D in an Asian population, and safety data were in-line with the known P safety profile. We present the final analysis of long-term efficacy (at 3 and 5 years) and safety from the study.

METHODS

Patients had centrally confirmed HER2-positive EBC (T2–3, N0–1) or LABC (T2–3, N2 or N3; T4, any N) and were randomized 2:1 to four neoadjuvant P+H+D or Pla+H+D cycles every 3 weeks. P: 840 mg loading/420 mg maintenance doses (or Pla); H: 8 mg/kg loading/6 mg/kg maintenance; D: 75 mg/m². Patients then received three fluorouracil, epirubicin, and cyclophosphamide cycles, followed by 13 of P+H or Pla+H in the adjuvant setting for up to 1 year.

Long-term outcomes (event-free survival [EFS], DFS, overall survival [OS]; all secondary endpoints) were assessed by Kaplan–Meier methods, Cox proportional hazards models, and a two-sided log-rank test (stratified by disease category and hormone receptor status).

RESULTS

Data cut-off was Mar 14, 2022, and 329 patients were randomized; 219 to P; 110, to Pla. Safety populations were 218 and 110 patients, respectively. Baseline characteristics were well balanced. Most patients received the full HER2-targeted cycles. Median follow-up was 62.9 months. Long-term efficacy data are shown in the table.

During the overall treatment period, 70.6% of patients in the P+H+D arm and 68.2% in the Pla+H+D arm experienced grade ≥3 adverse events (AEs); the most common (in ≥5% of

patients in either arm) being neutropenia (59.2% vs. 55.5%), leukopenia (34.4% vs. 34.5%), and febrile neutropenia (5.0% vs. 3.6%). Of the most common any-grade AEs (in $\geq 30\%$ of patients in either arm), diarrhea was more common in the P+H+D arm (40.8% vs. 17.3% in the Pla+H+D arm). Serious AEs were reported in 17.0% and 13.6% of patients, respectively. No primary cardiac events (heart failure [New York Heart Association grade III or IV] or significant decline of left ventricular ejection fraction) or secondary cardiac events occurred during any study periods.

CONCLUSIONS

Long-term efficacy endpoints (EFS, DFS, and OS) were supportive of the primary endpoint results (tpCR) and suggested a clinically meaningful improvement with P+H vs. Pla+H when administered before and after surgery for one year of anti-HER2- therapy. Safety data were in-line with the known P safety profile and generally comparable between arms, with the exception of diarrhea.

PEONY adds to the totality of data showing the benefit of the P+H+D regimen in HER2-positive EBC.

Long-term efficacy data

	P+H+D (n = 219)	Pla+H+D (n = 110)
EFS		
HR (95% CI)	0.53 (0.32–0.89)	
Event-free rate		
3-year	88.9%	79.7%
Δ (95% CI); p-value	9.2% (0.29–18.1); p = 0.043	
5-year	84.8%	73.7%
Δ (95% CI); p-value	11.1% (1.2–21.0); p = 0.027	
DFS		
HR (95% CI)	0.52 (0.30–0.88)	
Event-free rate		
3-year	90.1%	81.1%
Δ (95% CI); p-value	9.0% (0.30–17.7); p = 0.043	
5-year	86.0%	75.0%
Δ (95% CI); p-value	11.0% (1.2–20.7); p = 0.028	
OS		
HR (95% CI)	0.53 (0.23–1.19)	
Event-free rate		
3-year	97.0%	91.0%
Δ (95% CI); p-value	6.0% (0.08–12.1); p = 0.053	
5-year	93.9%	90.0%
Δ (95% CI); p-value	3.9% (2.9–10.7); p = 0.26	

CI, confidence interval; DFS, disease-free survival; EFS, event-free survival; HR, hazard ratio; OS, overall survival; Pla, placebo.

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PD18-04

PD18-04 Prognostic implications of PIK3CA mutation by hormone receptor status and intrinsic subtype in early stage HER2-positive breast cancer: a correlative analysis from CALGB 40601.

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Paola Zagami MD^{1,2}, Aranzazu Fernandez-Martinez MD, PhD^{1,3}, Naim U. Rashid PhD⁴, Katherine A. Hoadley PhD^{1,3}, Patricia A. Spears¹, Charles M. Perou PhD^{1,3} and Lisa A. Carey MD¹ ¹ Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, USA ² University of Milan, Milan, Italy ³ Department of Genetics, University of North Carolina, Chapel Hill, NC, USA ⁴ Department of Biostatistics, University of North Carolina, Chapel Hill, NC, USA Background PIK3CA mutations have been described in 20-25% of early-stage HER2-positive breast tumors [1], and are associated with reduced pathologic complete response (pCR) rate after chemotherapy and anti-HER2 agents [2]. However, the independence of this finding and association with long-term outcomes within HER2+ patients is still largely unknown. Here, we studied the prognostic implications of PIK3CA mutations by hormone receptor (HR) status and intrinsic subtype in patients with early stage HER2+ breast cancer enrolled in CALGB 40601. Method In CALGB 40601, gene expression profiling by RNA sequencing (RNAseq) with PAM50-determined intrinsic subtype and PIK3CA mutations from whole exome sequencing (WES) were obtained from 184/305 (60%) pretreatment core

biopsies. We examined the association of PIK3CA mutations with pCR and event free survival (EFS) by HR status and intrinsic subtype using logistic and Cox regression analyses. Results PIK3CA mutations were found in 32 patients (32/184, 17%). The most frequent mutation was H1047R (12/32,38%), followed by E545K (7/32,22%) and E542K (5/32,16%). PIK3CA mutations were present in 20% and 15% of HR-positive and HR-negative BC subpopulations, respectively. Within Luminal-B, Luminal-A and HER2-Enriched breast tumors, PIK3CA mutations occurred in 36%, 10% and 19% respectively. In the overall population there was lower rate of pCR in mutated-PIK3CA patients than wild-type (34% vs 49%). Using only the subset of patients treated with neoadjuvant trastuzumab-based therapy as standard of care (excluding the lapatinib plus paclitaxel arm), we found a statistically significant lower pCR rate among PIK3CA-mutated tumors using logistic regression model (30% vs 54%, OR=0.30, $p=0.045$). At a median follow-up of 9.1 years, the presence of PIK3CA mutation was significantly associated with worse EFS in the overall study population (HR 2.58, 95% CI 1.24-5.35, $p=0.011$). In a multivariable model including pCR status, HR status and intrinsic subtype (HER2-E vs. not), PIK3CA mutation was independently and significantly associated with worse EFS (HR 2.18, 95% CI 1.04- 4.56, $p=0.039$). The negative impact of PIK3CA mutation on EFS was statistically significant only in patients with HR-positive (HR 3.6, 95% CI 1.45-8.96, $p=0.06$) and luminal breast tumors (HR 4.84, 95% CI 1.08-21.7, $p=0.039$), but not in HR-negative and non-luminal subtypes. Conclusion In our study, the presence of PIK3CA mutation was significantly associated with lower pCR rates in patients treated with chemotherapy plus trastuzumab. Moreover, in uni- and multivariable Cox models, PIK3CA mutations were associated with worse long-term survival, which appeared to be driven by HR-positive and luminal HER2-positive breast tumors. References 1. Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumors. *Nature* 2012;490:61–70. 2. Loibl S, Majewski I, Guarneri V, Nekljudova V, Holmes E, Bria E, et al PIK3CA mutations are associated with reduced pathological complete response rates in primary HER2-positive breast cancer: pooled analysis of 967 patients from five prospective trials investigating lapatinib and trastuzumab. *Ann Oncol* 2016;27:1519–25.

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PD18-05

PD18-05 MEN1611, a PI3K inhibitor, combined with trastuzumab ± fulvestrant for HER2+/PIK3CA mutant advanced or metastatic breast cancer: updated safety and efficacy results from the ongoing phase 1b study (B-PRECISE-01)

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Background: MEN1611 (MEN) is an oral PI3K inhibitor active on the p110 α mutant and wild type, β and γ isoforms, while sparing the δ . B-PRECISE-01 is an open-label, 2-arm, phase 1b study investigating MEN1611 in combination with trastuzumab \pm fulvestrant in patients with HER2 positive/PIK3CA mutated metastatic breast cancer (MBC). No dose-limiting toxicities were observed during the dose-escalation step and MEN1611 48 mg BID was selected as the recommended phase 2 dose (RP2D) for cohort expansion (CE). Methods: Eligible patients had HER2+/PIK3CA-mutated MBC and were treated with at least 2 prior lines of anti-HER2-based

therapy in the advanced/metastatic setting including trastuzumab. Patients received MEN1611 + trastuzumab (MEN+T); hormone receptor positive (HR+) postmenopausal women received M+ T + fulvestrant (MEN+T+F). Recruitment was closed in December 2021. Pooled safety and efficacy data from the two subpopulations of CE are presented herein. Results: As of June 2022, 62 female patients were treated: 56 of them with MEN1611 48 mg BID (25 MEN+T and 31 MEN+T+F). Median age 55.5 years (range 34-78), 21% premenopausal, ECOG PS 0-1: 95.2%. Median metastatic regimens 4; 71.0% had prior pertuzumab and 91.9% had prior T-DM1. Common treatment-emergent adverse events (TEAEs, $\geq 20\%$) were diarrhea 66.1%, nausea 45.2%, hyperglycemia 43.6%, anemia 35.5%, asthenia 29.0%, decreased appetite 27.4%, rash 25.8%, aspartate aminotransferase increased 22.6%, vomiting 22.6%, and pyrexia 22.6%. Common TEAEs with CTCAE grade ≥ 3 ($\geq 10\%$) were hyperglycemia (22.6%) and diarrhea (11.3%). Most treatment-related AEs (TRAEs) were reversible and manageable by supportive care. TEAEs leading to permanent treatment discontinuation occurred in 9 patients (14.5%), the only TEAE occurring in more than one patient was lipase increased (3.2%). TEAEs caused temporary treatment interruptions in 32 patients (51.6%), the most common being hyperglycemia (21.0%) and diarrhea (9.7%). TEAEs leading to dose reduction occurred in 14 patients (22.6%), the most common being diarrhea (6.5%), hyperglycemia (3.2%) and stomatitis (3.2%). Serious TRAEs were experienced by 12 patients (19.4%): hyperglycemia 6 patients, diarrhea 3 patients, anemia, general physical health deterioration, generalized edema, lipase increased, ketoacidosis and pneumonitis (1 patient each). In the efficacy-evaluable population at the RP2D (n=41) 14 patients (34.1%) showed partial response (MEN+T 5/15, MEN+T+F 9/26), 1 patient (2.4%) had a complete response (MEN+T 1/15) and 23 patients (56.1%) had stable disease (MEN+T 6/15, MEN+T+F 17/26) as best response. At the RP2D, the median (95% CI) overall survival (OS) was 21.9 (11.9, NE) months and the median (95% CI) progression free survival (PFS) 5.6 (3.7, 7.2) months. In the MEN+T group, the median OS was 11.9 (5.7, NE) months and median PFS 3.9 (2.3, 6.7) months. In the MEN+T+F group the median OS was 21.9 (16.9, NE) months and median PFS 5.7 (3.7, 11.5) months. Five patients continue on treatment. Conclusions: Updated results from B-PRECISE-01 demonstrated that MEN1611 combined with trastuzumab \pm fulvestrant continued to show a manageable safety profile with encouraging anti-tumor activity and duration of response in heavily pre-treated patients with HER2+/PIK3CA-mutated advanced or metastatic breast cancer.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

PD18-06

PD18-06 Image-guided optimization of neoadjuvant chemotherapy duration in stage II and III HER2-positive breast cancer: radiologic and pathologic complete response (pCR) rates in the multicenter phase 2 TRAIN-3 study (BOOG 2018-01)

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Background

pCR rates in stage II – III HER2-positive breast cancer have greatly improved since the addition of HER2 targeted agents to neoadjuvant chemotherapy and are associated with excellent long-term survival. While longer treatment regimens increase pCR rate, early complete responses are also common. We evaluated an image-guided approach to tailor chemotherapy duration based on the identification of early complete responders.

Methods

45 hospitals across the Netherlands participated in the phase 2 TRAIN-3 trial. Patients received neoadjuvant systemic treatment consisting of paclitaxel, trastuzumab, carboplatin and pertuzumab (PTC-Ptz). Response to treatment was monitored every three cycles and patients were referred for surgery in case of a radiologic complete response (rCR) or after a maximum of 9 cycles. RCR was defined as the absence of pathological enhancement on MRI breast plus negative vacuum assisted core biopsies in case of hormone-receptor positive (HR+) tumors. In addition, negative fine needle aspiration or lymph node biopsy was required in patients with nodal involvement at baseline. The primary endpoint was 3-year event-free survival (EFS). Here, we report locally assessed rCR and pCR rates after 3, 6 and 9 cycles, the negative predictive value of rCR assessment and the incidence of adverse events (AEs). Analyses are stratified by HR-status.

Results

We included 467 patients between April 2019 and May 2021. Median age was 51 years, 69% had stage II disease and 232 had HR+ tumors. 33.6% of HR- patients and 15.5% of HR+ patients achieved pCR after 3 cycles of PTC-Ptz (see table). The NPV was higher in HR- patients and independent of the number of cycles. AE evaluation is currently ongoing.

Conclusion

Three cycles of PTC-Ptz induce an early pCR in one in three HR- and one in six HR+ tumors in patients with stage II-III HER2+ breast cancer. Dynamic contrast enhanced MRI-based response evaluation identifies these patients with $\pm 87\%$ certainty in HR- disease and $\pm 58\%$ in HR+ disease. Continuation of PTC-Ptz after 6 cycles further improves pCR rates and can be considered to reduce the need for adjuvant T-DM1. Efficacy and safety of this image-guided approach to tailor treatment duration need to be confirmed with follow-up in EFS and OS analyses.

Cumulative rCR & pCR according to HR-status

Table. Cumulative rCR & pCR according to HR-status

	1-3 cycles	1-6 cycles	1-9 cycles
HR- (n=235)			
rCR	83 (35.3%)	139 (59.1%)	168 (71.5%)
pCR	79 (33.6%)*	141 (60.0%)*	188 (80.0%)*
rCR & pCR	73 (31.1%)	123 (52.3%)	147 (62.6%)
NPV (rCR & pCR / rCR)	88.0%	88.5%	87.5%
HR+ (n=232)			
rCR	60 (25.9%)	107 (46.1%)	129 (55.6%)
pCR	36 (15.5%)*	73 (31.5%)*	99 (42.7%)*
rCR & pCR	34 (14.7%)	63 (27.2%)	76 (32.8%)
NPV (rCR & pCR / rCR)	56.7%	58.9%	58.9%

*Including patients who underwent surgery for other reasons than rCR

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

PD18-07

PD18-07 Omission of chemotherapy in the treatment of HER2-positive and hormone-receptor positive metastatic breast cancer – interim results from the randomized phase 3 DETECT V trial

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Background: Metastatic breast cancer (MBC) is an incurable disease and both the improvement of survival and maintenance of quality of life (QoL) are equally important aims of treatment planning. In patients with HER2-positive MBC, taxane-based chemotherapy in combination with dual HER2 targeted therapy with trastuzumab (T) and pertuzumab (P) is the standard of care first line therapy. However, adverse events are well-known side effects of any cytostatic treatment and can seriously impact the patients' QoL. In addition, in HER2-positive MBC

activated estrogen receptor (ER) signaling is associated with primary or secondary resistance. Thus, for patients with HER2-positive and hormone-receptor (HR) positive MBC, the synergistic combination of dual HER2-targeted therapy plus endocrine therapy might offer a better treatment option compared to cytotoxic chemotherapy-based treatments. Methods: Between 9/2015 and 11/2022, the multicenter phase III DETECT V trial randomized patients with HER2-positive and HR-positive (i.e. ER positive and/or progesterone-receptor positive) MBC in the 1st-3rd line setting 1:1 to receive T and P combined with either endocrine therapy or chemotherapy followed by maintenance therapy with T, P and endocrine therapy. Chemotherapy and the endocrine agents could be chosen from a variety of available regimens according to physicians' choice. Based on emerging data strongly suggesting an additional benefit of CDK4/6 inhibitors, an amendment came into effect in January 2019 with the addition of ribociclib to both treatment arms after 124 patients had been randomized. The primary objective of DETECT V is to compare tolerability between the chemotherapy-free and chemotherapy-containing treatment arm; secondary objectives comprise the comparison of PFS, OS and safety. Here we report results of an unplanned interim analysis with data cut off June 22th 2022. Results: The results reported here are based on 153 patients for whom end of study was documented at the time of data cut off for this interim analysis (120 patients randomized before and 33 patients randomized after the addition of ribociclib; 115 patients in the 1st line setting; 77 and 76 patients in the chemotherapy-free and chemotherapy-containing arm, respectively). Overall survival (OS) and progression-free survival (PFS) did not differ between patients receiving chemotherapy-free and chemotherapy-containing treatment (median OS not yet reached vs. 37.2 months, hazard ratio 0.87, 95% CI 0.51 – 1.50, p = 0.63; median PFS 15.6 vs. 14.9 months, hazard ratio 0.98, 95% CI 0.64 – 1.52, p = 0.93). Study treatment was terminated prematurely significantly less often in the chemotherapy-free treatment arm (43.9% vs. 72.2%, p = 0.001). Furthermore, tolerability was better for the chemotherapy-free treatment as there were less adverse events (AEs) of any grade (585 vs. 793; 70 vs. 71 patients affected), less AEs grade 3 or higher (66 vs. 90; 33 vs. 48 patients affected) and less serious adverse events (45 vs. 52; 28 vs. 29 patients affected) reported in the chemotherapy-free treatment arm as compared to the chemotherapy-containing treatment arm. Conclusion: These preliminary results suggest that chemotherapy-free treatment for patients with triple-positive MBC might be an effective and well tolerated option.

Disclosure(s):

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12/9/2022

7:00 AM - 8:15 AM

PD18-08

PD18-08 Efficacy and safety results of KN026, a HER2-targeted bispecific antibody combined with docetaxel in first-line treatment of HER2-positive recurrent/metastatic breast cancer

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Background: 1. The 3-drug combination therapy, trastuzumab, pertuzumab, and taxane chemotherapy is one of the standard treatment options for the first-line treatment of HER2-positive recurrent/metastatic breast cancer. 2. KN026 is a novel bispecific HER2-targeted antibody : Fully humanized, IgG1-like antibody binds to two distinct HER2 epitopes, the same domains as trastuzumab (ECD4) and pertuzumab (ECD2). IgG1 Fc fragment of KN026 binding FcγRIIIa mediates potent ADCC 3. Preliminary safety and efficacy results from Phase 1 study data (data as of January 22, 2020) of KN026 monotherapy in HER2-positive advanced breast cancer were presented at ASCO 2020, showed promising efficacy and well tolerated safety. Herein, we present the results from the phase 2 trial. Methods: □ Eligible subjects with HER2-positive and first-line systemic treatment-naïve (relapse ≥12 months after the end of

neoadjuvant/adjuvant therapy) recurrent or metastatic breast cancer were enrolled in this study. □ Subjects received KN026 30 mg/kg combined with docetaxel 75 mg/m² Q3W until disease progression, unacceptable toxicity, withdrawal of informed consent from subjects, or other circumstances that require drug discontinuation. □ The primary endpoints were ORR and duration of response (DoR). The secondary endpoints included safety, PFS and OS. Results: □ At data cut-off date (Mar 26, 2022), the median follow-up was 13.8 months (Interquartile Range [IQR] 12.22, 14.00). 57 subjects were enrolled, the median age was 52 years, 100% were female, and 89.5 % (51/57) were stage IV. □ Of the 55 subjects evaluable for efficacy, 21 had received prior taxane, 4 had received prior trastuzumab in combination with taxane, 30 without any prior trastuzumab and taxane. Nearly half of the subjects (25/55) had previously received trastuzumab and/or taxane chemotherapy. □ The confirmed ORR within 55 evaluable subjects was 76.4% (95% CI: 62.98, 86.77) and DoR was 18.1 months (95% CI: 12.45, NE). □ Median PFS was 19.3 months (95% CI: 13.86, NE) and median OS was not reached. Median PFS is not yet mature. The 12-, and 18-month OS rates were 93.5% (95% CI: 80.79, 97.89), and 88.3 % (95% CI: 68.93, 95.92), respectively. □ The confirmed ORR was 80% in 30 trastuzumab-and taxane-naïve subjects. Among these subjects, OS rates at 12, and 18 months were 100% (95% CI: 100,100), and 90.0% (95% CI: 47.30, 98.53), and the median PFS was 19.3 months (95% CI:13.77, NE). □ Treatment emergent adverse events with incidence rate ≥20% and TEAE≥Grade 3 were neutropenia (n=23, 40.4%) and leucopenia (n=16, 28.1%), respectively. □ The incidence of serious adverse events was 15.8%(9/57), including 5.3% (3/57) for febrile neutropenia, 3.5% (2/57) for leucopenia, and less than 2% for other SAEs □ There were no deaths due to KN026 drug-related AEs in this study. Conclusions: KN026 in combination with docetaxel is well tolerated and has shown promising clinical benefit as a 1L treatment for HER2-positive advanced breast cancer. At data cut-off date (Mar 26, 2022) , median PFS was 19.3 months while 18-month OS rate was 88.3%, which is very encouraging. Efficacy and safety require large-scale phase III studies to verify.

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Qingyuan Zhang, n/a: No financial relationships to disclose

Jingxuan Wang, n/a: No financial relationships to disclose

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12/9/2022

7:00 AM - 8:15 AM

PD18-09

PD18-09 ACE-Breast-03: Efficacy and safety of ARX788 in patients with HER2+ metastatic breast cancer previously treated with T-DM1

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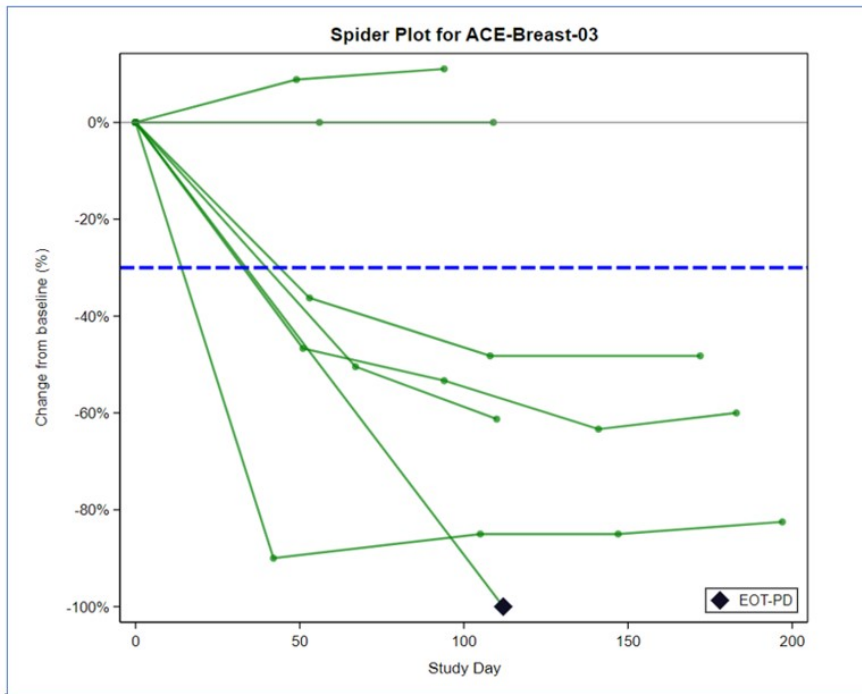
Background: Amplification of the human epidermal growth factor receptor 2 (HER2) gene with consequent HER2 protein overexpression occurs in approximately 20% of breast cancers (BC) and is a major driver of tumor development and progression. The HER2-targeted ADC trastuzumab emtansine (T-DM1) has been approved for the treatment of HER2-positive metastatic BC (mBC) after prior trastuzumab and taxane therapy. However, disease progression occurs in all patients requiring additional therapeutic options. The use of second-generation anti-HER2 ADCs using alternative molecules is being investigated to overcome drug resistance. ARX788 is a next-generation ADC using a technology platform whereby a HER2-specific monoclonal antibody is conjugated with Amberstatin269, a potent cytotoxic tubulin inhibitor. Site-specificity, high homogeneity, and stable covalent conjugation of ARX788 lead to its slow release and prolongation of the peak serum pAF-AS269 concentration, which may contribute to the lower systemic toxicity and increased targeted delivery of payload to tumor cells at a lower effective dose compared to other HER2 ADCs. Here, early evidence of activity of ARX788 in patients previously treated with T-DM1 is shown.

Methods: ACE-Breast-03 (NCT04829604) is an ongoing global, phase 2, single-arm study evaluating ARX788 in patients with HER2+ mBC whose disease has progressed following T-DM1, T-DXd, and/or tucatinib-containing regimens. The ARX788 is administered with an initial dose of 1.5 mg/kg Q4W and subsequent doses of 1.3 mg/kg Q4W. Eligibility criteria included central laboratory confirmed HER2+ mBC per ASCO/CAP guidelines, measurable disease, and adequate organ function. Stable treated brain metastases are allowed. Patients with interstitial lung disease (ILD) or pneumonitis in prior 12 months; active ocular infections or any chronic corneal disorder; are excluded. The primary endpoint is overall response rate (ORR).

Results: At the data cutoff of 11-Jul-2022, 7 patients were enrolled in ACE-Breast-03 (v1.0) who previously experienced disease progression on T-DM1 and had response-evaluable disease. Pts had a median age of 59 years and had received a median of 5 lines of prior anti-HER2 cancer therapy (range: 2-8). None of the pts in this subset had received T-DXd or tucatinib. 5 pts were previously treated with HER2-targeted TKIs (neratinib and lapatinib), as well as an investigational HER2 ADC and responded to ARX788 (3 PR; 2 SD). Two patients had hormone receptor (HR)-positive disease and 5 had HR-negative mBC. Treatment with ARX788 remains ongoing with the median time of ARX788 therapy of 4.5 months. The confirmed ORR was 57.1% (4/7 pts) and an unconfirmed ORR of 71.4% (5/7 pts) as one pt experienced an unconfirmed response with PR after 2 cycles. The disease control rate (DCR) was 100% (7/7 pts). No drug-related grade ≥ 3 AEs were reported; 57.1% (4/7 pts) reported ocular AEs including grade 1 events in 3 pts (i.e., dry eye, blurred vision) and a grade 2 event in one pt (lagophthalmos). No pneumonitis or ILD was observed. ARX788 was well-tolerated, and AEs were manageable.

Conclusion: In this small cohort of patients previously treated with T-DM1, ARX788 had a manageable AE profile and demonstrated promising clinical activity (confirmed ORR 57%; DCR 100%).

ACE-Breast-03 Spider Plot for patients with mBC who were previously treated with T-DM1



ARX788 demonstrated promising clinical activity in patients previously treated with T-DM1.

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7:00 AM - 8:15 AM

PD18-10

PD18-10 Treatment of HER2-positive (HER2+) hormone-receptor positive (HR+) metastatic breast cancer (mBC) with the novel combination of zanidatamab, palbociclib, and fulvestrant

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Background: HER2+ mBC remains incurable, with a need for new HER2-directed therapies and regimens, including chemotherapy-free options. Zanidatamab (zani) is a novel HER2-targeted bispecific antibody that binds HER2 in a unique trans configuration, driving multiple mechanisms of antitumor activity, including complement-dependent cytotoxicity. A CDK4/6 inhibitor combined with endocrine therapy is an approved treatment for HER2-negative/HR+ mBC and this combination has also demonstrated encouraging antitumor activity when paired with HER2-targeted therapy(ies) in HER2+/HR+ mBC. Here, we report results from ZWI-ZW25-202 (NCT04224272), an ongoing single-arm phase 2 study of zani combined with palbociclib (palbo) and fulvestrant (fulv) in pts with HER2+/HR+ mBC. Methods: Eligibility requirements include: HER2+/HR+ unresectable, locally advanced BC or mBC; ECOG PS of 0 or 1; prior treatment with trastuzumab, pertuzumab and T DM1 (additional prior HER2-targeting agents are permitted); and no prior treatment with CDK4/6 inhibitors. Part 1 of the study evaluated the safety and tolerability of the zani/palbo/fulv combination and determined the recommended doses for use in Part 2, where the antitumor activity of the combination is being evaluated. Endpoints include safety outcomes, progression-free survival at 6 months (PFS6), confirmed objective response rate (cORR) per RECIST v1.1; disease control rate (DCR=complete response [CR] plus partial response [PR] plus stable disease [SD]); duration of response (DOR); PFS; and overall survival. Results: As of 24 Feb 2022, 34 pts (33 HER2+/HR+ per central analysis) with a median age of 52 (range 36-77) have been treated. In the metastatic setting, pts had received a median (range) of 4 (1-10) prior systemic regimens, including 3 (1-8) different prior HER2 targeted therapies, and 1 (0-4) endocrine therapy. Seven pts (20%) had prior T DXd treatment and 7 pts had prior fulv treatment. All pts received zani (20 mg/kg Q2W) and standard doses of palbo and fulv. Eighteen pts (53%) remained on treatment; median duration of zani treatment was 6.9 mo (range 0.5-16.3). A dose-limiting toxicity (DLT) of neutropenia occurred in 1 of 7 DLT-evaluable pts in Part 1. Among all pts (n=34), the most

common (>20%) treatment (zani, palbo and/or fulv)-related adverse events (TRAEs) were diarrhea (74%), neutrophil count decreased/neutropenia (62%), stomatitis (41%), asthenia (26%), nausea (24%), and anemia (21%). Grade (Gr) ≥ 3 TRAEs in 2 or more pts included neutrophil count decreased/neutropenia (50%), anemia (6%), diarrhea (6%), and thrombocytopenia (6%). AEs of special interest were all Gr ≤ 2 and included 4 pts with cardiac events (LVEF decrease of $\geq 10\%$ from baseline) and 1 pt with infusion-related reaction. There were no treatment-related serious AEs. Palbo was discontinued for 1 pt due to an AE (AST increase); no pt discontinued zani treatment as a result of AEs. Two deaths occurred: 1 due to disease progression and 1 due to an unrelated AE of pneumonia caused by COVID-19. In 29 pts with measurable disease, the cORR was 34.5% (95% CI: 17.9, 54.3), all responses were cPRs, of which 1 is pending CR confirmation. DOR ranged from 2.3 to 14.9+ mo, with 8 confirmed responses ongoing, and the DCR was 93.1% (95% CI: 77.2, 99.2). Interim median PFS was 11.3 mo (range 0.03-16.7; 95% CI: 5.6, not estimable). PFS6 analysis is planned following the completion of enrollment. Conclusions: Zani in combination with palbo and fulv shows encouraging antitumor activity with durable responses in heavily pretreated pts and a manageable safety profile. This regimen has the potential to be a chemotherapy-free treatment option in pts with HER2+/HR+ mBC. Enrollment in the study is continuing.

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12/9/2022

7:00 AM - 8:15 AM

PD18-11

PD18-11 Dose-Expansion Study of Trastuzumab Deruxtecan as Monotherapy or Combined With Pertuzumab in Patients With Metastatic Human Epidermal Growth Factor Receptor 2-Positive (HER2+) Breast Cancer in DESTINY-Breast07 (DB-07)

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Background: In trials of HER2+ metastatic breast cancer (mBC), trastuzumab deruxtecan (T-DXd) monotherapy showed durable efficacy (DESTINY-Breast01) and significantly prolonged progression-free survival vs trastuzumab emtansine (DESTINY-Breast03). T-DXd is approved in the US for patients with HER2+ unresectable/mBC who received ≥ 1 prior anti-HER2-based treatment (tx) in the metastatic or neo-/adjuvant setting and recommended for approval in the EU as 2nd-line tx. Preclinical data suggest that T-DXd used in combination with other anticancer tx may lead to improved efficacy. The purpose of DB-07 is to assess the safety and efficacy of T-DXd alone or with other anticancer tx for patients with HER2+ mBC. Here we report preliminary data from the DB-07 dose-expansion phase for T-DXd monotherapy and T-DXd + pertuzumab (P) as 1st-line (1L) tx in mBC.

Methods: DB-07 (NCT04538742) is an ongoing, phase 1b/2, 2-part (part 1: dose finding; part 2: dose expansion), modular, open-label trial of T-DXd alone or with other anticancer tx in patients with HER2+ mBC. In part 2, patients in module (mod) 0 received T-DXd 5.4 mg/kg every 3 weeks (Q3W) and in mod 2, T-DXd 5.4 mg/kg + P 420 mg Q3W (loading dose: 840 mg), the recommended phase 2 dose. Patients in these mods must be mBC tx naive. For part 2, the primary objective is to assess safety and tolerability. A secondary objective is to assess the objective response rate (ORR) per local investigators by Response Evaluation Criteria In Solid Tumors v1.1. We report results for patients randomized before Oct 13, 2021 to mods 0 and 2 of part 2 (data cutoff [DCO]: Mar 4, 2022); recruitment is ongoing. Based on the distinct mechanism of action of T-DXd and P, we conducted preclinical studies with the drugs in HER2-overexpressing cell lines to elucidate their potential synergies. To assess the effects on T-DXd internalization, live cell imaging was performed using pH-dependent fluorescently labeled T-DXd. To assess the effects on HER2 signaling, total and p-HER2 levels and downstream substrates were evaluated by immunoblot.

Results: 23 patients were enrolled in the T-DXd monotherapy mod; 20 (87.0%) were receiving tx and 3 (13.0%) discontinued tx (withdrawal by patient, n=2; adverse event [AE], n=1) by DCO.

22 patients were enrolled in the T-DXd + P mod; 20 (90.9%) were receiving tx and 2 (9.1%) discontinued tx (AE, n=1; disease progression, n=1) by DCO. All patients experienced AEs (Table); 1 patient in each mod died. The unconfirmed ORR (80% CI) with T-DXd monotherapy and T-DXd + P was 82.6% (68.2%-92.2%) and 77.3% (61.9%-88.5%), respectively; updated data will be presented. Preclinical studies showed that T-DXd was more rapidly and effectively internalized in combination with P than when administered alone. Immunoblotting of cell lysates showed a greater reduction in total HER2 and HER2 signaling in response to combination tx than with T-DXd or P alone.

Discussion: In summary, 1L T-DXd monotherapy and T-DXd + P safety profiles and antitumor activity were consistent with those previously reported for T-DXd. Mature data in these mods are awaited, and other T-DXd combinations are being investigated in additional mods. Preclinical studies showed the potential for P to induce greater internalization of T-DXd and inhibition of HER2-driven signaling. These results support investigation of T-DXd in larger ongoing trials (eg, NCT04784715).

Table. Summary of treatment duration and safety data		
	T-DXd monotherapy (n=23) ^a	T-DXd + pertuzumab (n=22) ^a
Actual treatment duration, median (range), months		
T-DXd	5.6 (0.7-9.3)	5.5 (0.9-9.7)
Pertuzumab	NA	5.5 (0.9-9.7)
Any-grade AEs, n (%)	23 (100)	22 (100)
Any-grade AEs (≥30% in either module), n (%)		
Nausea	17 (73.9)	14 (63.6)
Diarrhea	6 (26.1)	14 (63.6)
Alopecia	11 (47.8)	8 (36.4)
Vomiting	7 (30.4)	9 (40.9)
Anemia	5 (21.7)	7 (31.8)
Fatigue	4 (17.4)	8 (36.4)
Grade ≥3 AEs, n (%)	6 (26.1)	8 (36.4)
Grade ≥3 AEs in >1 patient in either module, n (%)		
Neutropenia	1 (4.3)	4 (18.2)
Anemia	0	2 (9.1)
Diarrhea	0	2 (9.1)
Serious AEs, n (%)	2 (8.7)	3 (13.6)
AEs of special interest, n (%)		
Adjudicated interstitial lung disease/pneumonitis	1 (4.3) ^b	0
Left ventricular dysfunction	2 (8.7) ^c	0
Deaths, n (%)	1 (4.3) ^d	1 (4.5) ^e

AE, adverse event; NA, not applicable; T-DXd, trastuzumab deruxtecan.
^a All patients were female. ^b Interstitial lung disease/pneumonitis was possibly related to T-DXd, was grade 2, and led to discontinuation of T-DXd. ^c Left ventricular dysfunction was possibly related to T-DXd, was grade 2 in both patients and led to T-DXd interruption in 1 patient. ^d Death was due to disease progression (assessed by brain magnetic resonance imaging). ^e Death was due to disease under study (per autopsy report).

Disclosure(s):

Erika Hamilton, MD: Abbvie: Research Funding - Paid to Institution (Ongoing); Accutar Biotechnology: Research Funding - Paid to Institution (Ongoing); Acerta Pharma: Research Funding - Paid to Institution (Ongoing); ADC Therapeutics: Research Funding - Paid to Institution (Ongoing); AKESOBIO Australia: Research Funding - Paid to Institution (Ongoing); Amgen: Research Funding - Paid to Institution (Ongoing); Aravive: Research Funding - Paid to Institution (Ongoing); Arcus: Consulting Fees to Institution (Ongoing); ArQule: Research Funding - Paid to Institution (Ongoing); Artios: Research Funding - Paid to Institution (Ongoing); Arvinas: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); AstraZeneca: Study sponsor, consulting fees and research grant paid to institution (Ongoing);

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12/9/2022

8:30 AM - 9:00 AM

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12/9/2022

8:30 AM - 9:00 AM

Breast cancer prevention in premenopausal women: Accelerating transition from discoveries to clinical translation

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12/9/2022

9:00 AM - 9:15 AM

GS4-01

GS4-01 Impact of Breast Conservation Therapy on Local Recurrence in Patients with Multiple Ipsilateral Breast Cancer – Results from ACOSOG Z11102 (Alliance)

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12/9/2022

9:00 AM - 11:30 AM

General Session 4

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12/9/2022

9:15 AM - 9:30 AM

GS4-02

GS4-02 Oncological Outcomes Following Omission of Axillary Lymph Node Dissection in Node Positive Patients Downstaging To Node Negative with Neoadjuvant Chemotherapy:

the OPBC-04/EUBREAST-06/OMA study

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Background: Data on the oncologic safety of omission of axillary lymph node dissection (ALND) in node positive (N+) patients who downstage to ypN0 with neoadjuvant chemotherapy (NAC) is sparse. Additionally, there is no consensus on which axillary staging procedure should be used in this setting, sentinel lymph node biopsy (SLNB) alone or in combination with localization and retrieval of the clipped positive node, also known as targeted axillary dissection (TAD). Whether the reduction in the false negative rate observed with TAD translates into a significant reduction in the rate of axillary recurrence is unknown. We sought to evaluate oncologic outcomes after omission of ALND in a large, real-world cohort of breast cancer (BC) patients and to compare rates of axillary recurrence after SLNB with dual tracer mapping vs. TAD.

Methods: Data were collected from 19 centers in the Oncoplastic Breast Consortium (OPBC) and EUBREAST networks. Patients with T1-4 biopsy-proven N1-3 BC who underwent NAC followed by axillary staging with either SLNB with dual tracer mapping or TAD and who were pathologically node negative (ypN0) were included. ypN0 was defined as the absence of any tumor or isolated tumor cells. Competing risk analysis was performed to assess the cumulative incidence rates of axillary recurrence, locoregional recurrence, and any invasive (locoregional or distant) recurrence. Two-year cumulative incidence rates were compared between TAD and SLNB using the Gray's test. Type I error rate was set to 0.05 (α).

Results: We included 785 patients (565 treated with SLNB and 220 with TAD) treated with NAC followed by surgery from 01/2014-12/2020. Median patient age was 50 years. The majority (57%) of patients had clinical T2 tumors, and 95% had N1 disease. Most (55%) were HER2+, and 21% were triple negative. Most patients (81%) received anthracycline and taxane-based chemotherapy regimens, but NAC regimens differed between patients treated with TAD and those treated with SLNB (Table 1). All patients with HER2+ tumors received anti HER2 therapy. Nodal radiotherapy was administered to 76% of patients, and was more common in patients who underwent TAD (82% TAD vs 74% SLNB, $p=0.017$). Breast pathologic complete response (ypT0/is) was more frequent among those patients that had TAD (80% TAD vs. 66% SLNB, $p<$

0.001). TAD localization was with wire in 46%, radioactive seed in 40%, ultrasound in 5%, tattoo in 2%, and with a combination of these techniques in 7%. The clipped node was successfully retrieved in 94% of TAD cases. The median number of lymph nodes removed was lower in the TAD group compared to the SLNB group [3 (IQR 3-5) vs 4 (IQR 3-5), $p < 0.001$], as was the median number of sentinel lymph nodes [3 (IQR 2-4) vs 4 (IQR 3-5), $p < 0.001$] (Table 1).

The 5-year rates of any axillary recurrence, locoregional recurrence, and any invasive recurrence in the entire cohort were 1.1% (95%CI 0.39-2.4%), 3.1% (95%CI 1.6-5.3%) and 10% (95%CI 7.6-13%), respectively. The two-year cumulative incidence of axillary recurrence did not differ between patients treated with TAD compared to SLNB (0% vs 0.9%, $p=0.19$).

Conclusion: Early axillary recurrence after omission of ALND in patients who successfully downstage from N+ to ypN0 with NAC is a rare event following both SLNB or TAD, and was not significantly lower in TAD than SLNB. Although longer follow-up is needed to confirm these findings, the main advantage of TAD seems to be a reduction in the number of lymph nodes removed. Overall, these results support omission of ALND in patients who successfully downstage to node negative disease after NAC.

Table 1

Table 1: Clinicopathological Features of the Study Cohort, Stratified by Axillary Staging Technique

	Full cohort n = 785	SLNB only n = 565	TAD n = 220	p-value
Age, median (IQR)	50 (41, 59)	50 (41, 58)	50 (43, 59)	0.3
Race/ethnicity				<0.001
White	519 (66)	341 (60)	178 (81)	
Black	67 (8.5)	62 (11)	5 (2.3)	
Asian	109 (13)	81 (14)	22 (10)	
Hispanic	63 (8)	55 (9.7)	8 (3.6)	
Other/unknown	39 (4.2)	26 (4.6)	7 (3.2)	
Clinical T stage				0.13
1	156 (20)	108 (19)	48 (22)	
2	447 (57)	314 (56)	133 (60)	
3	150 (19)	117 (21)	33 (15)	
4	24 (3.1)	18 (3.2)	6 (2.7)	
X	8 (1)	8 (1.4)	0 (0)	
Clinical N stage				0.4
1	744 (95)	538 (95)	206 (94)	
2	27 (3.4)	19 (3.4)	8 (3.6)	
3	14 (1.8)	8 (1.4)	6 (2.7)	
Number of SLNs removed, median (IQR)	3 (3, 5)	4 (3, 5)	3 (2, 4)	<0.001
Total number of LNs removed, median (IQR)	4 (3, 5)	4 (3, 5)	3 (3, 5)	<0.001
Breast pCR (yp10/1s)				<0.001
Yes	547 (70)	372 (66)	175 (80)	
No	230 (29)	193 (33)	45 (20)	
Occult	8 (1)	8 (1.4)	0 (0)	
NAC regimens HER2- tumors ^a				<0.001
ACT	250 (71)	207 (81)	43 (45)	
ACT+Platinum	71 (20)	38 (15)	33 (35)	
AC free regimen	4 (1.1)	2 (0.8)	2 (2.6)	
Other	25 (7.3)	8 (3.3)	17 (19)	
NAC regimens HER2+ tumors ^b				<0.001
ACT-H	18 (4.1)	14 (4.6)	4 (3.2)	
ACT-HP	288 (66)	235 (76)	53 (42)	
TC-HP	95 (22)	40 (13)	55 (44)	
Other	34 (8)	21 (6.8)	13 (10.4)	
Histology				0.2
Ductal	733 (95)	530 (95)	203 (93)	
Lobular or mixed	29 (3.7)	18 (3.2)	11 (5.0)	
Other	12 (1.6)	7 (1.3)	5 (2.3)	
Unknown	11	10	1	
Tumor differentiation				<0.001
Well	20 (2.6)	10 (1.8)	10 (4.7)	
Moderately	174 (23)	99 (18)	75 (35)	
Poorly	561 (74)	432 (80)	129 (60)	
Unknown	30	24	6	
Subtype				0.6
HR+/HER2-	182(23)	136 (24)	46 (21)	
HR+/HER2+	261 (33)	189 (32)	78 (35)	
HR-/HER2+	174 (22)	129 (23)	45 (20)	
HR-/HER2-	168 (21)	117 (21)	51 (23)	
LVI				0.7
Yes	112 (15)	84 (15)	28 (14)	
Unknown	36	16	20	
Type of breast surgery				0.2
BCS	407 (52)	286 (51)	121 (55)	
Mastectomy	372 (47)	273 (48)	99 (45)	
No breast surgery ^c	6 (0.8)	6 (1.1)	0 (0)	
Whole breast radiotherapy ^d				>0.9
Yes	402 (98)	284 (98)	118 (98)	
No	5 (2)	2 (2)	3 (2)	
Post mastectomy radiotherapy ^e				>0.9
Yes	289 (78)	212 (78)	77 (78)	
No	83 (22)	61 (22)	22 (22)	
Nodal radiotherapy				0.017
Yes	595 (76)	415 (74)	180 (82)	
No	188 (24)	148 (26)	40 (18)	
Unknown	2	2	0	

Frequency (row percent) reported for categorical variables, and median (IQR) reported for continuous variables

SLNs Sentinel Lymph Nodes; LNs lymph nodes; pCR pathological complete response; ACT anthracycline and taxane; AC anthracycline; H Herceptin; HP, Herceptin and Pegjeta; TC taxol (or Taxotere) and carboplatinum; LVI lymphovascular invasion; BCS breast conserving surgery

^a Applies to HER2- tumors only (n=350)

^b Applies to HER2+ tumors only (n=435)

^c Applies to occult cases only

^d Applies to lumpectomy patients only (n=407)

^e Applies to mastectomy patients only (n=372)

Clinicopathological Features of the Study Cohort, Stratified by Axillary Staging Technique

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9:30 AM - 9:45 AM

GS4-03

GS4-03 Validation of Profile for the Omission of Local Adjuvant Radiotherapy (POLAR) in a meta-analysis of three randomized controlled trials of breast conserving surgery +/- radiotherapy

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9:45 AM - 10:00 AM

GS4-04

GS4-04 Population-based Estimates of contralateral Breast Cancer Risk among Carriers of Germline Pathogenic Variants in ATM, BRCA1, BRCA2, CHEK2, and PALB2

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Purpose To estimate the risk of contralateral breast cancer (CBC) among women in the general population with germline pathogenic variants (PVs) in ATM, BRCA1, BRCA2, CHEK2, and PALB2. **Methods** Among 15,104 prospectively followed women within the CARRIERS study treated with ipsilateral surgery for invasive breast cancer, a subset of 14,237 women were identified from population-based studies. The risk of CBC was estimated for PV carriers in each gene compared to women without PVs in a multivariate proportional hazard regression analysis accounting for the competing risk of death and adjusting for patient and tumor characteristics. The primary analyses focused on the overall cohort and on women from the general population. Secondary analyses examined associations by race/ethnicity, age at primary breast cancer diagnosis, menopausal status, and tumor estrogen receptor status. **Results** Germline BRCA1, BRCA2, and CHEK2 PV carriers with breast cancer were at significantly elevated risk (Hazard ratio ≥ 1.9 , $p < 0.05$) of CBC, whereas only the PALB2 PV carriers with ER-negative breast cancer had elevated risks. In contrast, ATM PV carriers did not have significantly increased CBC risks. African American PV carriers had similarly elevated risks of CBC as non-Hispanic White PV carriers. Among premenopausal women, the 15-year cumulative incidence of CBC was $>20\%$ for BRCA1, BRCA2 and CHEK2 PV carriers with breast cancer, and for PALB2 PV carriers with ER-negative breast cancer. The 15-year cumulative incidence of CBC among postmenopausal PV carriers was $< 20\%$ for PV carriers in any of the 5 genes. **Conclusions** Women diagnosed with breast cancer and known to carry germline PVs in BRCA1, BRCA2, CHEK2, or PALB2 are at substantially increased risk of CBC and may benefit from enhanced surveillance and risk-reduction strategies.

Disclosure(s):

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12/9/2022

10:00 AM - 10:15 AM

GS4-05

GS4-05 Phase II randomized trial of conventional versus hypofractionated post-mastectomy proton radiotherapy

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Purpose/Objectives: Proton therapy is under investigation in breast cancer as a strategy to reduce heart and lung exposure, which is associated with late cardiopulmonary adverse events and secondary malignancy. To date, studies investigating postmastectomy radiotherapy (PMRT) with protons have used conventional fractionation. We hypothesized that condensing treatment to 15 fractions would be safe based on evidence that breast cancer is more sensitive to higher dose fractions than surrounding normal tissues. **Materials/Methods:** We conducted a randomized non-inferiority phase II trial comparing conventional and hypofractionated proton PMRT with primary endpoint of 24-month complication rate (defined as grade 3 or higher late adverse events using CTCAE, v 4.0 and/or unplanned surgical intervention in patients undergoing mastectomy with reconstruction). With a 10% non-inferiority margin the study ensured 80% power and had a one sided-type I error rate of 0.05. Cardiotoxicity was assessed with serial transthoracic conventional and 2-dimensional speckle tracking echocardiography (2D-STE). Eligibility included age \geq 18 years with non-inflammatory breast cancer resected by mastectomy with indications for PMRT. Assignment of treatments was balanced with respect to immediate breast reconstruction (IBR). Conventional fractionation group received 50 Gy in 25 fractions of 2 Gy, and hypofractionation group received 40.05 Gy in 15 fractions of 2.67 Gy (RBE 1.1). Target volume included the chest wall and axillary, supraclavicular, and internal mammary lymph nodes. All patients were treated with multi-field optimized pencil beam scanning (intensity modulated proton therapy). **Results:** Between 2016 and 2018, 82 patients were enrolled and randomized (41 conventional, 41 hypofractionation). Median patient age was 52 years. 32.9% were staged T3-T4 and 79.3% node positive at diagnosis. 57 of 82 patients (69.5%) elected IBR. The median mean heart dose was 0.49 Gy and the median ipsilateral lung volume receiving 40% of prescription or greater (V40%) was 13.6%. No significant changes on conventional or 2D-STE at end-of-treatment or 3-month follow-up compared to baseline were observed. The rate of \geq grade 2 acute dermatitis was lower with hypofractionation (44% vs 15%, $p = 0.006$). Other \geq grade 2 acute adverse events including esophagitis (0 vs 5%), infection (5% vs 2.4%) and skin hyperpigmentation (7.3% vs 4.8%) were not significantly different between the two arms. With a median follow-up of 38.3 months, the 24-month complication rate was conventional 14.6% vs hypofractionation 17.1% (absolute difference 2.4%, $p=0.17$, 95% CI [-0.4, 15.7%]). In patients with IBR, 6 of 28 (21.4%) conventional and 7 of 29 (24.1%) hypofractionated patients developed complications ($p = 0.80$). There was no significant difference in 3-year disease-free survival between the conventional (89.4%; 95% CI 80.0 – 99.8%) and hypofractionated (92.4%, 95% CI 84.5 – 100.0%) arms ($p = 0.91$). One local recurrence occurred in the hypofractionated arm simultaneous with regional and distant relapse. The remaining 6 recurrences were isolated distant events. **Conclusions:** Proton PMRT provided excellent locoregional control and normal tissue sparing. There were no subclinical echocardiographic changes indicative of radiation-induced cardiac dysfunction. Hypofractionation resulted in comparable disease control, tolerability and reconstruction outcomes as conventional fractionation. Although non-inferiority of hypofractionation could not be established based on the upper bound of the 95% confidence interval for complication rate being greater than 10%, both conventional and hypofractionation may be considered appropriate regimens for ongoing phase 3 randomized trials comparing photon and proton radiotherapy.

Disclosure(s):

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12/9/2022

10:15 AM - 10:30 AM

GS4-06

GS4-06 Radiomic phenotypes of breast texture and association with breast cancer risk and masking

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Breast parenchymal patterns on radiologic images are associated with breast cancer risk. Radiomic features have been proposed as quantitative measures of parenchymal patterns. We defined intrinsic imaging phenotypes of breast parenchymal patterns based on radiomic features extracted from full field digital mammography (FFDM) in breast screening populations and assessed whether these phenotypes are associated with breast cancer risk and masking. We selected 30,000 women with 4-view FFDM exams from Hologic machines from three institutions (Hospital of the University of Pennsylvania, Mayo Clinic, and San Francisco Mammography Registry), randomly split into a training (20,000 women) and test set (10,000 women). In total, 390 radiomic features were automatically extracted from each image using a validated software pipeline, standardized, and adjusted for site differences using ComBat. We used two methods, hierarchical clustering and Principal Components (PCs) analysis, to classify significant variation among the features in the training set and replicate among the test set. Next, we applied the replicated clusters and PCs to an independent nested case-control set [1082 invasive breast cancer (BC) cases (of which 151 were Black and 893 White women, 38 other race) matched to 2837 controls (411 Black and 2345 White women, 81 other race) on age, race, timing of images, and site]. We examined associations of the clusters and PCs with invasive breast cancer risk, as well as masking [defined as a false-negative (FN) screen (124 cases and 319 matched controls) and additionally the subset with symptomatic interval cancer (IC) within 12 months of negative screen (88 cases and 223 matched controls)] using conditional logistic regression. We evaluated their association with breast cancer alone, and with adjustment for age, body mass index (BMI) and breast density assessed by Breast Imaging Reporting and Data System (BI-RADS) using likelihood ratio tests. We estimated discrimination using area under the curve (AUC) and compared AUCs for models that included the radiomic clusters and PCs with the model that included only age, BMI and density. We also stratified analyses by race (Black/White).

From hierarchical clustering, we defined six statistically significant phenotype clusters (each of at least 1000 women) in the training set which were replicated in the test set. For PC Analysis, we identified six PCs in the training set, explaining 85% of the variation in texture features and reproduced these in the test set. The six radiomic phenotype clusters ($P < 0.001$) and six PCs ($P < 0.001$) were both associated with invasive BC, including after adjusting for age, BMI, and density (cluster $P = 0.004$; PCs $P < 0.001$). Improvements in discrimination of invasive BC with inclusion of PCs or clusters were more pronounced among Black women (Table). Further, the PCs ($P < 0.001$) and clusters ($P < 0.001$) were significantly associated with FN overall and for symptomatic IC (PCs $P < 0.001$; clusters $P = 0.001$), but only PCs remained significant after adjusting for age, BMI and density (PCs $P = 0.004$ for FN; PCs $P = 0.007$ for symptomatic IC). Discrimination of masking also improved with inclusion of both clusters and PCs (Table). We identified reproducible radiomic phenotypes that are associated with invasive BC risk, above and beyond breast density with the strongest associations for invasive BC among Black women and symptomatic interval cancers.

Table

Group	AUC (95% CI)		
	Age+BMI+BIRADS	Age+BMI+BIRADS+6 Clusters	Age+BMI+BIRADS+ 6 PCs
Invasive BC - Overall	.603 (.585, .621)	.613 (.595, .631)	.616 (.598, .634)
Black Women	.627 (.580, .674)	.646 (.600, .693)	.685 (.640, .730)
White Women	.603 (.583, .623)	.606 (.586, .626)	.615 (.595, .634)
False Negative BC	.636 (.584, .689)	.671 (.619, .722)	.705 (.655, .755)
Symptomatic Interval	.686 (.625, .747)	.740 (.682, .797)	.762 (.706, .818)

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12/9/2022

10:30 AM - 10:45 AM

GS4-07

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12/9/2022

10:45 AM - 11:00 AM

GS4-08

GS4-08 10-year results of a phase 3 trial of low-dose tamoxifen in non-invasive breast cancer

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We have previously shown in a phase 3 trial that tamoxifen 5 mg/day for 3 years decreased by 52% the incidence of recurrence of invasive breast cancer or DCIS after a median follow-up of 5.1 years in women with excised non invasive breast disease, including atypical ductal hyperplasia, DCIS or LCIS (DeCensi et al. JCO 2019; 37:1629). Toxicity was negligible with only an extra hot flash per day in the tamoxifen arm compared with the placebo arm. These findings were incorporated into the ASCO clinical practice guidelines for breast cancer risk reduction as an alternative option to standard doses and duration of tamoxifen or aromatase inhibitors in women with non-invasive disease (Visvanathan et al. JCO 2019; 37:3152). In the present study we update the findings on breast cancer recurrence after a median of 9.14 years (interquartile range, IQR, 7.16-10.73) and a total of 10.57 person years of follow up to see if the treatment effect is retained with more events and after a median of approximately 6 years from treatment cessation. We conducted a national multicenter randomized trial of tamoxifen, 5 mg/d or placebo administered for 3 years after surgery in women with hormone-sensitive or unknown breast intraepithelial neoplasia, including atypical ductal hyperplasia and lobular or ductal carcinoma in situ. The primary end point was the incidence of invasive breast cancer or ductal

carcinoma in situ. Between November 1, 2008, and March 31, 2015, 1,160 women were screened and 500 aged 75 years of age or younger were included in the study. Women with high-grade or comedo/necrotic DCIS received adjuvant radiotherapy of 50 Gy in 25 courses. The mean age was 54 years (standard deviation, 9 years), and 55% of participants were postmenopausal. The mean (SD) body mass index, kg/m², was 25.7 (4.8) on tamoxifen and 25.3 (4.2) on placebo. Twenty percent had ADH, 11% had LCIS, and the remaining 69% had DCIS. After a median follow-up of 9.14 years, there were 22 neoplastic events (invasive breast cancer or DCIS) with tamoxifen and 37 with placebo (annual rate 11.09, 95% CI, 7-30-16.84 on T vs 19.71, 95% CI, 14.28-27.21 on P per 1,000 person-years; hazard ratio, 0.56; 95% CI, 0.33 to 0.95; P = .03), which resulted in a 5-year number needed to treat of 18. Overall, 71% of the recurrences were invasive breast cancer. The follow-up was updated with the most recent visit within 12 months in two thirds of the participants, so an update of all participants will be performed by Sept 30th with full analysis of neoplastic events, annual risk rate ratio, serious adverse events and deaths. Moreover, an updated analysis of potential effect modifiers will be conducted, including menopausal status, baseline estradiol levels, menopausal symptoms, BMI, smoking status and Ki-67 of the primary lesion. In conclusion, our findings indicate that low dose tamoxifen given for 3 years still significantly prevents recurrences from non-invasive breast cancer after a median of 6 years from treatment cessation, providing a valid prevention/interception option in this disease group. Supported by Ente Ospedaliero Ospedali Galliera, Genova, Italy, the Italian Ministry of Health (RFPS-2006-1-339898), the Italian Association for Cancer Research (IG 2008 Grant No. 5611), and the Italian League against Cancer (LILT 7-08).

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12/9/2022

11:00 AM - 11:15 AM

GS4-09

GS4-09 Pregnancy Outcome and Safety of Interrupting Therapy for women with endocrine responsive breast cancer: Primary Results from the POSITIVE Trial (IBCSG 48-14 / BIG 8-13)

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12/9/2022

11:15 AM - 11:30 AM

GS4-10

GS4-10 Discussant for GS4-09

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12/9/2022

10:00 AM - 5:00 PM

Exhibits

12/9/2022

11:30 AM - 12:00 PM

Brinker Award for Scientific Distinction in Clinical Research

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12/9/2022

11:30 AM - 12:00 PM

**The Contribution of NSABP Clinical Trials to the Management of Early Breast Cancer:
PAST AS PROLOGUE**

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12/9/2022

12:00 PM - 12:15 PM

GS5-01

GS5-01 Addition of platinum to sequential taxane-anthracycline neoadjuvant chemotherapy in patients with triple-negative breast cancer: A phase III randomized controlled trial

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Background: Despite several studies, the impact of adding platinum on long-term outcomes in triple-negative breast cancer (TNBC) has not been definitively established. We conducted a single-centre randomized phase III trial to evaluate the efficacy and toxicity of adding platinum to standard neoadjuvant chemotherapy in these patients. Methods: Patients with histopathological diagnosis of TNBC without evidence of distant metastases who were planned to be treated with neoadjuvant chemotherapy (NACT) were randomized to experimental or control arms after stratification by menopausal status (premenopausal or perimenopausal, and postmenopausal) and stage [operable breast cancer (OBC, clinical T1-3, N0-1, M0), and locally advanced breast cancer (LABC, cT4 or N2-3, M0)]. NACT in control arm included paclitaxel 100 mg/m² once per week for 8 weeks followed by doxorubicin (60 mg/m²) or epirubicin (90 mg/m²) plus cyclophosphamide (600 mg/m²) once every 21 days for 4 cycles while in experimental arm carboplatin (area-under-curve 2) was added once per week for 8 weeks with paclitaxel. After NACT patients received standard surgery for primary tumor and axillary lymph nodes (LN) followed by radiotherapy. The primary endpoint was disease-free survival (DFS) and the secondary endpoints were overall survival (OS), pathological complete response (pCR, absence of invasive cancer from breast and LN), and toxicity. Results: Between April 2010 and January 2020, 720 (355 control, 365 experimental) patients with a median age of 46 (25-69) years [< 50 years, 502 (69.7%), premenopausal 418 (58.2%)], were included in the study, of whom 285 (39.6%) had OBC and 435 (60.4%) had LABC, with a median clinical tumor size of 6.0 (1.2- 20.0) cm. At a median follow-up of 67.6 (18.9-142.2) months, in the experimental and control arms, the 5-year DFS were 70.6% (95% CI 65.7-75.5%) and 64.5% (95% CI 59.4-69.6%), respectively (HR 0.79, 95% CI 0.61-1.02, p=0.073), 5-year OS were 74.0 (95% CI 69.3-78.7%) and 66.7% (95% CI 61.6-71.8%), respectively (HR 0.75, 95% CI 0.57-0.98, p=0.034), and pCR were 55.2% (95% CI 49.7-69.5%) and 41.5% (95% CI 36.2-47.0%), respectively (p=0.0004). In subgroup analyses, the benefit of carboplatin was confined to patient's < 50 years, with significant interaction between treatment and age. In women < 50 years of age, in experimental versus control arms, 5-year DFS and OS were 74.5% vs 62.3% (p=0.003, interaction p=0.003) and 76.8% vs 65.7% (p=0.003, interaction p=0.004), respectively. Addition of carboplatin had a significant beneficial impact on OS after adjusting for baseline clinical tumor size and age in a Cox model (HR 0.75, 95% CI 0.58-0.98, p=0.038). In experimental and control arms, numbers of patients with any grade \geq 3 toxicity were 140 (38.5%) and 107/355 (30.14%), respectively, (p=0.02), grade \geq 3 neutropenia were 2/364 (0.55%) and 1/355 (0.28%), respectively, grade \geq 3 thrombocytopenia were 1/364 (0.27%) and 0 (0%), respectively, and febrile neutropenia were 26/364 (7.14%) and 18/355 (5.07%), respectively (p=0.25). Conclusions: This study, to our knowledge the largest reported trial of neoadjuvant platinum in TNBC thus far, suggests that addition of carboplatin to sequential taxane-anthracycline neoadjuvant chemotherapy results in substantial and clinically meaningful improvement in disease-free and overall survival in young patients with TNBC and should be the standard of care in these patients.

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12/9/2022

12:00 PM - 3:00 PM

General Session 5

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12/9/2022

12:15 PM - 12:30 PM

GS5-02

GS5-02 Neoadjuvant paclitaxel/olaparib in comparison to paclitaxel/carboplatinum in patients with HER2-negative breast cancer and homologous recombination deficiency – long-term survival of the GeparOLA study

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Background: The GeparOLA study was designed to evaluate the efficacy and safety of the combination of paclitaxel (P) plus olaparib (O) as part of neoadjuvant chemotherapy (NACT) in patients with human epidermal growth factor receptor 2 (HER2)-negative, either hormone receptor (HR)-positive or HR-negative and homologous recombination deficiency (HRD) defined as having a g/tBRCA mutation and/or a high HRD score. Primary analysis showed a pCR rate of 55.1% (90% CI 44.5%-65.3%) with PO and 48.6% (90% CI 34.3%-63.2%) with P plus carboplatinum (Cb). The PO combination could not exclude a pCR rate of $\leq 55\%$ in the PO arm but was significantly better tolerated. Analysis on the stratified subgroups showed higher pCR rates with PO in the cohorts of patients < 40 years and HR-positive tumors (Fasching Ann Oncol 2020). Here, we report long-term data. Methods: GeparOLA (NCT02789332) was a non-comparative, multicenter, prospective, randomized, open-label, phase II trial. Patients with primary HER2-negative breast cancer, HRD and indication for chemotherapy (cT2-cT4a-d or cT1c and cN+ or cT1c and pNSLN+ or cT1c and TNBC or cT1c and Ki-67 >20%) were randomly assigned to receive either P 80 mg/m² weekly plus O 100 mg twice daily for 12 weeks or P plus Cb area under the curve 2 (AUC2) weekly for 12 weeks, both followed by four cycles of either 2-weekly or 3-weekly epirubicin 90 mg/m² plus cyclophosphamide 600 mg/m². Primary endpoint was pCR (ypT0/is ypN0) rate after NACT with PO followed by EC. Long-term efficacy endpoints included invasive disease-free survival (iDFS), distant disease-free survival (DDFS) and overall survival (OS). The time-to-event endpoints analysis is planned with median follow-up of at least 4 years and a follow-up completeness of at least 80%. Results: Between

September 2016 and July 2018, 274 patients were screened, of whom 107 were randomized and 106 (PO N=69; PCb N=37) started treatment. The median age was 47.0 years (range 25.0-71.0); 32 patients were aged < 40 years; 36.2% of patients had cT1 tumors and 31.8% were cN-positive; the majority (86.8%) had grade 3 tumors and a Ki-67>20% (89.6%). Seventy-seven patients (72.6%) had TNBC. After a median follow-up of 49.8 months (range 0.1-69.1), 18 (15 in PO; 3 in PCb) iDFS events and 7 (6 in PO; 1 in PCb) deaths were reported. The 4-year survival rates are shown in the table below. iDFS (HR PO to PCb=2.86 [95%CI 0.83-9.9], log-rank p=0.081), DDFS (HR =3.03 [95%CI 0.67-13.67], log-rank p=0.129), and OS (HR=3.27 [95%CI 0.39-27.2], log-rank p=0.244) tended to be inferior with olaparib. Patients without g/tBRCA mutation seem to benefit from the use of carboplatinum (7/30 iDFS/DDFS events in PO; 0/16 in PCb, log-rank p=0.037, HR n.a.). Conclusions: In patients with HER2-negative and HRD breast cancer the use of olaparib instead of carboplatinum although showing comparable pCR rates, tended to result in an overall inferior outcome. This was mainly driven by the patients without a g/tBRCA mutation. In patients with a g/t BRCA mutation no difference between olaparib and carboplatinum was seen. Key words: Olaparib, HER2-negative breast cancer, HRD, survival Funding: The study was financially supported by AstraZeneca

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12/9/2022

12:30 PM - 12:45 PM

GS5-03

GS5-03 Evaluation of anti-PD-1 Cemiplimab plus anti-LAG-3 REGN3767 in early-stage, high-risk HER2-negative breast cancer: Results from the neoadjuvant I-SPY 2 TRIAL

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Background: I-SPY2 is a multicenter, phase 2 trial using response-adaptive randomization within biomarker subtypes defined by hormone-receptor (HR), HER2, and MammaPrint (MP) status to evaluate novel agents as neoadjuvant therapy for high-risk breast cancer. The primary endpoint is pathologic complete response (pCR). Cemiplimab is an anti-PD-1 inhibitor approved for the treatment of NSCLC and cutaneous basal and squamous cell CA. Lymphocyte activation gene 3 (LAG-3) binds MHC class II leading to inhibition of T-cell proliferation and activation and is often co-expressed with PD-1. REGN3767 is a fully humanized mAb that binds to LAG-3 and blocks inhibitory T-cell signaling. Concurrent blockade of LAG-3 with an anti-PD-1 may enhance efficacy of an anti-PD-1.

Methods: Women with tumors ≥ 2.5 cm were eligible for screening. Only HER2 negative (HER2-) patients were eligible for this treatment; HR positive (HR+) patients had to be MP high risk. Treatment included Paclitaxel 80 mg/m² IV weekly x 12 and Cemiplimab 350 mg and REGN3767 1600 mg both given q3weeks x 4, followed by doxorubicin/cyclophosphamide (AC) every 2 weeks x 4. The control arm was weekly paclitaxel x 12 followed by AC every 2-3 weeks x 4. Cemiplimab/REGN3767 was eligible to graduate in 3 of 10 pre-defined signatures: HER2-, HR-HER2-, and HR+HER2-. The statistical methods for evaluating I-SPY 2 agents has been previously described. To adapt to changing standard of care, we constructed "dynamic controls" comprising 'best' alternative therapies using I-SPY 2 and external data and estimated the probability of Cemiplimab/REGN3767 being superior to the dynamic control. Response predictive subtypes (Immune+ vs Immune-) were assessed using pre-treatment gene expression data and the ImPrint signature.

Results: 73 HER2- patients (40 HR+ and 33 HR-) received Cemiplimab/REGN3767 treatment. The control group included 357 patients with HER2- tumors (201 HR+ and 156 HR-) enrolled since March 2010. Cemiplimab/REGN3767 graduated in both HR-/HER2- and HR+/HER2- groups; estimated pCR rates (as of June 2022) are summarized in the table. Safety events of

note for Cemiplimab/REGN3767 include hypothyroidism 30.8%, adrenal insufficiency (AI) 19.2%, hyperthyroidism 14.1%, pneumonitis 1.3%, and hepatitis 3.8%. All were G1/2 except for 6 (7.7%) G3 AI and 3 (3.8%) G3 colitis. Rash occurred in 62.8%, 9% G3 and 2 pts (2.6%) had pulmonary embolism. X% of adrenal insufficiency cases required replacement therapy. 40 patients (11 HR+ and 29 HR-) in Cemiplimab/REGN3767 were predicted Immune+; 32 (29 HR+ and 3 HR-) were predicted Immune-. In the HR+ group pCR was achieved in 10/11 (91%) patients with Immune+ subtype compared with 8/29 (28%) with Immune- subtype. Additional biomarker analyses are ongoing and will be presented at the meeting.

Conclusion: The I-SPY 2 study aims to assess the probability that investigational regimens will be successful in a phase 3 neoadjuvant trial. Dual immune blockade with a LAG-3 inhibitor and anti-PD1 therapy resulted in a high predicted pCR rate both in HR-/HER2- (60%) and HR+/HER2- (37%) disease. The novel Imprint signature identified a group of HR+ patients most likely to benefit from this active regimen.

Signature	Estimated pCR rate		Probability Cemiplimab/REGN3767 Superior to Control	Predictive Probability of Success in Phase 3	Probability Cemiplimab/REGN3767 Superior to Dynamic Control
	Cemiplimab/REGN3767	Control			
HER2-	0.446	0.211	>0.999	0.960	N/A
HR-/HER2-	0.593	0.291	>0.999	0.973	0.529
HR+/HER2-	0.370	0.145	>0.999	0.939	0.761

Estimated pCR rates

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12:45 PM - 1:00 PM

GS5-04

GS5-04 Identification of symptoms that are associated with irAEs in the I-SPY clinical trial

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Title. Identification of symptoms that are associated with irAEs in the I-SPY clinical trial
Background. Immunotherapy has emerged as an important component of neoadjuvant therapy for some patients with breast cancer (BC). As a result, immune-related adverse events (irAEs) are increasing and have effects on both short and long term symptoms significantly impacting patient quality of life. BC patients may develop new conditions including arthralgias, gastrointestinal issues, endocrinopathies, and fatigue during or after cancer therapy that may be acute or long-lasting in nature. Monitoring for early onset and severity of symptoms, and adjusting treatment and symptom management could optimize therapy for a particular patient, maximizing potential efficacy while mitigating toxicity. We sought to identify patient demographic characteristics and symptom patterns associated with risk for development of irAEs in the context of a randomized trial for patients with early-stage high-risk breast cancer.
Methods. I-SPY2 is a multi-center, phase 2 trial using response-adaptive randomization for high-risk early-stage women with BC. The study population for this analysis includes enrolled patients receiving combinations of experimental immunotherapy and chemotherapy. Groups considered for statistical comparisons included those that developed an irAE versus those that did not develop an irAE up until the surgery timepoint. In I-SPY adverse events are documented through the Common Terminology Criteria for Adverse Events (CTCAEv5.0). Hypothyroidism, adrenal insufficiency, and pneumonitis were the irAEs considered in this study. A chi-square test was used to assess associations between race and ethnicity (White, Asian, Black, non-Hispanic) and irAEs. One-way ANOVA was used to evaluate the association between age (>50 vs < 50) and irAEs. 33 symptoms reported at CTCAE grade 2 or higher were included in the analyses and a symptom burden score was calculated using area under curve (AUC) which combined the duration of each symptom between baseline and week 6 of treatment, and grade of adverse event. Regularized regression using leave-one out cross validation was used to evaluate early symptoms (as quantified by the symptom burden score) as predictors, and irAEs as surrogate responses.
Results. Out of 461 patients, percentages of patients with irAEs of interest included hypothyroidism (13%), adrenal insufficiency (9%), and pneumonitis (4%). Demographic information was available for 333 patients, of which 270 (81%) were White, 23 (7%) were Asian, 37 (11%) were African American (AA) and 278 (17%) were non-Hispanic. There were proportionately higher number of white patients that developed hypothyroidism than non-white patients (35 of 265 (13%) vs 2 of 63 (3%), $P < 0.04$). Pneumonitis was more common in patients over 50 years old than under 50 years old ($P < 0.02$). Symptoms that were most commonly reported up to week 6 of treatment among patients who developed an irAE included: diarrhea (36%), fatigue (15%), dizziness (12%) and shortness of breath (SOB) (11%). Symptoms associated with the development of hypothyroidism included fatigue (15%, mean AUC=11.8 vs 5.8 for those that did not develop irAE), SOB (11%, 4.3 vs 2.8), and blurry vision (1%, 1.0 vs 0.12). Development of adrenal insufficiency was associated with early reports of

diarrhea (36%, 19.0 vs 10.5), SOB (11%, 7.8 vs 2.6), joint pain (3%, 2.29 vs 0.58), decreased appetite (3%, 3.55 vs 0.91), and constipation (1%, 3.6 vs 0.02). No significant early symptoms emerged for pneumonitis due to a limited number of events. Conclusion. Our study utilizes an analysis framework that is aimed to determine symptom clusters that predict the development of irAEs. We describe specific symptoms presenting early with the development of hypothyroidism and adrenal insufficiency, in recognition of allowing physicians to be more diligent in active and post treatment monitoring.

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1:00 PM - 1:15 PM

GS5-05

GS5-05 ZNF689 deficiency promotes intratumor heterogeneity and resistance to immune checkpoint blockade in triple-negative breast cancer

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Background: Triple-negative breast cancer (TNBC) is an aggressive disease characterized by remarkable intratumor heterogeneity (ITH), which poses a significant therapeutic challenge. However, the key determinants and underlying mechanisms of ITH in TNBC remain to be fully elucidated. Methods: We used multi-omics data from our cohort (n = 260) and The Cancer Genome Atlas (n = 134) cohort to comprehensively characterize ITH at the genetic and histologic levels. Transcriptomic differences between high ITH and low ITH tumors were compared to identify the core genes contributing ITH in TNBC. Xenograft models were used to examine the role of key determinants in TNBC ITH. The molecular mechanism was investigated by mass spectrometry, coimmunoprecipitation, pull-down, RNA-seq, long interspersed element-1 (LINE-1) reporter, ATAC-seq, luciferase reporter assays, chromatin immunoprecipitation, flow cytometry and coculture assay. Results: We found that high ITH was associated with poor patient survival and immune checkpoint blockade (ICB) resistance, which were validated in four independent ICB-treated trials. Further analysis indicated zinc finger protein 689 (ZNF689) deficiency as an important determinant of TNBC ITH. Mechanistically, the ZNF689-TRIM28 complex directly bound to the promoter of LINE-1, inducing H3K9me3-mediated transcriptional silencing. ZNF689 deficiency reactivated LINE-1 retrotransposition to exacerbate genomic instability, which promoted ITH. ZNF689 deficiency-induced ITH inhibited antigen presentation and CD8+ T cell infiltration, leading to ICB resistance. Pharmacological inhibition of LINE-1 retrotransposition reduced ITH, augmented antitumor immunity, and eventually sensitized ZNF689-deficient tumors to ICB. Consistently, ZNF689 expression positively correlated with favorable prognosis and ICB responsiveness in clinical samples. Conclusions: Our study uncovers a new mechanism underlying ZNF689 deficiency-induced ITH and suggests LINE-1 inhibition combined with ICB as a novel treatment strategy in TNBC.

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1:15 PM - 1:30 PM

GS5-06

GS5-06 InteractPrint predicts clinically meaningful interactions between cancer epithelial cells and immune cells: Lessons from a single-cell breast cancer atlas

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BACKGROUND: While immunotherapy has revolutionized the treatment of many solid tumors, the efficacy of immunotherapy regimens is comparatively lower in breast cancer. Immunotherapy efficacy is often negatively correlated with intratumor heterogeneity. Novel immunotherapy approaches in breast cancer should leverage how cancer epithelial cell heterogeneity affects immune cells in the tumor microenvironment. However, current definitions of cancer epithelial cell heterogeneity in breast cancer have limited resolution. Single cell RNA-seq (scRNA-seq) provides an unprecedented opportunity to further define cancer epithelial cell heterogeneity and identify how heterogeneity influences interactions with immune cells. **METHODS:** We generated a novel scRNA-seq dataset of 236,363 cells from 119 primary breast tumors biopsied from 88 patients taken from 8 publicly available datasets, currently the largest published scRNA-seq dataset in breast cancer. To define cancer epithelial cell heterogeneity, we performed unsupervised clustering and supervised clustering based on molecular subtype and expression of clinical target genes on all cancer epithelial cells. This identified 11 gene elements (GEs), which reflect key molecular features that vary between cancer epithelial cells. Receptor-ligand pairing analysis allowed us to determine how cells that

highly express each GE interact with various immune cells. We developed InteractPrint, a score to predict the predominant tumor-interacting immune cells, based on the GE composition of an individual patient tumor. RESULTS: In our dataset, 17% of samples were HER2+, 41% were HR+, and 42% were TNBC. This dataset was statistically powered to characterize cancer epithelial cell heterogeneity. For each of the 11 GEs, we predicted interactions with immune cells. Experimentally, GEs with predicted NK cell interactions showed sensitivity to NK cell cytotoxicity. In a spatially resolved transcriptomics dataset, GEs with predicted T cell interactions demonstrated colocalization with CD8+ T cells, while those with limited predicted T cell interactions did not. To infer GE-immune interactions at the patient level (GEs define cell-level interactions), we developed InteractPrint. To validate InteractPrint, we assessed the accuracy of the T cell InteractPrint in predicting response to anti-PD-1 therapy. Across two trials and all breast cancer subtypes, T cell InteractPrint demonstrated significant improvement over PD-L1 in predicting response to anti-PD-1 therapy. In an scRNA-seq dataset of samples from patients treated with pembrolizumab, we observed AUC of 85% ($p < 0.005$) for T cell InteractPrint vs. 61% ($p > 0.05$) for PD-L1 in predicting response to anti-PD-1 therapy. In patients treated with paclitaxel + pembrolizumab in the I-SPY 2 trial, we observed AUC of 81% ($p < 0.00001$) for T cell InteractPrint versus 72% ($p = 0.001$) for PD-L1. CONCLUSIONS: Our results demonstrate considerable cancer epithelial cell heterogeneity across primary breast tumor samples and clinical subtypes. We defined this heterogeneity and leveraged it to predict immune cell interactions within a patient's tumor. We developed T cell InteractPrint to capture heterogeneous interactions between cancer epithelial cells and CD8+ T cells. T cell InteractPrint is predictive of response to anti-PD-1 immune checkpoint inhibition at higher AUC than PD-L1. This provides a path forward for the interpretation of cancer epithelial cell heterogeneity in a clinically meaningful way.

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GS5-07

GS5-07 Estradiol represses anti-tumoral immune response to promote progression of triple-negative breast cancer brain metastases

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Background: Younger women with breast cancer have increased risk of development of brain metastases irrespective of the tumor subtype. We have shown that pre-menopausal levels of 17- β -Estradiol (E2) contributes to the promotion of brain metastases by influencing the tumor microenvironment. E2 promotes brain metastasis (BM) of estrogen receptor negative (ER⁻) BC cells by inducing neuroinflammatory ER⁺ astrocytes in the brain niche to secrete pro-metastatic factors critical for early brain colonization. Ovarieectomy (OVX) in combination with the aromatase inhibitor (Letrozole) prevented brain colonization of triple negative (TNBC) (ER-PR-HER2-) human xenografts (MDA231BR/NSG) and murine models (E0711/C57Bl6, 4T1/BALBc) through paracrine activation of EGFR and TRKB, pathways involved in increased invasion and early tumor initiation. Yet, the extent to which E2-depletion therapies can decrease progression of established BM in combination with current standard of care for brain metastasis remains unknown. Goal: Current standard of care (SOC) for patients with TNBC brain metastasis includes irradiation (SRS, whole brain) and immunotherapy (PD-1/PDL-1 inhibitors). The goal of this study was to assess how E2-depletion therapies affects brain immune function in the context of SOC for brain metastatic progression of TNBC. Results: To assess whether E2-depletion could decrease BM progression in a model that mimics standard of care for BM,

TNBC E0771-GFP-luc cells were injected intracardially in syngeneic ovariectomized (OVX)-female C57Bl6 mice supplemented with pre-menopausal levels of E2. Seven days after injection (when cancer cells have colonized), mice received a single 15Gy dose brain irradiation and were randomized to continue receiving E2, E2 withdrawal (E2WD) or E2WD plus the aromatase-inhibitor letrozole (E2WD+LET). Brain metastatic burden significantly decreased in E2WD and E2WD+Letrozole treated mice as compared to E2-treated mice. Injection of E0711 cells in immunocompromised NSG mice or in the absence of brain irradiation abolished this effect, suggesting that E2-depletion therapies decrease BM progression through boosting radiation-induced anti-tumor immunity. Accordingly, there were no differences in BM progression in E2, E2WD or E2WD+let treated mice in a xenograft model (F2-7 TNBC cells) in NSG mice, even in the presence of brain irradiation. Immune-profiling of brains from OVX+E2, OVX and OVX+Let C57BL6 mice carrying BMs showed dynamic changes in immune populations at early and late stages of brain metastatic colonization. At early stages post brain colonization (3 days post ic injection) E2-treated mice showed a decreased fraction of CD11b+CD45int CD206+ microglia/CNS macrophages as compared to OVX+LET-treated mice, without significant changes in the fraction of infiltrated lymphocytes, suggesting E2 represses early immunosurveillance through repression of microglia/CNS macrophage activation. At later stages of brain colonization (7 days post ic injection), E2-treated mice showed an increased fraction of proinflammatory microglia and decreased fraction of T and B cells as compared to OVX or OVX+let treated mice. While E2-depletion increased the recruitment of T cells to the brain niche, the fraction of CD279 (PD1+) brain T cells was similar among groups. Ongoing studies assess the efficacy of E2-depletion therapies in combination with brain radiation and PD-1 inhibitors to decrease metastatic burden and improve survival in preclinical models. Conclusion: Our results support the hypothesis that estradiol promotes brain metastatic progression by stimulating an immunosuppressive brain microenvironment. As such, FDA-approved E2-depletion therapies (aromatase inhibitors and selective-estrogen modulators) could be used in combination with brain irradiation and PD-1 inhibitors to promote a more effective anti-tumoral immune response.

Disclosure(s):

Maria J. Contreras-Zarate, MSc, PhD: No financial relationships to disclose

Karen Alvarez-Eraso, n/a: No financial relationships to disclose

Vesna Tesic, PhD: No financial relationships to disclose

Nicole Tsuji, BS: No financial relationships to disclose

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Peter Kabos, MD: AstraZeneca: Contracted Research (Ongoing); Genentech: Contracted Research (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Pfizer: Contracted Research (Ongoing); Radius Health: Contracted Research (Ongoing); Sanofi: Contracted Research (Ongoing)

Diana Cittelly, PhD: No financial relationships to disclose

12/9/2022

1:45 PM - 2:00 PM

GS5-08

GS5-08 Soluble E-cadherin: a novel prognostic biomarker and driver of brain metastasis in inflammatory breast cancer

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Background: Inflammatory breast cancer (IBC) is a highly aggressive form of breast cancer with rapid onset and a strong propensity to spread to distant organs. Five-year overall survival (OS) rates remain poor, in part because of the high risk of brain metastasis: 19% of patients with IBC have brain metastases within the first 2 years after diagnosis. Our hypothesis for this study was that soluble E-cadherin (sEcad), an 80-kDa extracellular proteolytic fragment of full-length E-cadherin - a tumor promoter in IBC, is crucial for driving brain metastasis in IBC. **Methods:** We analyzed serum sEcad levels in from 348 IBC patients by ELISA. Four IBC cell lines [ER-/HER2+ (MDA-IBC3; SUM190) and ER-/HER2- (SUM149; BCX010)], human brain microvascular endothelial cells, and immortalized human astrocytes were used in this study. Stable overexpression of sEcad in IBC cell lines was achieved using lentiviral vectors. Mass spectrometry and Bio-ID-based proteomics assays, and RNA sequencing were used to identify sEcad-interacting proteins and potential mechanisms. **In vivo,** we studied tumor growth and brain metastasis in mice by injecting IBC cells into the mammary fatpad or tail vein, respectively, of SCID/Beige mice. **Results:** In IBC patients, higher serum sEcad levels correlated with poorer OS ($p=0.02$), earlier development of metastasis ($p=0.006$), and development of brain metastasis ($p=0.04$). On multivariable analysis, sEcad independently predicted OS (hazard ratio [HR]=2.07 [95% CI 1.19-3.60], $p=0.01$). **In vitro,** sEcad overexpression in IBC cell lines promoted anchorage-independent growth, migration, invasion, and resistance to anoikis. **In vivo,** sEcad-overexpressing SUM149 cells promoted primary tumor growth ($p=0.007$). Mice injected with sEcad-overexpressing MDA-IBC3 cells also had higher incidence of brain metastasis (100% vs 50%, $p=0.03$), metastatic burden ($p=0.02$) and number of metastases per mouse ($p=0.0009$), and had worse OS ($p=0.0016$), and brain metastasis-free survival ($p=0.04$), relative to controls. We further found that sEcad increased cancer cell adhesion to brain endothelial cells ($p=0.01$) and promoted induction of reactive astrocytes (as identified by high glial fibrillary acidic protein levels) **in vitro** and **in vivo**. Mechanistically, mass spectrometry and Bio-ID assays identified X-linked inhibitor of apoptosis protein (XIAP), a potent inhibitor of apoptotic cell death, as a novel binding partner of sEcad, which was validated through co-immunoprecipitation. Further analysis showed that sEcad bound to the BIR2 domain of XIAP. XIAP is the most potent and best-defined anti-apoptotic IAP family member, and it could induce NF- κ B activation to inhibit tumor cell apoptosis. Gene set enrichment analysis of RNA-seq profiling data showed activation of NF- κ B signaling and downregulation of apoptotic pathways in the sEcad-overexpressing SUM149 cells compared with controls. Immunoblotting revealed that sEcad enhanced XIAP expression, activated NF- κ B signaling, and inhibited cleavage of caspase-3 in IBC cells. **Conclusions:** We found that higher serum sEcad correlates with development of brain metastases and independently predicts poor OS in patients with IBC. We further found that sEcad promotes tumor growth and brain metastasis, perhaps via activation of XIAP/NF- κ B signaling in breast cancer cells and promotion of endothelial cell adhesion and reactive astrocytosis in the brain microenvironment. These findings uncover a novel and crucial role for sEcad in brain metastasis and provide new insights and potential therapeutic targets for patients with metastatic IBC.

Disclosure(s):

Xiaoding Hu, Ph.D.: No financial relationships to disclose

yun xiong, Ph.D.: No financial relationships to disclose

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Juhee Song, Ph.D.: No financial relationships to disclose

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12/9/2022

2:00 PM - 2:15 PM

GS5-09

GS5-09 Discussant for GS5-07 and GS 5-08

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Nancy U. Lin, MD: Affinia Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Aleta Biopharma: Consulting Fees (e.g., advisory boards) (Ongoing); Artera: Ownership Interest (stocks, stock options, patent or other intellectual property or other ownership interest excluding diversified mutual funds) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Daichii-Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Denali Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Genentech: Contracted Research (Ongoing); Janssen: Consulting Fees (e.g., advisory boards) (Ongoing); Merck: Contracted Research (Ongoing); Olema Pharmaceuticals: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Pfizer: Contracted Research (Ongoing); Prelude Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Seattle Genetics: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Up to Date: Royalty (Ongoing); Voyager Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Zion Pharmaceuticals: Contracted Research (Ongoing)

12/9/2022

2:15 PM - 2:30 PM

GS5-10

GS5-10 Utility of the 70-gene MammaPrint test for prediction of extended endocrine therapy benefit in patients with early-stage breast cancer in the IDEAL Trial

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Background: The IDEAL trial showed no significant benefit of 5 years extended endocrine therapy (EET) using letrozole in postmenopausal patients with hormone receptor positive (HR+) breast cancer (BC) versus 2.5 years. Genomic classifiers may assist with treatment decisions by predicting EET benefit. The 70-gene MammaPrint (MP) test classifies tumors as having a higher or lower risk of distant metastasis in HR+ early-stage BC. A MP lower risk result can be further classified as either Ultra-Low risk or Low risk of distant metastasis. In the NSABP B42 trial, MP predicted a statistically significant absolute benefit from EET in patients with a MP Low Risk result. Here, we aimed to determine the utility of MP in identifying a subgroup of patients enrolled in the IDEAL trial for which 5 years of EET is beneficial compared to 2.5 years.

Methods: A total of 869 patients had available primary tumor tissue for testing. MP results were available for 545/869 patients, of which 515 did not have an event at 2.5 year after randomization and were used for our analyses. The MP result for each patient was calculated by Agendia while blinded to patient clinical outcomes. The primary endpoint was distant recurrence (DR). Secondary endpoints were recurrence free interval (RFI) and breast cancer free interval (BCFI) as defined by STEEP criteria. Patients were classified as higher risk (score $-1.000 - 0$) or lower risk (score $0.001 - 1.000$). Lower risk tumors were further classified as either MP Ultra-Low (score > 0.355) or MP Low Risk (score $\geq 0.001, \leq 0.355$). Likelihood ratio

test based on stratified Cox proportional hazards (PH) model were used to evaluate treatment by risk group interaction. Differences in endpoints between treatment groups were assessed by stratified log-rank tests. Hazard ratios (HR) and 95% Confidence Intervals (CI) were computed based on the stratified Cox PH model.

Results: The clinical characteristics of the 515 IDEAL samples with a MP result were comparable to the whole IDEAL cohort (n=1820). Within the 2.5 year EET group, 50.6% (n=134) were MP higher risk and 49.4% (n=131) MP lower risk, of which 14.5% (n=19/131) were MP Ultra-Low. Within the 5 year EET group, 50.0% (n=125) were MP higher risk and 50.0% (n=125) MP lower risk, of which 11.2% (n=14/125) were MP Ultra-Low. Among patients with MP lower risk tumors, 5 years vs. 2.5 years of EET resulted in a significant absolute benefit of 9.8% for DR (HR=0.42, [95% CI 0.174-0.996]), 9.8% for RFI (HR=0.43, [95% CI 0.198-0.934]), and 8.8% (HR=0.53, [95% CI 0.264-1.055]) for BCFI, whereas patients with MP higher risk tumors did not derive significant benefit (Table 1). Within the MP lower risk group, 5 year vs 2.5 year EET benefit was more pronounced in MP Low tumors, which exhibited a significant benefit of 10.1% for DR (HR=0.32, [95% CI 0.116-0.866]), 11.7% for RFI (HR=0.35, [95% CI 0.147-0.824]), and 9.7% for BCFI (HR=0.48, [95% CI 0.225-1.015]); MP Ultra Low tumors did not derive significant benefit. Treatment-by-risk group interaction was statistically significant for RFI.

Conclusion: A significant EET benefit was observed for MammaPrint lower risk tumors but not for MP higher risk tumors. MammaPrint Low tumors exhibited the largest absolute benefit of 5 years of EET compared to 2.5 years. Consistent with the findings in the NSABP B42 trial, the results from this second randomized trial provide clinically meaningful implications in patient selection for extended endocrine therapy.

Table 1. IDEAL: 10-year outcome analysis comparing 5 years vs. 2.5 years of EET using letrozole stratified by MP risk.

Table 1. IDEAL: 10-year outcome analysis comparing 5 years vs. 2.5 years of EET using letrozole stratified by MP risk.

Endpoint	MammaPrint Result	10-yr outcome 2.5y EET (%)	10-yr outcome 5y EET (%)	Absolute benefit (%)	HR	95% CI		p	P interaction*
DR	Higher Risk (n=259)	90.0	90.9	0.9	0.882	0.395	1.968	0.758	Ref
	Lower Risk (n=256)	82.5	92.3	9.8	0.416	0.174	0.996	0.049	0.217**
	MP Low (n=223)	85.2	95.3	10.1	0.317	0.116	0.866	0.025	0.120***
RFI	Higher Risk (n=259)	90.1	86.5	-3.6	1.283	0.617	2.667	0.505	Ref
	Lower Risk (n=256)	82.5	92.3	9.8	0.430	0.198	0.934	0.033	0.045
	MP Low (n=223)	81.5	93.2	11.7	0.349	0.147	0.824	0.016	0.024
BCFI	Higher Risk (n=259)	87.0	84.8	-2.2	1.101	0.567	2.136	0.777	ref
	Lower Risk (n=256)	80.9	89.7	8.8	0.528	0.264	1.055	0.071	0.133
	MP Low (n=223)	80.6	90.3	9.7	0.478	0.225	1.015	0.055	0.103

MammaPrint Lower Risk & Higher Risk (n=515) and * MammaPrint Low Risk & High Risk (n=482)

MammaPrint Lower Risk & Higher Risk (n=515) and * MammaPrint Low Risk & High Risk (n=482)

Disclosure(s):

Gerrit-Jan Liefers, MD: Astra Zeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Biotheranostics: Consulting Fees (e.g., advisory boards) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing)

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12/9/2022

2:30 PM - 2:45 PM

GS5-12

GS5-12 Hypofractionated Radiotherapy in patients with Breast Cancer (HRBC): Acute toxicity data of a phase III randomized study

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Background HRBC is a phase III randomized open label study of adjuvant radiotherapy in patients with breast cancer. In this study we compared a 3 weeks radiation schedule with 2 weeks. Materials and methods Patients with breast cancer, stage I-III, post mastectomy or after breast conservative surgery who needed adjuvant locoregional radiotherapy were randomized to 34Gy in 10 fractions over 2 weeks (study arm) or 35Gy in 15 fractions over 3 weeks to the chest wall and 40Gy/15#/3wks to breast and supraclavicular fossa (control arm). Boost dose when indicated was 8Gy/2# in both the arms. Patients were planned on simulator with 2 tangential fields to breast/chest wall and incident supraclavicular fossa field. Acute toxicity was assessed using a RTOG grading system. Assessment was carried out weekly during radiotherapy and at 4 weeks after treatment by the physician. Cosmetic outcome was assessed using Harvard/NSABP/RTOG scale. The toxicity between the two arms was compared using Fisher's exact test. The trial was approved by institutional ethics committee. This trial is registered with ClinicalTrials.gov, number NCT04075058. Results This study included 1121 patients. Median follow up was 35 months (range 6-84 months). Mean age was 48 year (range 24-80 years). The patient characteristics were comparable between the two arms except for more mastectomies in the 3 week arm and more node positive patients in the 2 week arm. There were more oestrogen receptor positive tumors in the 3 week arm. Acute skin toxicities were comparable between the two arms. Grade 2 and 3 skin toxicity was 98(17%) and 82(15%); and 16(3%) and 10(2%) in the 3 week and 2 week arm (p=0.15), respectively. Cosmetic outcome was significantly better in 2 week arm 94% as compared to 90% in the 3 week arm (p=0.016). Conclusion The two radiation schedules were comparable in terms of acute skin toxicity. Cosmetic outcome was better in the 2 week schedule.

Disclosure(s):

Budhi Singh Yadav, n/a: No financial relationships to disclose

Divya Dahiya, MS, General Surgery: No financial relationships to disclose

Manish Gupta, MD: No financial relationships to disclose

12/9/2022

3:00 PM - 3:40 PM

Updates in the pathology of PABC

Presenting Author(s) and Co-Author(s):

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Updates in the Pathology of Pregnancy Associated Breast Cancer (PABC)

Pregnancy associated breast cancer is defined as a breast cancer diagnosed during gestation, lactation and within 1 to 5 years postpartum. While the development of malignancy during pregnancy is rare, the incidence is increasing; breast cancer is one of the most common cancers diagnosed during pregnancy and the postpartum period occurring in up to 1 in 3000 deliveries. Of interest, breast cancer is the leading cause of cancer death in US women age 15-29. Pregnancy has a dual effect on breast cancer development: on one hand cancer protective and on the other cancer promoting. While a number of hypotheses have been proposed over the years to explain these effects, the most likely hypothesis for the development of PABC is the involution hypothesis. This hypothesis proposes that the involution pathways activated during pregnancy and the immediate postpartum period are remodeling programs similar to wound healing and inflammation that may be associated with tumor development and progression. Although PABCs can be any subtype of breast carcinomas, they are usually invasive ductal carcinomas of high tumor grade and large tumor size with higher stage at presentation and higher rates of lymph node involvement. Most PABCs are hormone receptor negative tumors with high Ki-67 proliferation rates; most frequently, they are either triple negative or HER2-positive carcinomas. A number of studies have shown that PABCs have different genomic signatures than the non-PABC tumors with PABCs having an increased expression of immune response mediators. Better understanding of the molecular pathways of tumor initiation and progression and prompt diagnosis and state-of-art treatment protocols in PABC is expected to lead to better outcomes for these young breast cancer patients.

12/9/2022

3:00 PM - 5:00 PM

Educational Session: Advances in Pregnancy Associated Breast Cancer - (PEOPLE'S CHOICE)

Presenting Author(s) and Co-Author(s):

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12/9/2022

3:40 PM - 4:20 PM

Special treatment issues in this young patient population

Presenting Author(s) and Co-Author(s):

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Disclosure(s):

Ann Partridge, MD, MPH: Patient-Centered Outcomes Research Institute (AFT-25 COMET):

Contracted Research (Ongoing); UpToDate: Royalty (Ongoing)

12/9/2022

4:20 PM - 5:00 PM

Oncofertility and other quality of life issues

Presenting Author(s) and Co-Author(s):

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The current availability of effective systemic treatment strategies has significantly improved the prognosis of patients with early breast cancer. However, this survival gain is often obtained at the cost of higher toxicity. The increase in life span among breast cancer survivors calls for the need to address both early and late potential adverse effects of anticancer therapies to maximize their quality of life. Among them, the potential gonadotoxicity of anticancer therapies and its implications on fertility and ovarian function need to be discussed with all young patients. According to available guidelines, oncofertility counseling should now be considered mandatory in the care of young women with newly diagnosed cancer. This counselling should focus on the risk of developing treatment-induced premature ovarian insufficiency and on the available techniques to preserve fertility and/or ovarian function. Oocyte/embryo cryopreservation, or ovarian tissue cryopreservation in those not eligible for gamete cryopreservation, are standard strategies to be offered to young patients interested in preserving fertility, i.e. to increase their chances of post-treatment pregnancies. Ovarian suppression with gonadotrophin-releasing hormone agonists (GnRHa) during chemotherapy can be offered to premenopausal patients interested in ovarian function preservation, i.e. to decrease their risk of developing chemotherapy-induced early menopause.

Current available data confirm that pregnancy occurring following proper treatment for breast cancer and period of follow-up is safe, both in terms of long-term clinical outcomes for the patients and safety for the babies. However, there is a slightly higher incidence of obstetric and birth complications that require the need for a closer monitoring of these pregnancies.

Beyond fertility and pregnancy-related issues, a long-term follow-up of young women with breast cancer by the oncofertility unit is recommended for improving the management of other additional gynecological-related issues faced by these women. Among them, contraception should be considered during active treatment and in the follow-up of women who do not wish to get pregnant. Moreover, in the current era of more complex endocrine therapy approaches with a major negative impact on the quality of life of premenopausal patients with breast cancer, it is essential to properly and proactively care about their treatment-related side effects. Among them, menopause related-symptoms and sexual dysfunction may be better managed by implementing a close collaboration between oncologists and gynecologists within the oncofertility unit.

Disclosure(s):

Matteo Lambertini, MD, PhD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead: Consulting Fees (e.g., advisory boards) (Ongoing), Travel support (Ongoing); Ipsen: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Knight: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Libbs: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g.,

speakers' bureaus) (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Sandoz: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing); Seagen: Consulting Fees (e.g., advisory boards) (Ongoing); Takeda: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing)

12/9/2022

3:00 PM - 3:40 PM

Overview of the current state of the art – what patients and oncologists need to know

Presenting Author(s) and Co-Author(s):

Rachel Jimenez, MD - *Massachusetts General Hospital*

City: Boston

State: MA

Country: United States

While radiation therapy plays a significant role in the treatment of breast cancer for many patients, the nuances of modern day radiation therapy are often poorly understood by both patients and referring providers. Radiation therapy techniques to reduce toxicity and improve treatment accuracy have rapidly evolved in the past decade. This session will introduce non-radiation oncologists to recent innovations that allow increased personalization of treatment based on anatomical variations. Methods to improve patient positioning will be discussed. Frequently utilized dosimetric techniques for breast radiotherapy will be described and compared, including Volumetric Modulated Arc Therapy (VMAT), Intensity Modulated Radiation Therapy (IMRT), and 3D conformal planning. New methods for patient monitoring during treatment and the purpose of respiratory gating will be reviewed. Finally, the impact of surgical therapies on radiation planning and delivery will also be examined. Attendees should leave the session having a greater understanding of the current available options for radiotherapy and rationale for the choice of treatment technique.

12/9/2022

3:00 PM - 5:00 PM

Educational Session: State of the Art Radiotherapy: Reducing Toxicity and Increasing Options

Presenting Author(s) and Co-Author(s):

Wendy Woodward, MD, PhD - *UT MD Anderson Cancer Center*

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State: Texas

Country: United States

Disclosure(s):

Wendy Woodward, MD: No financial relationships to disclose

12/9/2022

3:40 PM - 4:20 PM

The role of advanced radiation technology in reducing toxicity

Presenting Author(s) and Co-Author(s):

Melissa Mitchell, MD, PhD - *UT MD Anderson Cancer Center*

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State: Texas

Country: United States

Over the past decade, breast cancer radiotherapy has increasingly focused on techniques to improve treatment precision and limit toxicity. Surface guided radiotherapy and respiratory gating has allowed for improved cardiac sparing and the elimination of permanent skin tattoos in women receiving breast radiation, while rapid developments in the technological delivery of radiation via both volumetric arc therapy and proton beam radiation have shown promise in further improving target coverage and normal tissue sparing for breast cancer patients. Cutting edge innovations, including MR-guided radiotherapy and FLASH technology are now being explored as means to further improve treatment precision and decrease toxicity. The purpose of this talk is to highlight and discuss these advances in radiotherapy, review the existing evidence to support their use in the treatment of breast cancer, and detail specific patient populations that are most likely to benefit. Discussion will also focus on ongoing and future research aimed at improving our understanding and utilization of these novel advances in care.

12/9/2022

4:20 PM - 5:00 PM

Evidence for ablative radiation in metastatic breast cancer

Presenting Author(s) and Co-Author(s):

Chiaojung Jillian Tsai, MD, PhD - *Princess Margaret Cancer Centre*

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Country: United States

12/9/2022

3:00 PM - 3:30 PM

Influence of bone microenvironment on metastasis

Presenting Author(s) and Co-Author(s):

Igor Bado, PhD - *Baylor College of Medicine*

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Country: United States

12/9/2022

3:00 PM - 5:00 PM

Educational Session: Targeting the Tumor Microenvironment for Clinical Impact

Presenting Author(s) and Co-Author(s):

Diana Cittelly, PhD - *University of Colorado Anschutz Medical Campus*

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Disclosure(s):

Diana Cittelly, PhD: No financial relationships to disclose

12/9/2022

3:30 PM - 4:00 PM

The contribution of the tumor microenvironment to cancer dormancy

Presenting Author(s) and Co-Author(s):

Jose Javier Bravo-Cordero, PhD - *Icahn School of Medicine at Mount Sinai*

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Country: United States

In this seminar I will discuss how breast cancer DTCs modify the metastatic microenvironment to favor seeding and dormancy. In order to extravasate efficiently and form metastasis, cancer cells have to become migratory and coordinate both invasive and proliferative programs at distant organs. High-resolution lattice light-sheet with adaptive optics imaging in living cells revealed that DTCs extravasate from the blood vessels by forming actin-rich invadopodium protrusions. We have identified a population of breast cancer DTCs with pro-invasive and pro-dormancy capacities. These cells downregulate srGAP1, a GTPase regulator, favoring dissemination and dormancy at metastatic organs. Our findings describe a novel mechanism mediating the shift from a proliferative to an invasive/dormant phenotype in breast cancer cells *in vivo*. srGAP1 is a new regulator of dormancy that regulates the formation of dormancy-permissive microenvironments through increased secretion of TGF β 2 and SMAD2 activation.

12/9/2022

4:00 PM - 4:30 PM

Effects of age on the tumor microenvironment

Presenting Author(s) and Co-Author(s):

Sandra McAllister, PhD - *Harvard Institutes of Medicine*

City: Boston

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Country: United States

Dr. McAllister's translational research group studies breast cancer as a systemic disease with an emphasis on the role of immune fitness in disease control and response to therapy. In this education session, Dr. McAllister will introduce the concept of "immunological age". She will discuss her team's ongoing efforts to understand how age sets the stage for triple-negative breast cancer (TNBC) progression and response to immune checkpoint blockade therapy.

Her team was the first to report that bone marrow derived immune cells from 8–10-week-old young mice promote more aggressive TNBC growth when transferred to 12–15-month-old aged mice (Marsh, et al., *Cancer Research*, 2016). They subsequently identified cellular and molecular mechanisms that promote aggressive disease, as typically observed in younger individuals. Likewise, her group was the first to report that immune checkpoint blockade therapy is less effective in older mice with TNBC and discovered a treatment strategy that improved outcomes in pre-clinical TNBC models (Sceneay, et al., *Cancer Discovery*, 2019). The same tumor cellular and molecular pathways that stratified by age in their pre-clinical models also defined age-stratified differences between younger (65) TNBC patients in the METABRIC dataset.

She will present her team's new work on functional aspects of immunological age in TNBC and the ongoing efforts of the Older Women with Breast Cancer Research and Treatment Team at the Dana-Farber/Brigham Cancer Center. Ultimately, she and her team wish to eliminate age- and race-based disparities in breast cancer outcomes.

12/9/2022

4:30 PM - 5:00 PM

Can inflammation be targeted?

Presenting Author(s) and Co-Author(s):

Angela DeMichele, MD, MSCE - *University of Pennsylvania*

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Disclosure(s):

Angela DeMichele, MSCE: Calithera: Contracted Research (Ongoing); Genentech: Contracted Research (Ongoing); Inivata: Contracted Research (Ongoing); Novartis: Contracted Research (Ongoing); Pfizer: Contracted Research (Ongoing)

12/9/2022

5:00 PM - 5:15 PM

Refreshment Break

12/9/2022

5:15 PM - 7:15 PM

View from the Trenches: What to do on Monday Morning?

Presenting Author(s) and Co-Author(s):

Andrea V. Barrio, MD, FACS - *Memorial Sloan Kettering Cancer Center*

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Panel discussion and critical review of practice changing presentations from SABCS 2022.

Disclosure(s):

Andrea Barrio, MD: No financial relationships to disclose

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Marianna Chavez, MD, MSC, FASCO: Abbott: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing); Exact Sciences: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Terminated, January 31, 2021), Contracted Research (Terminated, January 31, 2021); Pfizer: Consulting Fees (e.g., advisory boards) (Terminated, January 31, 2021), Contracted Research (Terminated, January 31, 2021); Roche/Genentech: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing), Contracted Research (Ongoing), Third-party writing assistance for this abstract, furnished by Daniel Clyde, PhD, of Health Interactions, was provided by F. Hoffmann-La Roche Ltd (Ongoing)

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12/10/2022

8:00 AM - 8:30 AM

Basic Science

Presenting Author(s) and Co-Author(s):

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12/10/2022

8:00 AM - 10:00 AM

Year In Review

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Country: United States

Disclosure(s):

Virginia Kaklamani, MD: AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Daiichi Sankyo: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Genentech: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Genomic Health: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Gilead Sciences: Honoraria (Ongoing); Novartis: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Pfizer: Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing); Puma Biotechnology: Consulting Fees (e.g., advisory boards) (Ongoing), Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g., speakers' bureaus) (Ongoing), Honoraria (Ongoing)

Carlos Arteaga, MD: Arvinas: Consulting Fees (e.g., advisory boards) (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Daiichi Sankyo: Consulting Fees (e.g., advisory boards) (Ongoing), Research Funding (Ongoing); Lilly: Consulting Fees (e.g., advisory boards) (Ongoing), Research Funding (Ongoing); MERCK: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing); OrigiMed: Consulting Fees (e.g., advisory boards) (Ongoing); Pfizer: Research Funding (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing); TAIHO Oncology: Consulting Fees (e.g., advisory boards) (Ongoing); Takeda: Research Funding (Ongoing)

12/10/2022

8:30 AM - 9:00 AM

Translational Research

Presenting Author(s) and Co-Author(s):

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12/10/2022

9:00 AM - 9:30 AM

Early Breast Cancer

Presenting Author(s) and Co-Author(s):

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Country: Netherlands

Disclosure(s):

Marleen Kok, MD, PhD: AZ/Daiichi: Consulting Fees (e.g., advisory boards) (Ongoing), funding to institute (Ongoing); BMS: Consulting Fees (e.g., advisory boards) (Ongoing), funding to institute (Ongoing); MSD: Consulting Fees (e.g., advisory boards) (Ongoing); Roche: Consulting Fees (e.g., advisory boards) (Ongoing), funding to the institute (Ongoing)

12/10/2022

9:30 AM - 10:00 AM

Advanced Breast Cancer

Presenting Author(s) and Co-Author(s):

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Disclosure(s):

Melinda Telli, MD: AbbVie: Contracted Research (Ongoing); Arvinas: Contracted Research (Ongoing); AstraZeneca: Consulting Fees (e.g., advisory boards) (Ongoing); Bayer: Contracted Research (Ongoing); Biothera: Contracted Research (Ongoing); Blueprint Medicines: Consulting Fees (e.g., advisory boards) (Ongoing); Calithera Biosciences: Contracted Research (Ongoing); EMD Serono: Contracted Research (Ongoing); G1 Therapeutics: Consulting Fees (e.g., advisory boards) (Ongoing); Genentech: Contracted Research (Ongoing); Genentech/Roche: Consulting Fees (e.g., advisory boards) (Ongoing); Gilead Sciences: Consulting Fees (e.g., advisory boards) (Ongoing); GSK: Contracted Research (Ongoing); Guardant Health: Consulting Fees (e.g., advisory boards) (Ongoing); Hummingbird Biosciences: Contracted Research (Ongoing), Contracted Research (Ongoing); Immunomedics: Consulting Fees (e.g., advisory boards) (Ongoing); Medivation: Contracted Research (Ongoing); Merck: Consulting Fees (e.g., advisory boards) (Ongoing); Natera: Consulting Fees (e.g., advisory boards) (Ongoing); Novartis: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); OncoSec: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); Pfizer: Consulting Fees (e.g., advisory boards) (Ongoing), Contracted Research (Ongoing); PharmaMar: Contracted Research (Ongoing); Reflexion Medical: Consulting Fees (e.g., advisory boards) (Ongoing); Sanofi: Consulting Fees (e.g., advisory boards) (Ongoing); Tesaro: Contracted Research (Ongoing); Vertex: Contracted Research (Ongoing)

12/10/2022

10:00 AM - 10:15 AM

Adjournment

