



2018

DECEMBER 4-8

HENRY B. GONZALEZ CONVENTION CENTER,
SAN ANTONIO, TEXAS, USA

NEOADJUVANT ENDOCRINE THERAPY: THE TIMES THEY ARE A-CHANGING

Ingrid A. Mayer, MD, MSCI
Vanderbilt University Medical Center, Nashville, TN
Hall 3

“Neoadjuvant endocrine therapy breast cancer trials can be used as a platform to help design larger phase III trials,” says Dr. Ingrid A. Mayer from the Vanderbilt University Medical Center in Nashville, TN.

Dr. Mayer’s plenary lecture, an overview of neoadjuvant endocrine therapy trials and their relevance to patient outcomes, takes place at the Symposium on Thursday morning.

“Most neoadjuvant endocrine trials are phase II trials and are not definitive trials. They will not change practice,” says Dr. Mayer. “However, I can envision these trials as a testing platform to inform the design of bigger trials.”

In general, neoadjuvant endocrine therapy studies lack power to look at the long-term end points that larger metastatic breast cancer therapy trials and some neoadjuvant chemotherapy trials examine, such as disease-free survival or overall survival. This is partly due to the fact that neoadjuvant endocrine therapy trials tend to be smaller, and also because trial participants are not completing definitive treatment during the time the study is conducted. “In endocrine therapy trials, patients are getting treatment for perhaps 6 months, when the full treatment takes 5 to 10 years. With chemotherapy, you’re getting the whole thing.”

But Dr. Mayer explains that neoadjuvant endocrine trials that use intermediate outcome markers are useful in inferring a patient’s prognosis. Correlating outcomes such as the Preoperative Endocrine Prognostic Index (PEPI), which considers tumor size, lymph node status, hormone receptor status, and Ki67 blood levels, to larger trials with similar design can predict long-term outcomes. Her lecture cites several neoadjuvant endocrine therapy trials that use surrogate end points to predict results of phase III adjuvant therapy and metastatic endocrine therapy trials.

Dr. Mayer is hopeful that neoadjuvant endocrine therapy trials will inform the design of larger clinical trials. “We can test novel combinations and strategies with quick turnaround of results and use those results for more definitively designed trials.” Testing agents in the neoadjuvant setting provides investigators with insight about the success of a trial, prioritization of drug combinations, and efficacy of novel strategies. Ultimately, neoadjuvant endocrine therapy trials form an excellent platform for the development of effective breast cancer therapy, and can reduce costs, time, and need for large numbers of patients.

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- 2: Connect to **SABCS2018**
- 3: Open your favorite browser.
- 4: When symposium welcome page loads you are connected!

**THE FOLLOWING SESSION
HAS BEEN REVISED:**

**Thursday, December 6
1:00 PM - 2:00 PM**

TRANSLATIONAL SCIENCE FORUM 1
Stars at Night Ballroom 3&4
3rd Level

PI3K Pathway in Breast Cancer
Moderator: Carlos L. Arteaga, MD
UT Southwestern
Simmons Comprehensive Cancer
Center
Dallas, TX

**The complexity of targeting PI3K for
cancer therapy**
Lewis C. Cantley, PhD
The Sandra and Edward Meyer
Cancer Center
New York, NY

**Lessons learned from the clinical
development of PI3K inhibitors in
metastatic breast cancer**
Dejan Juric, MD
Massachusetts General Hospital
Boston, MA

**SPOTLIGHT SESSION
PRESENTATION UPDATE:**

PD2-07 has moved to Spotlight
Session 5

*AT PRESS TIME

**ANNUAL AACR DISTINGUISHED LECTURESHIP
IN BREAST CANCER RESEARCH**

Thursday, December 6, 11:30 am, Hall 3

This lectureship recognizes an outstanding scientist whose work has inspired or has the potential to inspire new perspectives on the etiology, diagnosis, treatment, or prevention of breast cancer.

**WHAT CAN WE LEARN FROM BREAST CANCERS THAT
METASTASIZE OR DON'T?**

Zena Werb, PhD
University of California San Francisco, San Francisco, CA

Zena Werb, PhD is honored for her pioneering studies involving elucidation of the mechanistic role of the extracellular microenvironment in regulating breast epithelial cell function, which has led to a paradigm shift in the understanding of mammary gland development as well as breast cancer progression and metastasis.

Dr. Werb received her B.Sc. in Biochemistry from the University of Toronto, and her Ph.D. in Cell Biology from Rockefeller University, New York. After postdoctoral studies at the Strangeways Research Laboratory in Cambridge England, she was recruited to the University of California San Francisco faculty, where she is currently Professor of Anatomy and Associate Director for Basic Science, Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco.

Dr. Werb is recognized internationally for her fundamental discoveries about the role of matrix metalloproteinases, the cellular microenvironment and intercellular communication in the normal functioning and pathogenesis of tissues, in particular, breast cancer. She has published over 450 papers. Her honors include a Guggenheim Fellowship, the E. B. Wilson Medal, American Society for Cell Biology and election to the National Academy of Sciences, the National Academy of Medicine, and the American Academy of Arts and Sciences.



A TRIBUTE TO DR COLTMAN

The San Antonio Breast Cancer Symposium community was saddened by news of the passing of symposium co-founder and oncology trailblazer Charles A. Coltman Jr., MD Wednesday, Nov. 28. He was 88.

Coltman, along with William L. McGuire, MD started the symposium in 1978 during Breast Cancer Awareness Week. At that time, there were 140 attendees from around South Texas. It has grown over the following four decades to an international conference spanning five days drawing nearly 8,000 attendees.

"It was their vision that really made it what it is today," said SABCS Co-Sponsor C. Kent Osborne, MD, director of the Dan L Duncan Comprehensive Cancer Center at Baylor College of Medicine in Houston. "It was their vision

WITHDRAWN ABSTRACTS

- P2-06-18
- P3-06-21
- P3-03-28
- P3-07-11
- P3-03-33
- P3-08-02

**The following abstract & poster has
appears in our publications and
website with incomplete author/
institution information.**

**P3-09-07: The role of MLK4
amplification in progression of triple
negative breast cancer**

Prelowska MK, Mehlich D, Lazniewski M, Kaminska K, Gorczynski AS, Korwat A, Sokolowska O, Golab J, Biernat W, Plewczynski D, Brognard J, Nowis D, Marusiak AA Centre of New Technologies, University of Warsaw, Warsaw, Poland; Genomic Medicine, Medical University of Warsaw, Poland; Medical University of Warsaw, Warsaw, Poland; Postgraduate School of Molecular Medicine, Medical University of Warsaw, Warsaw, Poland; Medical University of Gdansk, Gdansk, Poland; Medical University of Warsaw, 7Centre for Preclinical Research and Technology, Medical University of Warsaw, Warsaw, Poland; Faculty of Mathematics and Information Science, Warsaw University of Technology, Warsaw, Poland; National Cancer Institute, Frederick, Maryland

to always have basic scientists and clinicians in the same room hearing each other talk."

Osborne described him as an educator who, "had a major impact in the cancer world early on when we were just getting started as a specialty." Coltman's primary focus was on blood cancers and his work advancing research in this area earned him several awards, including the Outstanding Achievement in Clinical Research Award from the Association of Community Care Centers and ASCO's David A. Karnofsky Memorial Award.

Coltman was an Air Force veteran and chief of hematology and oncology at Wilford Hall Medical Center in San Antonio. He was named chief medical director of the Cancer Therapy & Research Center in 1977, now part of UT Health San Antonio, and remained until his departure in 2003. In 1964 - just eight years after its founding by the National Cancer Institute - Coltman joined the Southwest Oncology Group, now the SWOG Cancer Research Network. Coltman served as the group's chair for 24 years. SWOG is a member of the National Cancer Institute's National Clinical Trials Network, which has run over 1,300 cancer clinical trials that have saved more than 3 million years of human life. Coltman is a former ASCO president and member of the ASCO board of directors.

Coltman was a faculty member of UT Health San Antonio from 1977 through 2010. "With his influence locally, regionally, and through SABCS, Dr. Coltman impacted the prevention and treatment of cancer throughout the world," said William L. Henrich, MD, President of UT Health San Antonio.

**PD-L1 AS A MARKER OF RESPONSIVENESS TO TREATMENT
WITH ATEZOLIZUMAB PLUS NAB-PACLITAXEL**

PD-L1 expression can identify patients with triple negative breast cancer (TNBC) who will benefit from first-line therapy with atezolizumab plus nab-paclitaxel (nabPx), Leisha A. Emens, MD, PhD, of the UPMC Hillman Cancer Center at the University of Pittsburgh, reported here on Wednesday morning. The findings come from the first interim analysis of IMpassion 130, the first phase III study to demonstrate a benefit of immunotherapy for TNBC.

In this study, the investigators sought to determine whether immune biology and BRCA 1/2 status might be associated with clinical benefit from the treatment regimen. They assigned 902 women with treatment-naive metastatic, inoperable, locally advanced TNBC to receive nabPx plus either atezolizumab or placebo in a 1:1 randomized, double-blind design. Tumor PD-L1 expression was analyzed in pre-treatment biopsies, as were intratumoral CD8+ T cells and stromal tumor-infiltrating lymphocytes (TILs). The patients were then followed for a median time of 12.9 months.

Among women with PD-L1-positive tumors, the combination regimen was associated with a median overall survival (OS) time of 25.0 months, compared with 15.5 months for women receiving nabPx plus placebo. Progression-free survival (PFS) times were 7.5 months and 5.0 months, respectively. For women testing negative for PD-L1, the median OS and PFS were virtually equal for both regimens. Patients testing positive for the other immune markers derived a similar clinical benefit only if their tumors also were PD-L1 positive.

"These findings suggest that newly diagnosed patients [with TNBC] should be tested for PD-L1 status," Dr. Emens concluded.

T-DM1 IMPROVES SURVIVAL AFTER NEOADJUVANT THERAPY AMONG WOMEN WITH HER2-POSITIVE CANCER AND RESIDUAL DISEASE

Findings from the KATHERINE study suggest that treatment with T-DM1 confers a significant invasive disease-free survival (IDFS) advantage over trastuzumab in women with HER2 positive cancer and residual disease after neoadjuvant therapy, Charles E. Geyer, Jr, MD, reported today.

KATHERINE is an international phase III, open-label study of 1,486 patients who have residual breast or axillary disease after undergoing neoadjuvant chemotherapy plus HER2-targeted therapy, said Dr. Geyer, of the Virginia Commonwealth University School of Medicine, Richmond, VA. The neoadjuvant therapy must have included at least 9 weeks of taxane and trastuzumab. The patients were randomized within 12 weeks of surgery to receive 14 cycles of T-DM1 or trastuzumab.

Each group consisted of 743 women. Median duration of follow-up was 40.9 months in the trastuzumab group and 41.4 months in the T-DM1 group. The patients were roughly similar in terms of median age, race, and region of residence. Prior anthracycline had been received by 564 women in the trastuzumab group (75.9%) and 579 women in the T-DM1 group (77.9%).

T-DM1 was associated with a total of 91 IDFS events, such as distant recurrence or contralateral breast cancer, compared with 165 with trastuzumab, and an unstratified hazard ratio of 0.50 (95% CI, 0.39-0.64; $p < 0.0001$). Three-year IDFS was 88.3% with T-DM1 and 77% with trastuzumab.

These data “will likely form the foundation of a new standard of care in this population and increase the use of neoadjuvant therapy in HER2-positive EBC,” Dr. Geyer said.

However, 133 patients (18%) discontinued T-DM1 due to side effects such as decreased platelet count or increased bilirubin, compared with only 15 (2.1%) patients given trastuzumab, although most adverse events were considered mild.

“The standard of care has changed,” Eric P. Winer, MD, of the Dana-Farber Cancer Institute, Boston, MA, said in a discussion following Dr. Geyer’s presentation. “T-DM1 should be recommended to the vast majority of patients with residual disease after a taxane-based neoadjuvant regimen.” Its role in the adjuvant and neoadjuvant settings is still limited, “but I predict this will change dramatically over time.” He also recommended that new trials be developed to optimize its use.

EFFICACY RESULTS OF ADDING ADJUVANT CAPECITABINE TO STANDARD CHEMOTHERAPY IN EARLY TRIPLE-NEGATIVE BREAST CANCER

Investigators of the randomized phase III trial, GEICAM/2003-11_CIBOMA/2004-01, hypothesized a 9% increase in 5-yr disease-free survival (DFS) with the addition of capecitabine (an oral agent approved for the treatment of metastatic breast cancer) to standard neo/adjuvant chemotherapy in early triple-negative BC (TNBC).

On Wednesday afternoon, Dr. Miguel Martín, from Madrid Spain, presented results of the study, showing that adding capecitabine to anthracycline-based chemotherapy (with or without taxane-based therapy) did not significantly increase DFS or overall survival (OS) in early TNBC. The study reported a 5-yr DFS in the capecitabine arm of 79.6% vs 76.8% in the observation arm. OS in the capecitabine arm was reported as 86.2% vs 85.9% in the observation arm.

“An interesting thing we saw in the trial refers to the basal vs non-basal phenotype,” said Dr. Martín. A subgroup analysis found that patients with non-basal type (TNBC with no expression of EGFR and CK5/6 markers) had a statistically significant increase in 5-yr DFS (from 72.9% to 82.6%) when extended adjuvant capecitabine was added to the regimen. However, there was no DFS improvement with treatment in the basal-type TNBC group. Five-year OS was similarly improved in the non-basal type treatment subgroup, but not the basal type.

Dr. Martín added that capecitabine was able to significantly reduce distant recurrence in the non-basal type population, particularly in terms of reduction in liver and brain metastases.

Dr. Martín concluded with a report on adverse events associated with the use of 8 cycles of capecitabine at a relative median dose intensity of 86.3%. Toxicity of capecitabine was as expected. Hand-foot syndrome was the most common adverse event, followed by diarrhea, nausea, and fatigue. Two toxic deaths involving septic shock and liver failure were also reported.