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2017 DEC. 5-9

Henry B. Gonzalez Convention Center, San Antonio, Texas, USA

ISSUE 3

Plenary Lecture 3: Individualizing Management of the Axillary Nodes

Tari A. King, MD
Dana-Farber Cancer Institute • Boston, MA

HALL 3

This morning, Dr. Tari A. King from Dana-Farber Cancer Institute in Boston, MA will be presenting on individualizing the management of the axillary nodes.

With the field evolving to afford more women with the opportunity to avoid axillary node dissection and its resultant increased risk of lymphedema, Dr. King will review recent data focused on identifying appropriate patients and treatment strategies for a "less is more" approach: minimizing local therapy used in the axillary lymph node area without compromising oncological outcomes.

Since its introduction and widespread adoption in the mid-1990s, the sentinel lymph node (SLN) biopsy procedure has been proven effective for women presenting with clinically negative axilla. For those who are ultimately proven to not have cancer in the lymph nodes, the accumulated data provides a clear understanding of the accuracy of this procedure and the risk of axillary recurrence after SLN biopsy alone. Similarly, women who present with a clinically negative axilla and are found to have limited disease in the SLNs, generally defined as one or two positive nodes, can also safely avoid axillary node dissection in favor of observation or axillary radiation, as demonstrated by several recent clinical trials (ACOSOG Z0011, IBCSG 23-01, and EORTC 10981-22023 AMAROS).

However, data on the use of SLN biopsy in women who present with clinically positive axillary nodes are still evolving, and the big question is can we attempt to eradicate the cancer in the axillary nodes with preoperative chemotherapy and then use the SLN procedure to demonstrate, with a high level of certainty, that the cancer has been completely eradicated? Early trials, which include ACOSOG Z1071, SENTINA, and SN-FNAC, tested this approach. These trials demonstrated important technical aspects of using SLN biopsy in this setting and documented that the false negative rate is highly dependent on the number of SLNs removed. Importantly, because all participants in these trials received completion axillary lymph node dissection, these trials do not provide information on the risk of axillary recurrence when SLN biopsy alone is used to stage the axilla following preoperative chemotherapy in women who were known to have node positive disease. These trials have, however, opened up the possibility that axillary node dissection may be avoidable in patients who have had a complete response to preoperative chemotherapy; the challenge lies in patient selection and optimization of the SLN procedure.

Dr. King emphasizes the importance of two ongoing clinical trials on the management of the axilla after preoperative chemotherapy. The Alliance A11202 trial addresses whether or not axillary irradiation can replace axillary node dissection for patients with residual nodal disease after preoperative chemotherapy, while the NRG 9353 trial asks, "Can we de-escalate therapy and

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ISSUE AT A GLANCE

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SYMPOSIUM UPDATES

FRIDAY, DECEMBER 8

WITHDRAWN

POSTER SESSION 4

- P4-03-08
- P4-10-10

POSTER SESSION 5

- P5-12-03
- P5-14-03
- P5-15-03
- P5-21-05
- P5-22-18

PROGRAM NUMBER CORRECTION

GS5-08. A validation of DCIS biological risk profile in a randomised study for radiation therapy with 20 year follow-up (SweDCIS)

Wärnberg F, Garmo H, Folkvaljon Y, Holmberg L, Karlsson P, Sandelin K, Linke S, Lyle S, Simin K, Leesman G, Barry T, Savala J, Whitworth P and Bremer T. Uppsala University, Uppsala, Sweden; King's College London, Medical School, Division of Cancer Studies, King's College London, London, United Kingdom; Sahlgrenska University Hospital, Göteborg, Sweden; Karolinska Institutet, Stockholm, Sweden; PreludeDx, Laguna Hills, CA; University of Massachusetts Medical School, Worcester, MA; Spectrum Pathology, Mission Viejo, CA; Nashville Breast Center, Nashville, TN and Regional Cancer Centre, Uppsala University, Uppsala, Sweden.

*AT PRESS TIME

omit regional nodal irradiation in patients who have had a complete response to preoperative therapy?"

With a large and evolving body of data that allows moving away from a one-size-fits-all approach to management of the axillary lymph nodes, clinicians can increasingly offer patients a "less is more" approach. As more is discovered on the interplay between breast cancer biology, response to treatment, and local therapy, local therapy strategies can be individualized to minimize the risks of long-term arm morbidity without compromising outcomes.

AACR Outstanding Investigator Award for Breast Cancer Research, funded by Susan G. Komen® 2017 Award Recipient

FRIDAY, DECEMBER 8, 11:30 AM, HALL 3

Tackling Breast Cancer Diversity
Nicholas C. Turner, PhD, FRCP
Institute of Cancer Research and Royal, Marsden London, England

The AACR Outstanding Investigator Award for Breast Cancer Research, funded by Susan G. Komen®, recognizes an investigator of no more than 50 years of age whose novel and significant work has had or may have a far-reaching impact on the etiology, detection, diagnosis, treatment, or prevention of breast cancer. Such work may involve any discipline across the continuum of biomedical research, including basic, translational, clinical and epidemiological studies.

Dr. Nicholas C. Turner is honored for his seminal work in developing novel targeted therapy approaches for breast cancer, and directing treatment with circulating tumor DNA analysis.

His work on targeted therapies in breast cancer has focused on amplification of FGFR1/2 and targeting the cell cycle for therapy. He identified FGFR1 and FGFR2 amplification as oncogenic drivers that promote endocrine resistance, demonstrating that high-level and clonal amplification are required for response to FGFR inhibitors in the clinic. He has had a major role in targeting aberrant regulation of the cell cycle for breast cancer treatment, discovering mechanisms of action of WEE1 inhibitors and CDK4/6 inhibitors, and he has led translational efforts, turning insights from basic science into clinical trials of targeted therapy in breast cancer.

His work on circulating tumor DNA (ctDNA) analysis has demonstrated how ctDNA analysis can more accurately deliver treatment in breast cancer. In particular, he has shown that ctDNA analysis can detect minimal residual disease, and, as well, predict who will relapse after treatment for early stage breast cancer. His work has also demonstrated the potential clinical utility of ctDNA analysis in advanced breast cancer.

Dr Nicholas Turner is Professor at the Institute of Cancer Research and Consultant Medical Oncologist at the Royal Marsden Hospital, in London. He leads the Molecular Oncology at the Breast Cancer Now Research Centre at the Institute of Cancer Research (ICR), and is the Genotype, Phenotype and Cancer Evolution Lead for The Royal Marsden NIHR Biomedical Research Centre. He is the Breast Domain Lead of the Genomics England Clinical Interpretation Partnerships, and has co-chaired of the ASCO/CAP review committee on circulating tumor DNA analysis in patients with cancer.

Hot Topic: Ovarian Suppression

Dr. Matteo Lambertini, a San Antonio Breast Cancer Symposium clinical scholar awardee, presented the results of a study investigating temporary ovarian suppression with gonadotropin-releasing hormone analogs (GnRHa) during chemotherapy as a strategy to preserve ovarian function and fertility in premenopausal early breast cancer (eBC) patients.

The study evaluated individual patient data from five randomized control trials (PROMISE-GIM6, POEMS/SWOG S0230, Anglo Celtic Group OPTION, GBG-37 ZORO, and the Moffitt-led trial).

Results revealed the premature ovarian insufficiency (POI) rate, according to the definition used as primary endpoint in each trial, to be improved to 14.1% in the GnRHa group from 30.9% in the control group. The effect of GnHRa reducing the risk of chemotherapy-induced POI was homogeneous across all subgroups. The treatment was effective regardless of patient age at time of diagnosis, estrogen receptor (ER) status, and type and duration of chemotherapy.

No significant difference was observed in amenorrhea one year after the end of chemotherapy between the two subgroups. However, the results diverged favoring the use of GnHRa in the two-year amenorrhea rate (GnRHa group: 18.2% vs control group: 30.0%). No significant difference in disease-free survival (DFS) and overall survival (OS) was observed regardless of ER status of the tumor.

The study concluded that the administration of GnHRa during chemotherapy is associated with a significant reduction in the risk of chemotherapy-induced POI, so that the strategy could be an option to improve the preservation of future fertility in premenopausal eBC patients undergoing adjuvant or neoadjuvant chemotherapy.

Following Dr. Lambertini's talk, Dr. Prudence Francis (on behalf of Dr. Olivia Pagani) presented an update of the combined TEXT and SOFT trials. After a median 9-year follow-up, results confirm statistically significant improvements in disease outcomes with exemestane plus ovarian function suppression (E+OFS). Adjuvant E+OFS, compared to tamoxifen plus ovarian function suppression (F+OFS), shows a sustained absolute improvement in DFS (4%) and reduction in distant recurrence (2.1%). In patients with HER2-negative tumors, E+OFS improved disease outcomes in all treatment cohorts.

Dr. Gini Fleming then further discussed the SOFT Trial, revealing that the addition of OFS to tamoxifen significantly improves DFS in premenopausal women with HR+ eBC at the 8-year median follow-up. A small OS benefit is seen at 8 years in women with prior chemotherapy, and the population not receiving chemotherapy has a low risk of distant metastases at 8 years with tamoxifen alone. Follow-up for both studies continues.

In her discussion, Dr. Ann Partridge summarized that patients with higher risk disease should consider OFS. However, "ultimately, patient preference and tolerance is key. After all, the best treatment is the one the patient will take."

Acupuncture for Aromatase Inhibitor-Related Joint Pain in Early Breast Cancer

Joint pain is one of the leading causes of noncompliance in aromatase inhibitor (AI) therapy in women with early breast cancer. Data about acupuncture for AI-related arthralgia have been conflicting and/or unclear due to study designs using small sample sizes or varying methodologies. On Wednesday afternoon, Dawn Hershman, MD, from Columbia University, New York, presented findings from a multicenter, randomized, phase III trial looking at the efficacy of acupuncture in reducing AI-related joint pain in 226 women.

The study randomized participants to 1 of 3 arms. 110 women in the true acupuncture (TA) arm received standardized, joint-specific point prescriptions twice weekly for 6 wk. The sham acupuncture (SA) group (59 women) underwent shallow insertions of thinner and shorter needles near non-acupuncture points near affected joints twice weekly for 6 wk. An additional 57 women served as a waitlist control (WC) group. The primary endpoint of worst pain score on the Brief Pain Inventory was evaluated at 6 wk, again after 6 more weeks of once-weekly treatment, and again after 12 further weeks with no treatment.

The data presented by Dr. Hershman showed a significant improvement in the worst pain score in women who received TA, compared to those in the SA or WC group. There was no difference in women who received SA, compared to those in the WC group. 58% of patients who received TA had a 2-point drop in worst pain score, compared to 31% who received SA, and 30% in the WC group. At the end of 24 wk, overall, TA was still more effective than SA and WC in reducing worst pain scores.

TA was also found more effective than SA and WC in improving secondary outcomes, such as average pain, worst stiffness, and symptoms in hips, knees, and hands. At 24 wk, TA was still more effective than SA and WC

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in these outcome measures, though results in the hands were less significant.

Dr. Hershman added that these effects persisted for 12 wk following completion of the intervention, and the main adverse event was grade 1 bruising (47% in the TA group vs 25% in the SA group).

"We feel that acupuncture provides a non-pharmacologic option that can improve symptoms, possibly increase AI adherence, and (improve) subsequent breast cancer outcomes," Dr. Hershman concluded.

PD7-13: Molecular Characterization and Mortality from Breast Cancer in Men

Suleiman A. Massarweh[1, 2*] George W. Sledge,[1, 2] Dave P. Miller,[3] Debbie McCullough,[3] Valentina I. Petkov,[4] Steven Shak.

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BACKGROUND: Limited data exist on the molecular biology, treatment, and outcomes of breast cancer in men and much of our understanding in this area remains largely an extrapolation from data in women with breast cancer.

METHODS: We studied men and women with hormone receptor (HR)-positive breast cancer and 21-gene test (RS) results. Patients with negative nodes, micrometastasis, and 1-3 positive nodes were included. Differences in clinical characteristics and gene expression were determined and distribution of RS results was analyzed and correlated with 5-year breast cancer specific survival (BCSS) and overall survival (OS).

Results: There were 3806 men and 571115 women. Men were older than women (mean age 64.2 vs. 59.1 years, p<0.001). RS <18 predominated in both genders, but RS ≥31 was more frequent in men (12.4% vs. 7.4%, p<0.001) as were very low scores (RS <11) (33.8% vs. 22.1%, p<0.001). Mean gene expression was higher in men for the ER, proliferation, and invasion groups. ER was lowest and PR highest in women <50 years, with a progressive increase in ER with age. Men <50 years had slightly lower ER and PR compared to older men. Survival data was available from SEER for 322 men and 55842 women. 5-year estimates for BCSS differed significantly between RS groups for both men (p=0.003) and women (p<0.001). For men, the 5-year BCSS was 99.0% and 95.9% with RS <18 and RS 18-30, respectively, and for women it was 99.5% and 98.6%, regardless of nodal status. RS ≥31 was associated with a 5-year BCSS of 81.0% in men and 94.9% in women. The prognostic utility of RS was evident in both men and women, despite the progressive increase in adjuvant chemotherapy use with higher RS results. 5-year BCSS and OS were overall lower in men than in women.

CONCLUSION: This large genomic study reveals some distinctive biologic features of breast cancer in men and an important prognostic role for 21-gene testing in both men and women, regardless of nodal status. Future adjuvant trials in ER-positive breast cancer should focus on targeting endocrine-resistance in those patients with RS ≥31, and need to consider the weight of competing causes of mortality when investigating the value of any additional treatment beyond endocrine therapy.