



# Newsletter 2014

ISSUE 3

## Plenary Lecture #3: Adjuvant Endocrine Therapy in 2015

Nancy E. Davidson, MD

Adjuvant endocrine therapy has made a significant impact on the way women with breast cancer (BC) have been treated, and now ideas about new treatment strategies are emerging. Tamoxifen has primarily been used in the treatment of premenopausal women with hormone receptor-positive BC, but the use of aromatase inhibitors (AIs) with ovarian function suppression in premenopausal women has been gaining significant interest. On Friday, Dr. Nancy Davidson will discuss emerging data about new endocrine therapy strategies with the premenopausal patient in mind, along with other issues such as medication compliance and BC resistance. Can exemestane plus ovarian suppression provide a new adjuvant treatment option for premenopausal women? The Tamoxifen and Exemestane Trial (TEXT) and the Suppression of Ovarian Function Trial (SOFT) were designed to compare the AI exemestane with tamoxifen in premenopausal women with early BC who received ovarian function suppression. Dr. Davidson will answer that question, and will also focus on the key question about how this approach compares with tamoxifen used alone. Those answers lie in the full results of SOFT, which are being presented during SABCS this week.

"There is a lot of concern and interest in the importance of compliance for these therapies," Dr. Davidson said. She added that the emerging literature on compliance with long-term oral therapies for BC show that there is room for improvement. Despite the positive outcomes associated with tamoxifen use, many women stop taking their medications because of side effects such as hot flashes, decreased libido, and arthritis pain. Long-term use has also been associated with blood clotting and endometrial cancer. Studies indicate that women who adhere to tamoxifen therapy less than fully are more likely to die than the women who are more compliant. Dr. Davidson will discuss the emerging literature about these issues.

Which patients would benefit from longer therapy? With the possibility of using biomarkers to predict development of earlier or late BC recurrence, Dr. Davidson raises the question of whether a woman predicted to have late recurrence might need longer or additional therapy. She will draw from the results of the aTTom (Adjuvant Tamoxifen: To Offer More?) and ATLAS (Adjuvant Tamoxifen, Longer Against Shorter) trials to help weigh the decisions about giving 5 years of treatment vs 10 years of treatment.

Friday, December 12th - 9:00am. - Hall D

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Scan the QR code to hear brief interviews and commentaries from faculty who presented this year's hot topics and plenary lectures as they become available during the Symposium.



[www.audiodigest.org/sabcs14](http://www.audiodigest.org/sabcs14)

# Symposium UPDATES

## POSTER SESSION 5

FRIDAY, DEC 12<sup>TH</sup>

### POSTERS WITHDRAWN

- P5-01-16
- P5-06-02
- P5-07-03
- P5-11-02
- P5-16-04
- P5-18-03
- P5-18-04
- P5-19-18
- P5-20-05

### PRESENTER UPDATES

- P5-12-02 – will be presented by Dr. Bernardo Bonanni
- OT3-2-01 – will be presented by Dr. Carolien Schröder

## POSTER SESSION 6

SATURDAY, DEC 13<sup>TH</sup>

### POSTERS WITHDRAWN

- P6-03-14
- P6-08-12
- P6-08-51
- P6-10-05
- P6-13-07
- P6-14-04

## AACR Distinguished Lectureship in Breast Cancer Research

### Genomic Analysis of Inherited Breast and Ovarian Cancer

*Dr. Mary-Claire King*

Friday, December 12, 11:30 am, Hall D

The AACR Distinguished Lectureship in Breast Cancer Research has been established to recognize outstanding science that has inspired or has the potential to inspire new perspectives on the etiology, diagnosis, treatment, or prevention of breast cancer.

Dr. Mary-Claire King is honored for her many outstanding research accomplishments, including the discovery of the BRCA1 locus' association with hereditary breast cancer. Her work has focused on understanding the inherited genetic factors that can increase a person's risk of developing breast and ovarian cancer and the molecular mechanisms of action of BRCA1, BRCA2, and other genes associated with an increased risk for developing cancer.

Dr. King's breast cancer research encouraged the study of other complex diseases to examine if there could be an underlying inherited component in some families. Her other medical research interests include genetic analysis of inherited deafness, identifying genetic causes of schizophrenia and other severe mental illnesses, and understanding the genetics of systemic lupus erythematosus. Dr. King also is interested in human genetic diversity and evolution, and in the application of her genetic skills to human rights problems.

Dr. King has received many honors and awards for her seminal contributions to genetics research, as well as her humanitarian efforts. She was elected to the Fellows of the AACR Academy, the National Academy of Sciences (NAS), the Institute of Medicine (IOM), the American Academy of Arts and Sciences, and as a Fellow of the American Association for the Advancement of Science (AAAS). Dr. King's awards include the Gruber Genetics Prize from the Peter and Patricia Gruber Foundation, the Clowes Award for Basic Research from the American Association for Cancer Research, the Jill Rose Award from the Breast Cancer Research Foundation, and the Brinker Award from the Susan G. Komen Foundation. King was also named as honorary chair for the state of Washington at the 50th Anniversary of the United Nations.

Dr. King holds a B.A. in Mathematics from Carleton College in Minnesota and a Ph.D. in Genetics from the University of California at Berkeley. She carried out her postdoctoral training at the University of California, San Francisco. Prior to joining the Department of Medicine (Medical Genetics) and the Department of Genome Sciences at the University of Washington, Seattle, in 1995, King served as a Professor of Genetics in the Departments of Molecular and Cell Biology and of Epidemiology at the University of California at Berkeley from 1976 to 1995.

\* At Press Time

## AROME Special Satellite Symposium: Minimal Requirements and Radiation Therapy Standards for Breast Cancer in Countries with Limited Resources

On Friday, a special satellite symposium will be presented by the Association of Radiotherapy and Oncology of the Mediterranean Area (AROME). This course will focus on breast radiotherapy practice in the context of limited resources, such as lack of access to technology and hands-on training, and inequalities in countries that provide care using only local and regional resources. The workshop will feature presentations by internationally recognized experts from France, Tunisia, Turkey, Lebanon, and Mexico.

SABCS welcomes Dr. Joseph Gligorov (France), President of AROME, Dr. Hamouda Bousse (Tunisia), and Dr. Adeal Poitevin (Mexico), who will discuss ways of adapting means, new drugs, and evidence-based radiotherapy in countries with

limited resources. Attendees will also learn ways to implement multidisciplinary and adapt guidelines from a discussion led by Dr. Fady Geara (Lebanon). Issues about radiotherapy techniques and indications according to means will be addressed by Drs. Nuran Bese (Turkey) and Yazid Belkacemi (France). Dr. Alphonse G. Taghian (United States) will discuss ways to prevent toxicities when providing regional radiation therapy.

This symposium will be an important educational opportunity for general attendees of SABCS, but will be a particularly important resource for attendees who provide day-to-day care in areas with limited resources.

Friday, December 12, 7:30 to 9:30 PM, Ballroom B

## Suppression of Ovarian Function Trial (SOFT): Efficacy and Tolerability of Tamoxifen and Ovarian Function Suppression

On Thursday, presenters from the International Breast Cancer Study Group shared results from SOFT trial, a landmark study designed to assess the value of ovarian function suppression (OFS) added to tamoxifen in reducing recurrence in young, premenopausal women with early hormone receptor-positive (HR+) breast cancer (BC). The secondary objective was to compare exemestane plus OFS with tamoxifen alone.

“Maximum suppression of estrogen levels appears to be important in young women with hormone-sensitive breast cancer,” Dr. Prudence Francis said. Although the addition of OFS did not lead to significant benefits in the overall population of premenopausal women, addition of OFS to tamoxifen improved disease outcomes in women with HR+ disease who are at sufficient risk for recurrence to warrant adjuvant chemotherapy, and who remain premenopausal after such chemotherapy.

In the cohort of women with no prior chemotherapy, no meaningful benefit from OFS was seen, as women who received tamoxifen alone demonstrated a 95% chance of remaining BC-free for 5 years.

Women who received prior chemotherapy saw improved outcomes with OFS. Their chance of remaining BC-free at 5 years with tamoxifen alone was 78%, 82.5% with tamoxifen and OFS, and up to 85.7% with exemestane and OFS. The most striking advantage of OFS was seen in women under 35 years of age, 94% of whom had prior chemotherapy.

In addition to assessing the effectiveness of the treatments at reducing risk for BC recurrence, investigators also collected patient-reported quality-of-life assessments. These results were presented by Dr. Karin Ribí. “Overall, we are seeing that patients receiving tamoxifen plus OFS experienced worse endocrine symptoms and sexual functioning than those receiving tamoxifen alone,” she said. Most of the differences in symptoms, such as hot flashes and sweats between treatments were seen during the first 2 years of treatment, and were no longer apparent at 5 years.

Drawing from the SOFT results, Dr. Hope Rugo presented a new algorithm for early premenopausal HR+ disease. She suggested that low-risk women who received no chemotherapy could be well-treated with tamoxifen alone for at least 5 years. And while OFS appears to provide significant reduction in BC recurrence in high-risk women, she pointed out that treatment of intermediate-risk women remains uncertain. “My argument would be in premenopausal women, ovarian suppression and endocrine therapy would be reasonable,” she said.

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## Adjuvant Chemotherapy: Rational Regimens and Combination Therapies

The rationale for combination adjuvant chemotherapy is to use agents with different mechanisms of action to yield better outcomes without intolerable side effects. When combining breast cancer drugs with different effects, optimal doses and schedules must be determined.

Dr. Charles Geyer presented NSABP B-36 data that compared 4 cycles of standard adjuvant chemotherapy (doxorubicin and cyclophosphamide) every 3 weeks to 6 cycles of 5-fluorouracil, epirubicin, and cyclophosphamide (FEC-100) every 3 weeks in patients with node-negative BC. He reported that the 8-year DFS and overall survival did not improve in the FEC-100 arm, compared to the standard therapy arm. Toxicities were higher with the FEC-100 regimen, and there were 5 deaths in the FEC-100 arm compared to 2 deaths in the standard therapy group.

Next, Dr. Joseph Sparano presented a 10-year update of E1199, a study that looked at patients with axillary node-positive or high-risk node-negative BC who received 4 cycles of doxorubicin and cyclophosphamide every 3 weeks, followed by either paclitaxel or docetaxel, either weekly or every 3 weeks. His group found that in their entire patient population, adjuvant weekly paclitaxel

and docetaxel every 3 weeks were associated with significant improvements in DFS, and marginal improvements in overall survival, compared with paclitaxel given every 3 weeks. Among patients with triple-negative disease, the 10-year DFS rate with weekly paclitaxel was 69%, and the 10-year overall survival rate was 75%.

Then, Dr. Gunter von Minckwitz presented data from the ICE study, showing that adding adjuvant capecitabine failed to improve invasive DFS in patients over 65 years of age who were receiving ibandronate. He stated that outcomes in patients with moderate- or high-risk early BC receiving ibandronate alone were favorable, with a 5-year DFS rate of 77% and 5-year overall survival rate of 88%.

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## New Concepts in Translational Science

Clinical and translational developments in breast cancer (BC) research set the framework for transforming laboratory models and findings into new treatments for patients.

“There’s beginning to be more interest now in the fact that the preexisting inflammatory state of a gland can really influence how fast tumors are initiated,” said Nicholas Brady, who presented a genetic mouse model of the role of STAT5 protein and macrophages in mammary gland development and ductal elongation. His group hypothesized that loss of inflammatory homeostasis by macrophage-specific deletion would predispose mammary glands to tumor initiation. They saw exacerbation of the iFGFR1 phenotype and increased proliferation of mammary epithelial cells in mice with STAT5-deficient macrophages.

Then, Dr. Christos Sotiriou discussed how his group aimed to characterize the extent of A-to-I RNA editing in BC. Dr. Sotiriou presented data showing that mean editing frequency is significantly and positively correlated with ADAR protein expression, as they saw high ADAR expression with more

edited sites and higher editing frequency. He added that ADAR expression appears to be regulated by both ADAR copy number gains and the type I interferon response.

Next, Dr. Kathy Albain presented a presurgical window model to identify a Notch-driven BC stem cell gene set modulated by anti-Notch therapy in estrogen receptor-positive BC patients. According to Dr. Albain, Notch signaling regulates 18 genes that promote BC stem cell growth, which can be inhibited by gamma-secretase inhibitors (GSIs) during endocrine therapy. Moreover, these genes reflect the efficacy of anti-Notch GSI therapy. She added, “DAXX and potentially others may be predictive markers of GSI’s inhibition of stem cell survival.”

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