Breast Cancer Update for Surgeons
A Continuing Medical Education Audio Series

OVERVIEW OF ACTIVITY

Historically, surgery has been the primary mode of treatment for early breast cancer. The diagnostic, surgical and medical management of breast cancer, however, has escalated in complexity because of numerous advances in novel technologies and available adjunctive medical therapies. Hence, the multifaceted treatment of breast cancer now requires the input of an interdisciplinary group of expert care providers. This paradigm shift has created the challenge of ensuring that major clinical advances in local and systemic breast cancer therapy are effectively disseminated among all members of the cross-functional team. To bridge the gap between research and patient care, Breast Cancer Update for Surgeons uses one-on-one interviews with leading breast cancer investigators to efficiently distill the latest research developments in the field so that they may be incorporated into clinical practice when appropriate. By providing access to the latest data and expert perspectives, this CME program assists breast surgeons in the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

• Critically appraise and develop an evidence-based approach to the management of the axilla in carefully selected patients with localized breast cancer and a positive sentinel lymph node biopsy.
• Adopt criteria for the selection of patients who can safely be considered for nipple-sparing mastectomy.
• Determine the utility of genomic assays in counseling patients with DCIS or ER-positive early breast cancer about their risk of developing invasive disease or recurrence and the potential benefits of radiation therapy or adjuvant chemotherapy, respectively.
• Evaluate recently presented data supporting the extended use of adjuvant tamoxifen beyond 5 years for patients with ER-positive early breast cancer, and, where appropriate, integrate these findings into clinical practice.
• Counsel appropriately selected patients with breast cancer about participation in ongoing clinical trials.

ACCREDITATION STATEMENT

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HOW TO USE THIS CME ACTIVITY

This CME activity contains an audio component. To receive credit, the participant should review the CME information, listen to the CDs, complete the Post-test with a score of 75% or better and fill out the Educational Assessment and Credit Form located in the back of this booklet or on our website at ResearchToPractice.com/BCUS113/CME.

This activity is supported by an educational grant from Genomic Health Inc.

Last review date: July 2013; Release date: July 2013; Expiration date: July 2014
FACULTY INTERVIEWS

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San Francisco, California

4 Shawna C Willey, MD
Vice-Chairman of Clinical Affairs, Department of Surgery
MedStar Georgetown University Hospital
Director, Betty Lou Ourisman Breast Health Center
Lombardi Comprehensive Cancer Center
Washington, DC

5 SELECT PUBLICATIONS

6 POST-TEST

7 EDUCATIONAL ASSESSMENT AND CREDIT FORM
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**FACULTY** — Dr Wolmark had no real or apparent conflicts of interest to disclose. The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process: **Dr Borgen** — Advisory Committee and Consulting Agreement: Genomic Health Inc. **Dr Rugo** — Contracted Research: Agensys Inc, a subsidiary of Astellas Pharma US, Amgen Inc, Eisai Inc, Genentech BioOncology, GlaxoSmithKline, ImClone Systems, a wholly owned subsidiary of Eli Lilly and Company, MacroGenics Inc, Merck, Novartis Pharmaceuticals Corporation, Plexxikon Inc; Speakers Bureau: Genomic Health Inc. **Dr Willey** — Advisory Committee and Speakers Bureau: Genomic Health Inc, Invuity Inc.

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**RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS** — The scientific staff and reviewers for Research To Practice have no real or apparent conflicts of interest to disclose.
**Tracks 1-12**

**Track 1** ACOSOG-Z0011 study: Axillary lymph node dissection in women with clinical T1-2N0M0 breast cancer and a positive sentinel node

**Track 2** Role of the breast cancer surgeon in personalized cancer care: Clinical utility of the Oncotype DX® assay

**Track 3** Multidisciplinary breast center approach to ordering an Oncotype DX assay

**Track 4** Role of the Oncotype DX assay in clinical decision-making about adjuvant chemotherapy

**Track 5** Prognostic and predictive value of the Oncotype DX assay versus other genomic platforms

**Track 6** Results from ATLAS, a Phase III trial of 5 versus 10 years of adjuvant tamoxifen for women with ER-positive breast cancer

**Track 7** Long-term hormonal therapy for breast cancer

**Track 8** Perspective on nipple-sparing mastectomy

**Track 9** Use of the Oncotype DX DCIS Score™ to facilitate decision-making on the value of radiation therapy

**Track 10** Partial breast irradiation

**Track 11** Impact of surgical margins on local recurrence in women with DCIS

**Track 12** Increasing mastectomy rates in the United States

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**Tracks 1-13**

**Track 1** Timing of sentinel lymph node biopsy in patients receiving neoadjuvant chemotherapy

**Track 2** Results from the CALOR (IBCSG-27-02, NSABP-B-37, BIG 1-02) trial: Adjuvant chemotherapy prolongs survival for patients with isolated local or regional recurrence of breast cancer

**Track 3** Use of the Oncotype DX assay for patients with breast cancer and locoregional recurrence

**Track 4** Historical perspective on the initial development of the Oncotype DX assay for ER-positive, node-negative breast cancer

**Track 5** Rationale for next-generation sequencing in breast cancer

**Track 6** RxPONDER: A Phase III trial of adjuvant endocrine therapy with or without chemotherapy for patients with ER-positive, HER2-negative, node-positive breast cancer and a Recurrence Score® (RS) of 25 or lower

**Track 7** NSABP-B-28 study: Prognostic impact of the Oncotype DX RS in patients with ER-positive, node-positive breast cancer treated with adjuvant chemotherapy

**Track 8** Viewpoint on the Oncotype DX and PAM50 genomic tests

**Track 9** Critical evaluation of the ACOSOG-Z0011 trial results

**Track 10** Use of the Oncotype DX DCIS Score to identify patients who will not benefit from radiation therapy

**Track 11** NSABP-B-50-I: A Phase III trial of the newly FDA-approved agent T-DM1 versus trastuzumab in women with HER2-positive breast cancer who have residual tumor present after neoadjuvant therapy

**Track 12** Mechanism of action of T-DM1

**Track 13** Risk of recurrence for patients with residual disease after neoadjuvant therapy for HER2-positive breast cancer

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Patrick I Borgen, MD

Norman Wolmark, MD
Tracks 1-10

Track 1  **Case discussion:** A 27-year-old woman who is pregnant with a 1.2-cm, ER/PR-positive, HER2-negative, node-positive, BRCA2-mutant, Grade I invasive ductal carcinoma (IDC) and DCIS with an Oncotype DX RS of 16

Track 2  Risk of recurrence and chemotherapy benefit for ER-positive, node-negative breast cancer: RS alone and integrated with pathologic and clinical factors

Track 3  Clinical decision-making regarding neoadjuvant versus adjuvant chemotherapy

Track 4  ATLAS trial: Benefits and risks associated with continuing adjuvant tamoxifen to 10 years versus stopping at 5 years for ER-positive early breast cancer

Track 5  Long-term endocrine therapy and potential considerations for longer-duration, intermittent treatment

Track 6  **Case discussion:** A 27-year-old woman who is pregnant with a 1.2-cm, ER/PR-positive, HER2-negative, node-positive, BRCA2-mutant, Grade I invasive ductal carcinoma (IDC) and DCIS with an Oncotype DX RS of 16

Track 7  Timing of mastectomy for a pregnant patient with breast cancer

Track 8  Long-term treatment options for a young patient with ER-positive, node-positive, BRCA-mutant breast cancer

Track 9  **Case discussion:** A 59-year-old woman with a strongly ER-positive, PR-negative, HER2-negative, Grade III IDC is enrolled on the neoadjuvant I-SPY 2 trial

Track 10  I-SPY 2: A Phase II trial of neoadjuvant chemotherapy and personalized adaptive novel agents for invasive breast cancer

Tracks 1-13

Track 1  **Case discussion:** A 23-year-old woman with a strong family history of cancer and a known BRCA1 mutation desires prophylactic, bilateral, nipple-sparing mastectomy

Track 2  Applications and potential complications of nipple-sparing mastectomy

Track 3  Oophorectomy in patients with known BRCA1 mutation

Track 4  Screening and MRI evaluation in patients with BRCA1 mutation

Track 5  Chemoprevention in BRCA carriers and other patients at high risk for breast cancer

Track 6  Viewpoint on the ATLAS trial results of 5 versus 10 years of adjuvant tamoxifen

Track 7  **Case discussion:** A 76-year-old woman with strongly ER/PR-positive, HER2-negative, Grade II IDC and 2 negative sentinel lymph nodes

Track 8  Use of partial breast irradiation and oncoplastic reconstruction

Track 9  Counseling women about the use of mastectomy versus lumpectomy

Track 10  Advising elderly patients on the role of the Oncotype DX assay and potential administration of adjuvant chemotherapy

Track 11  Differences in the use of the Oncotype DX and MammaPrint® assays in the United States and Europe

Track 12  **Case discussion:** A 30-year-old woman with ER/PR-positive, HER2-positive, Stage IV breast cancer and liver metastases achieves a complete response to taxane/pertuzumab/trastuzumab

Track 13  ECOG-E2108: A Phase III trial evaluating the value of early local therapy for intact primary tumor in patients with metastatic breast cancer
SELECT PUBLICATIONS

A phase III, randomized clinical trial of standard adjuvant endocrine therapy +/- chemotherapy in patients with 1-3 positive nodes, hormone receptor-positive and Her2-negative breast cancer with Recurrence Score (RS) of 25 or less. RxPONDER: A clinical trial Rx or positive node, endocrine responsive breast cancer. NCT01272037

A randomized, multicenter, open-label phase III study to evaluate the efficacy and safety of trastuzumab emtansine versus trastuzumab as adjuvant therapy for patients with HER2-positive primary breast cancer who have residual tumor present pathologically in the breast or axillary lymph nodes following preoperative therapy. NCT01772472

A randomized phase III trial of the value of early local therapy for the intact primary tumor in patients with metastatic breast cancer. NCT01242800


Gray RG et al. aTTom: Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years in 6,953 women with early breast cancer. Proc ASCO 2013; Abstract 5.

I-SPY 2 Trial (Investigation of Serial studies to Predict Your Therapeutic Response with Imaging And moLecular analysis 2). NCT01042379


1. The Phase III ACOSOG-Z0011 trial randomly assigned patients with clinical T1-2N0M0 breast cancer and a positive sentinel node to axillary lymph node dissection versus no axillary lymph node dissection.
   a. True
   b. False

2. The Phase III CALOR trial evaluating no chemotherapy versus chemotherapy as adjuvant therapy for isolated local or regional recurrence of breast cancer demonstrated a significant improvement in 5-year disease-free and overall survival for patients who received chemotherapy.
   a. True
   b. False

3. The ongoing Phase III NSABP-B-50-I trial is evaluating ____________ versus trastuzumab as adjuvant therapy for patients with HER2-positive primary breast cancer who have residual tumor present pathologically in the breast or axillary lymph nodes after preoperative therapy.
   a. Lapatinib
   b. Pertuzumab
   c. T-DM1
   d. All of the above

4. The Phase III RxPONDER study randomly assigns patients with node-negative, ER-positive, HER2-negative breast cancer and an Oncotype DX RS of 25 or higher to adjuvant endocrine therapy with or without chemotherapy.
   a. True
   b. False

5. A retrospective analysis of data from the NSABP-B-28 trial, which compared doxorubicin/cyclophosphamide to doxorubicin/cyclophosphamide followed by paclitaxel, reported that the Oncotype DX RS was a significant predictor of disease-free survival for patients with ER-positive, node-positive breast cancer treated with adjuvant chemotherapy.
   a. True
   b. False

6. The MammaPrint assay continues to require fresh frozen tissue specimens.
   a. True
   b. False

7. The Phase III ATLAS trial of 5 versus 10 years of adjuvant tamoxifen for women with ER-positive early breast cancer demonstrated that the most beneficial effect on breast cancer mortality of continuing tamoxifen to 10 years was observed during which period after diagnosis?
   a. 0 to 4 years
   b. 5 to 9 years
   c. After 10 years

8. The I-SPY 2 trial is a Phase II study of neoadjuvant chemotherapy and personalized adaptive novel agents for the treatment of invasive breast cancer.
   a. True
   b. False
EDUCATIONAL ASSESSMENT AND CREDIT FORM

Breast Cancer Update for Surgeons — Issue 1, 2013

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

**PART 1 — Please tell us about your experience with this educational activity**

How would you characterize your level of knowledge on the following topics?

<table>
<thead>
<tr>
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<th>BEFORE</th>
<th>AFTER</th>
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<tr>
<td>Prognostic impact of the Oncotype DX RS in patients with ER-positive, node-positive breast cancer treated with adjuvant chemotherapy in the NSABP-B-28 study</td>
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<td>4 3 2 1</td>
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<tr>
<td>Benefits and risks associated with continuing adjuvant tamoxifen to 10 years versus stopping at 5 years for ER-positive early breast cancer (ATLAS trial)</td>
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<td>Use of the Oncotype DX DCIS Score to identify patients who will not benefit from radiation therapy</td>
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Was the activity evidence based, fair, balanced and free from commercial bias?
- ☐ Yes  ☐ No

If no, please explain: ........................................................................................................................................................................

Please identify how you will change your practice as a result of completing this activity (select all that apply).
- ☐ This activity validated my current practice
- ☐ Create/revise protocols, policies and/or procedures
- ☐ Change the management and/or treatment of my patients
- ☐ Other (please explain): ........................................................................................................................................................................

If you intend to implement any changes in your practice, please provide 1 or more examples:

...........................................................................................................................................................................................................

The content of this activity matched my current (or potential) scope of practice.
- ☐ Yes  ☐ No

If no, please explain: ........................................................................................................................................................................

Please respond to the following learning objectives (LOs) by circling the appropriate selection:

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<th>4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = LO not met N/A = Not applicable</th>
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<tbody>
<tr>
<td>As a result of this activity, I will be able to:</td>
<td>4 3 2 1 N/M N/A</td>
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<tr>
<td>- Critically appraise and develop an evidence-based approach to the management of the axilla in carefully selected patients with localized breast cancer and a positive sentinel lymph node biopsy.</td>
<td>4 3 2 1 N/M N/A</td>
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<td>- Adopt criteria for the selection of patients who can safely be considered for nipple-sparing mastectomy.</td>
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<td>4 3 2 1 N/M N/A</td>
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<tr>
<td>- Evaluate recently presented data supporting the extended use of adjuvant tamoxifen beyond 5 years for patients with ER-positive early breast cancer, and, where appropriate, integrate these findings into clinical practice.</td>
<td>4 3 2 1 N/M N/A</td>
</tr>
<tr>
<td>- Counsel appropriately selected patients with breast cancer about participation in ongoing clinical trials.</td>
<td>4 3 2 1 N/M N/A</td>
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EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

Please describe any clinical situations that you find difficult to manage or resolve that you would like to see addressed in future educational activities:

Would you recommend this activity to a colleague?
☐ Yes       ☐ No
If no, please explain:

Additional comments about this activity:

As part of our ongoing, continuous quality-improvement effort, we conduct postactivity follow-up surveys to assess the impact of our educational interventions on professional practice. Please indicate your willingness to participate in such a survey.
☐ Yes, I am willing to participate in a follow-up survey.
☐ No, I am not willing to participate in a follow-up survey.

PART 2 — Please tell us about the faculty and editor for this educational activity

<table>
<thead>
<tr>
<th>Faculty</th>
<th>Knowledge of subject matter</th>
<th>Effectiveness as an educator</th>
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<tbody>
<tr>
<td>Patrick I Borgen, MD</td>
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<td>Norman Wolmark, MD</td>
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<td>Hope S Rugo, MD</td>
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<td>Shawna C Willey, MD</td>
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Please recommend additional faculty for future activities:

Other comments about the faculty and editor for this activity:

REQUEST FOR CREDIT — Please print clearly

Name: ................................................................. Specialty: .................................................................

Professional Designation:
☐ MD     ☐ DO    ☐ PharmD ☐ NP ☐ RN ☐ PA ☐ Other

Street Address: ................................................................. Box/Suite: .................................................................

City, State, Zip: .................................................................

Telephone: ................................................................. Fax: .................................................................

Email: .................................................................

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I certify my actual time spent to complete this educational activity to be ________ hour(s).

Signature: ................................................................. Date: .................................................................

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