BCU SURGEONS | 2013 VOL 12 | ISSUE 1

Breast Cancer® UPDATE

An Audio Review Journal for Surgeons

Bridging the Gap between Research and Patient Care

FACULTY INTERVIEWS

Patrick I Borgen, MD
Norman Wolmark, MD
Hope S Rugo, MD
Shawna C Willey, MD

EDITOR

Neil Love, MD

CONTENTS

2 Audio CDs

CME Certified

Subscribe to Podcasts or download MP3s of this program at ResearchToPractice.com/BCUS113

Follow us at Facebook.com/ResearchToPractice Follow us on Twitter @DrNeilLove

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 where 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

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Research To Practice designates this enduring material for a maximum of 2.75 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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

TABLE OF CONTENTS

FACULTY INTERVIEWS

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantor.

EDITOR

Neil Love, MD
Research To Practice
Miami, Florida

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess potential conflicts of interest with faculty, planners and managers of CME activities. Real or apparent conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

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.

EDITOR — Dr Love is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Algeta US, Allos Therapeutics, Amgen Inc, ArQule Inc, Astellas, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, Biodesix Inc, Biogen Idec, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Daiichi Sankyo Inc, Dendreon Corporation, Eisai Inc, EMD Serono Inc, Foundation Medicine Inc, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, Incyte Corporation, Lilly USA LLC, Medivation Inc, Merck, Millennium: The Takeda Oncology Company, Mundipharma International Limited, Novartis Pharmaceuticals Corporation, Onyx Pharmaceuticals Inc, Prometheus Laboratories Inc, Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Spectrum Pharmaceuticals Inc and Teva Oncology.

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.

Have Questions or Cases You Would Like Us to Pose to the Faculty?

Submit them to us via Facebook or Twitter
and we will do our best to get them answered for you

Facebook.com/ResearchToPractice or Twitter @DrNeilLove

Patrick I Borgen, MD

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 Onco*type* DX® assay

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

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

Track 5 Prognostic and predictive value of the Onco*type* 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 Onco*type* 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

Norman Wolmark, MD

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 Onco*type* DX assay for patients with breast cancer and locoregional recurrence

Track 4 Historical perspective on the initial development of the Onco*type* 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 Onco*type* DX RS in patients with ER-positive, node-positive breast cancer treated with adjuvant chemotherapy

Track 8 Viewpoint on the Onco*type* DX and PAM50 genomic tests

Track 9 Critical evaluation of the ACOSOG-Z0011 trial results

Track 10 Use of the Onco*type* 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

Hope S Rugo, MD

Tracks 1-10

Track 1 Neoadjuvant chemotherapy to facilitate breast conservation

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 Onco*type* 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

Shawna C Willey, MD

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 Onco*type* DX assay and potential administration of adjuvant chemotherapy

Track 11 Differences in the use of the Onco*type* 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

Aebi S et al. **Chemotherapy prolongs survival for isolated local or regional recurrence of breast cancer: The CALOR trial (Chemotherapy as Adjuvant for Locally Recurrent Breast Cancer; IBCSG 27-02, NSABP B-37, BIG 1-02).** San Antonio Breast Cancer Symposium 2012;**Abstract S3-2**.

Davies C et al. **Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial.** *Lancet* 2013;381(9869):805-16.

Dowsett M et al. **Prediction of risk of distant recurrence using the 21-gene Recurrence Score in node-negative and node-positive postmenopausal patients with breast cancer treated with anastrozole or tamoxifen: A TransATAC study.** *J Clin Oncol* 2010;28(11):1829-34.

Giuliano AE et al. **Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: A randomized clinical trial.** *JAMA* 2011;305(6):569-75.

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

Laronga C et al. **The role of the breast cancer surgeon in personalized cancer care: Clinical utility of the 21-gene assay.** *Am J Surg* 2012;203(6):751-8.

Latosinsky S et al. **CAGS and ACS Evidence Based Reviews in Surgery. 40. Axillary dissection versus no axillary dissection in women with invasive breast cancer and sentinel node metastasis.** *Can J Surg* 2012;55(1):66-9.

Mallon P et al. **The role of nipple-sparing mastectomy in breast cancer: A comprehensive review of the literature.** *Plast Reconstr Surg* 2013;131(5):969-84.

Mamounas EP et al. **Association between the 21-gene Recurrence Score (RS) and benefit from adjuvant paclitaxel (Pac) in node-positive (N+), ER-positive breast cancer patients (pts): Results from NSABP B-28.** San Antonio Breast Cancer Symposium 2012;**Abstract S1-10**.

Mamounas EP et al. **Association between the 21-gene Recurrence Score assay and risk of locoregional recurrence in node-negative, estrogen receptor-positive breast cancer: Results from NSABP B-14 and NSABP B-20.** *J Clin Oncol* 2010;28(10):1677-83.

Mitchell SD et al. **Incidence rate of nipple areolar complex ischemia after nipple sparing mastectomy. Analysis of the American Society of Breast Surgeons Nipple Sparing Mastectomy Registry.** San Antonio Breast Cancer Symposium 2012;**Abstract P4-14-01**.

Powles TJ. **Extended adjuvant tamoxifen for breast cancer — A new era?** *Lancet* 2013;381(9869):782-3.

Solin LJ et al. **A multigene expression assay to predict local recurrence risk for ductal carcinoma in situ of the breast.** *J Natl Cancer Inst* 2013;105(10):701-10.

Tang G et al. **Comparison of the prognostic and predictive utilities of the 21-gene Recurrence Score assay and Adjuvant! for women with node-negative, ER-positive breast cancer: Results from NSABP B-14 and NSABP B-20.** *Breast Cancer Res Treat* 2011;127(1):133-42.

Tang G et al. **Risk of recurrence and chemotherapy benefit for patients with node-negative, estrogen receptor-positive breast cancer: Recurrence Score alone and integrated with pathologic and clinical factors.** *J Clin Oncol* 2011;29(33):4365-72.

QUESTIONS (PLEASE CIRCLE ANSWER):

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 Onco*type* 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 Onco*type* 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?

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

	BEFORE	AFTER
Prognostic impact of the Onco*type* DX RS in patients with ER-positive, node-positive breast cancer treated with adjuvant chemotherapy in the NSABP-B-28 study	4 3 2 1	4 3 2 1
Benefits and risks associated with continuing adjuvant tamoxifen to 10 years versus stopping at 5 years for ER-positive early breast cancer (ATLAS trial)	4 3 2 1	4 3 2 1
Use of the Onco*type* DX DCIS Score to identify patients who will not benefit from radiation therapy	4 3 2 1	4 3 2 1
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	4 3 2 1	4 3 2 1
NSABP-B-50-I: A Phase III trial of the newly FDA-approved agent T-DM1 versus trastuzumab as adjuvant therapy for HER2-positive primary breast cancer	4 3 2 1	4 3 2 1

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:

4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = LO not met N/A = Not applicable

As a result of this activity, I will be able to:

- 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. . . . . 4 3 2 1 N/M N/A
- Adopt criteria for the selection of patients who can safely be considered for nipple-sparing mastectomy. . . . . 4 3 2 1 N/M N/A
- 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. . . . . 4 3 2 1 N/M N/A
- 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. . . . . 4 3 2 1 N/M N/A
- Counsel appropriately selected patients with breast cancer about participation in ongoing clinical trials. . . . . 4 3 2 1 N/M N/A

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

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

Faculty	Knowledge of subject matter	Effectiveness as an educator
Patrick I Borgen, MD	4 3 2 1	4 3 2 1
Norman Wolmark, MD	4 3 2 1	4 3 2 1
Hope S Rugo, MD	4 3 2 1	4 3 2 1
Shawna C Willey, MD	4 3 2 1	4 3 2 1
Editor	**Knowledge of subject matter**	**Effectiveness as an educator**
Neil Love, MD	4 3 2 1	4 3 2 1

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: .....

Research To Practice designates this enduring material for a maximum of 2.75 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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

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

The expiration date for this activity is July 2014. To obtain a certificate of completion and receive credit for this activity, please complete the Post-test, fill out the Educational Assessment and Credit Form and fax both to (800) 447-4310, or mail both to Research To Practice, One Biscayne Tower, 2 South Biscayne Boulevard, Suite 3600, Miami, FL 33131. You may also complete the Post-test and Educational Assessment online at www.ResearchToPractice.com/BCUS113/CME.

QID 1129

Breast Cancer®
UPDATE

PRSRT STD
U.S. POSTAGE
PAID
MIAMI, FL
PERMIT #1317

Neil Love, MD
Research To Practice
One Biscayne Tower
2 South Biscayne Boulevard, Suite 3600
Miami, FL 33131

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

Research
To Practice®

Sponsored by Research To Practice.

Last review date: July 2013
Release date: July 2013
Expiration date: July 2014
Estimated time to complete: 2.75 hours

This program is printed on MacGregor XP paper, which is manufactured in accordance with the world's leading forest management certification standards.