The Practical Application of Research Advances and Emerging Data in the Management of Breast Cancer

A special audio supplement to a CME conference held during the 2015 San Antonio Breast Cancer Symposium featuring expert comments on the application of emerging research to patient care

Faculty Interviews
Kimberly L Blackwell, MD
Lisa A Carey, MD

Editor
Neil Love, MD

From the publishers of:

Subscribe to Podcasts or download MP3s of this program at ResearchToPractice.com/SanAntonioBC15
Follow us at Facebook.com/ResearchToPractice Follow us on Twitter @DrNeilLove
The Practical Application of Research Advances and Emerging Data in the Management of Breast Cancer

OVERVIEW OF ACTIVITY
Breast cancer (BC) continues to be one of the most rapidly evolving fields in medical oncology. Results from numerous ongoing trials lead to the continual emergence of new therapeutic agents, treatment strategies and diagnostic and prognostic tools. A number of pivotal data sets indicate that additional therapeutic options may soon be available that warrant consideration. In order to offer optimal patient care — including the option of clinical trial participation — the practicing cancer clinician must be well informed of these advances. This CME program uses one-on-one interviews with 2 leading investigators who served as faculty at a recent satellite symposium to discuss key data sets presented at the 2015 San Antonio Breast Cancer Symposium and questions submitted by attendees. This program will assist practicing clinicians in formulating up-to-date and appropriate clinical management strategies.

LEARNING OBJECTIVES
• Develop an evidence-based algorithm for the treatment of hormone-sensitive advanced BC.
• Implement a long-term clinical plan for the management of metastatic HER2-positive BC.
• Evaluate available and emerging data guiding the use of genomic assays to optimize decision-making regarding adjuvant chemotherapy and extended endocrine therapy.
• Appraise novel treatment strategies under investigation in advanced BC (eg, anti-PD-1/PD-L1 antibodies, androgen receptor inhibitors).
• Apply the results of current clinical data to the management of triple-negative BC.

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 1.5 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AMERICAN BOARD OF INTERNAL MEDICINE (ABIM) — MAINTENANCE OF CERTIFICATION (MOC)
Successful completion of this CME activity enables the participant to earn up to 1.5 MOC points in the American Board of Internal Medicine’s (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider’s responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialty: medical oncology.

Personal information and data sharing: Research To Practice aggregates deidentified user data for program-use analysis, program development, activity planning and site improvement. We may provide aggregate and deidentified data to third parties, including commercial supporters. We do not share or sell personally identifiable information to any unaffiliated third parties or commercial supporters. Please see our privacy policy at ResearchToPractice.com/Privacy-Policy for more information.

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 CD, complete the Post-test with a score of 80% 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/SanAntonioBC15/CME. A complete list of supporting references may also be accessed at ResearchToPractice.com/SanAntonioBC15.

This activity is supported by educational grants from Astellas Pharma Global Development Inc/ Medivation Inc, AstraZeneca Pharmaceuticals LP, bioTheranostics Inc, Celgene Corporation, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Lilly and Myriad Genetic Laboratories Inc.

Release date: April 2016; Expiration date: April 2017
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 grantors.

If you would like to discontinue your complimentary subscription to Breast Cancer Update, please email us at Info@ResearchToPractice.com, call us at (800) 648-8654 or fax us at (305) 377-9998. Please include your full name and address, and we will remove you from the mailing list.
SELECT PUBLICATIONS


Gianni L et al. Five-year analysis of the phase II NeoSphere trial evaluating four cycles of neoadjuvant docetaxel and/or trastuzumab and/or pertuzumab. Proc ASCO 2015; Abstract 505.

Harbeck N et al. Final analysis of WSG-ADAPT HER2+/HR+ phase II trial: Efficacy, safety, and predictive markers for 12-weeks of neoadjuvant TDM1 with or without endocrine therapy versus trastuzumab + endocrine therapy in HER2-positive hormone-receptor-positive early breast cancer. San Antonio Breast Cancer Symposium 2015; Abstract S5-03.


Slamon DJ et al. Ten year follow-up of BCIRG-006 comparing doxorubicin plus cyclophosphamide followed by docetaxel (AC → T) with doxorubicin plus cyclophosphamide followed by docetaxel and trastuzumab (AC → TH) with docetaxel, carboplatin and trastuzumab (TCH) in HER2+ early breast cancer. San Antonio Breast Cancer Symposium 2015; Abstract S5-04.


Turner NC et al. PALOMA3: A double-blind, phase III trial of fulvestrant with or without palbociclib in pre- and post-menopausal women with hormone receptor-positive, HER2-negative metastatic breast cancer that progressed on prior endocrine therapy. *Proc ASCO* 2015; Abstract LBA502.

Tutt A et al. The TNT trial: A randomized phase III trial of carboplatin (C) compared with docetaxel (D) for patients with metastatic or recurrent locally advanced triple negative or BRCA1/2 breast cancer (CRUK/07/012). San Antonio Breast Cancer Symposium 2014; Abstract S3-01.


1. Results of the Phase III CREATE-X (JBCRG-04) trial of adjuvant capecitabine in patients with HER2-negative BC who have pathologic residual invasive disease after neoadjuvant chemotherapy demonstrated an improvement in ___________ with the addition of capecitabine.
   a. Disease-free survival
   b. Overall survival
   c. Both a and b

2. Five-year analysis of the NeoSphere trial evaluating the addition of neoadjuvant pertuzumab to trastuzumab and/or docetaxel in locally advanced or inflammatory HER2-positive BC demonstrated that the addition of pertuzumab resulted in a higher pathologic complete response rate.
   a. True
   b. False

3. The Phase II ADAPT trial investigated the efficacy and safety of neoadjuvant ___________ with or without endocrine therapy versus trastuzumab and endocrine therapy in HER2-positive hormone receptor-positive early BC.
   a. Pertuzumab
   b. T-DM1

4. A 10-year follow-up analysis of the BCIRG 006 study evaluating adjuvant AC → T compared to AC → TH and TCH for HER2-positive early BC showed ___________.
   a. A significant benefit with trastuzumab
   b. No significant difference in efficacy between AC → TH and TCH
   c. Both a and b

5. The results of the Phase III GeparSepto (GBG 69) trial evaluating neoadjuvant chemotherapy with weekly nanoparticle albumin-bound (nab) paclitaxel versus solvent-based paclitaxel followed by anthracycline and cyclophosphamide for patients with early-stage BC yielded a statistically significant improvement in pathologic complete response rate with solvent-based paclitaxel.
   a. True
   b. False

6. A retrospective analysis of patients with HER2-positive advanced BC who had preexisting asymptomatic central nervous system metastases and who received T-DM1 versus lapatinib with capecitabine in the EMILIA study demonstrated no difference in overall survival.
   a. True
   b. False

7. The CDK4/6 inhibitor palbociclib was approved by the FDA for use in combination with letrozole for postmenopausal women with ER-positive, HER2-negative advanced BC in the ___________ setting.
   a. First-line
   b. Second-line
   c. Late-line

8. Which of the following is true regarding the use of everolimus in the treatment of hormone receptor-positive BC?
   a. Its mechanism of action involves the inhibition of CDK4/6
   b. It is effective in combination with exemestane
   c. It is commonly associated with mucositis
   d. All of the above
   e. Both b and c

9. The Phase III TNT study comparing carboplatin to docetaxel for patients with metastatic or recurrent locally advanced triple-negative or BRCA1/2 mutation-positive BC demonstrated a benefit with carboplatin versus docetaxel with respect to ___________.
   a. Objective response rate in BRCA1/2 mutation carriers
   b. Overall survival in the unselected population

10. Which of the following CDK4/6 inhibitors has demonstrated significant response rates as a single agent among patients with hormone receptor-positive metastatic BC?
    a. Abemaciclib
    b. Palbociclib
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>
<th>Topic</th>
<th>BEFORE</th>
<th>AFTER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Results of the Phase III CREATE-X (JBCRG-04) trial of adjuvant capecitabine in patients with HER2-negative BC who have pathologic residual invasive disease after neoadjuvant chemotherapy</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Use of genomic assays to predict risk of recurrence and benefit of extended endocrine therapy</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>GeparSepto GBG 69: A Phase III trial comparing nab paclitaxel to solvent-based paclitaxel as neoadjuvant chemotherapy for early BC</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Available data with and ongoing evaluation of novel CDK4/6 inhibitors</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Efficacy of T-DM1 in patients with CNS metastases</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Selection of chemotherapy regimen for patients with BRCA1/2 mutations</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Recent clinical trial results with enzalutamide in patients with androgen receptor-positive, triple-negative BC</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Five-year analysis of the Phase II NeoSphere trial evaluating neoadjuvant docetaxel and/or trastuzumab and/or pertuzumab</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
</tbody>
</table>

**Practice Setting:**
- ☐ Academic center/medical school
- ☐ Community cancer center/hospital
- ☐ Group practice
- ☐ Solo practice
- ☐ Government (eg, VA)
- ☐ Other (please specify)

Approximately how many new patients with breast cancer do you see per year? ........... patients

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:

As a result of this activity, I will be able to:
- Develop an evidence-based algorithm for the treatment of hormone-sensitive advanced BC. ......................................................... 4 3 2 1 N/M N/A
- Implement a long-term clinical plan for the management of metastatic HER2-positive BC. ......................................................... 4 3 2 1 N/M N/A
EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

- Evaluate available and emerging data guiding the use of genomic assays to optimize decision-making regarding adjuvant chemotherapy and extended endocrine therapy. ........................................4 3 2 1 N/M N/A
- Appraise novel treatment strategies under investigation in advanced BC (eg, anti-PD-1/PD-L1 antibodies, androgen receptor inhibitors) .................4 3 2 1 N/M N/A
- Apply the results of current clinical data to the management of triple-negative BC .......................................................................4 3 2 1 N/M N/A

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: ________________________________________________________________

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>
</tr>
</thead>
<tbody>
<tr>
<td>Kimberly L Blackwell, MD</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Lisa A Carey, MD</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Editor</th>
<th>Knowledge of subject matter</th>
<th>Effectiveness as an educator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neil Love, MD</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
</tbody>
</table>

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: _______________________

Email: ___________________________ Fax: ___________________________

Research To Practice designates this enduring material for a maximum of 1.5 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: ___________________________

☐ I would like Research To Practice to submit my CME credits to the ABIM to count toward my MOC points. I understand that because I am requesting MOC credit, Research To Practice will be required to share personally identifiable information with the ACCME and ABIM.

Additional information for MOC credit (required):

Date of Birth (Month and Day Only): ___/___  ABIM 6-Digit ID Number: ___________________________

If you are not sure of your ABIM ID, please visit http://www.abim.org/online/findcand.aspx.

The expiration date for this activity is April 2017. 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/SanAntonioBC15/CME.