ATLAS OF MOLECULAR ONCOLOGY

Critical Pathways in Breast Cancer Treatment

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CME Information: Critical Pathways in Breast Cancer Treatment

OVERVIEW OF ACTIVITY
The diagnosis and treatment of breast cancer have undergone a fundamental shift with the advent of molecular disease subtyping and the availability of genomic assays that enable individualized therapeutic decision-making through the identification of oncogenic pathways responsible for tumor growth.

This unique educational activity will combine the powers of art and science to communicate the complex pathways, processes and structures that define the current and emerging breast cancer treatment landscape. The Atlas of Molecular Oncology: Critical Pathways in Breast Cancer Treatment will provide clinicians with a concise, easy to understand slide resource to facilitate their knowledge and application of novel therapeutic approaches.

TARGET AUDIENCE
This activity is intended for medical, surgical and radiation oncologists and other healthcare providers involved in the treatment of breast cancer.

LEARNING OBJECTIVES
- Differentiate among the unique HER2-directed investigational agents currently in Phase III clinical development.
- Recognize practical and investigational strategies to maximize the clinical utility of endocrine therapy in the management of ER-positive breast cancer.
- Educate patients about the benefits and risks of bevacizumab in combination with evidence-based chemotherapeutic partners.
- Critique the available data with multi-kinase inhibitors in the management of metastatic breast cancer.
- Assess the scientific rationale for continuation of biologic therapy at the time of first disease progression.
- Define the role of the immune system in mediating the activity of cancer vaccine therapy.
- Explain the scientific rationale for selectively treating triple-negative and/or BRCA-deficient breast tumors with PARP inhibitors.
CME Information (continued)

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 educational activity for a maximum of 2.5 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

HOW TO USE THIS CME ACTIVITY
To receive credit, the participant should review the CME information, review the slides on the enclosed CD and complete the Post-test and Educational Assessment and Credit Form located in the back of this booklet or on our website at CME.ResearchToPractice.com.

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 Goss 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 Chang — Consulting Agreement: Boehringer Ingelheim Pharmaceuticals Inc; Speakers Bureau: GlaxoSmithKline. Dr Miller — Consulting Agreement: Bristol-Myers Squibb Company; Speakers Bureau: Genentech BioOncology, Roche Laboratories Inc. Dr Shulman — Advisory Committee and Study PI: EMD Serono Inc. Dr Slamon — Honoraria: Genentech BioOncology, Pfizer Inc, Roche Laboratories Inc, Sanofi-Aventis; Paid Travel: Genentech BioOncology, Roche Laboratories Inc, Sanofi-Aventis; Stock Ownership: Amgen Inc, Pfizer Inc, Schering-Plough Corporation. Dr Tutt — Advisory Committee: AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Novartis Pharmaceuticals Corporation, Pfizer Inc,
CME Information (continued)

Sanofi-Aventis; Honoraria: AstraZeneca Pharmaceuticals LP, Sanofi-Aventis.

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: Abraxis BioScience, Allos Therapeutics, Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals/Onyx Pharmaceuticals Inc, Biogen Idec, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Cephalon Inc, Eisai Inc, EMD Serono Inc, Genentech BioOncology, Genomic Health Inc, Genzyme Corporation, GlaxoSmithKline, ImClone Systems Incorporated, Lilly USA LLC, Millennium Pharmaceuticals Inc, Monogram BioSciences Inc, Novartis Pharmaceuticals Corporation, OSI Oncology, Roche Laboratories Inc, Sanofi-Aventis and Spectrum Pharmaceuticals Inc.

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.

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Post-test: Critical Pathways in Breast Cancer Treatment

1. T-DM1 is a novel agent that combines the highly potent antimicrotubule agent DM1 with _________.
   a. Docetaxel
   b. Trastuzumab
   c. Bevacizumab
   d. None of the above

2. Which of the following is true regarding the efficacy results of the MA17 trial with respect to patients with ER-positive disease who were premenopausal at the time of diagnosis and became postmenopausal after five years of tamoxifen versus women who were postmenopausal at diagnosis?
   a. Extent of improvement with letrozole was greater for the premenopausal than for the postmenopausal patients
   b. Extent of improvement with letrozole was less for the premenopausal than for the postmenopausal patients
   c. No improvement in efficacy was observed in premenopausal patients with extended adjuvant letrozole

3. The monoclonal antibodies trastuzumab and pertuzumab target the same extracellular region of the HER2 receptor.
   a. True
   b. False

4. The TAnDEM trial evaluated the impact of adding trastuzumab to _________ for patients with HER2-positive, ER-positive metastatic breast cancer.
   a. Fulvestrant
   b. Lapatinib
   c. Exemestane
   d. Anastrozole
   e. Letrozole

5. In the randomized Phase III EGF30008 trial for women with hormone receptor-positive metastatic breast cancer, the combination of lapatinib/letrozole demonstrated a statistically significant increase in progression-free survival compared to letrozole alone for those patients with _________ disease.
   a. HER2-positive
   b. HER2-negative
   c. Both a and b
   d. None of the above
6. BLP25 is a liposome-encapsulated vaccine consisting of a synthetic peptide derived from the MUC-1 antigen with potential antineoplastic activity.
   a. True
   b. False

7. A Phase II trial of the PARP inhibitor olaparib demonstrated that the agent was well tolerated and highly active in patients with refractory, advanced _______ breast cancer.
   a. HER2-positive
   b. BRCA1-mutant
   c. None of the above

8. In the randomized Phase II trial of gemcitabine/carboplatin with or without BSI-201 for triple-negative breast cancer, median overall survival was improved by approximately _______ with the addition of the PARP inhibitor.
   a. One month
   b. 4.5 months
   c. 7.7 months

9. In the Phase III ToGA trial for patients with HER2-positive advanced gastric cancer, the addition of trastuzumab to first-line chemotherapy was associated with a relative reduction in the risk of death of approximately __________.
   a. Five percent
   b. 26 percent
   c. 47 percent

10. The combination of lapatinib and trastuzumab showed greater antitumor efficacy than either drug alone when evaluated in HER2-amplified human gastric cancer cells.
    a. True
    b. False

11. The synthetic lethality of PARP inhibitors refers to ____________.
    a. Unblocking all repair pathways in a damaged cell
    b. Blocking a second repair pathway in a cell with a single blocked pathway
    c. Repairing the BRCA mutation
    d. None of the above

Post-test answer key: 1b, 2a, 3b, 4d, 5a, 6a, 7b, 8b, 9b, 10a, 11b
Educational Assessment and Credit Form: Critical Pathways in Breast Cancer Treatment

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 ONE — 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>4 = Excellent</th>
<th>3 = Good</th>
<th>2 = Adequate</th>
<th>1 = Suboptimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Targeting the HER2 signaling pathway and evolving therapeutic options</td>
<td>BEFORE</td>
<td>4 3 2 1</td>
<td>3 2 1</td>
</tr>
<tr>
<td>Endocrine therapy dose and schedule for patients with hormone receptor-positive breast cancer</td>
<td>BEFORE</td>
<td>4 3 2 1</td>
<td>3 2 1</td>
</tr>
<tr>
<td>Synergistic effect of chemotherapy with anti-angiogenic agents</td>
<td>BEFORE</td>
<td>4 3 2 1</td>
<td>3 2 1</td>
</tr>
<tr>
<td>Potential of vaccines to elicit immune response to target cancer cells</td>
<td>BEFORE</td>
<td>4 3 2 1</td>
<td>3 2 1</td>
</tr>
<tr>
<td>BRCA mutations and “BRCA-ness”</td>
<td>BEFORE</td>
<td>4 3 2 1</td>
<td>3 2 1</td>
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<tr>
<td>Therapeutic targeting of the oncogenic pathway</td>
<td>BEFORE</td>
<td>4 3 2 1</td>
<td>3 2 1</td>
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</tbody>
</table>

Was the activity evidence based, fair, balanced and free from commercial bias?

☐ Yes ☐ No

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

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Educational Assessment and Credit Form (continued)

Will this activity help you improve patient care?
☐ Yes    ☐ No    ☐ Not applicable
If no, please explain: ..........................................................................................................................

Did the activity meet your educational needs and expectations?
☐ 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:

• Differentiate among the unique HER2-directed investigational agents currently in Phase III clinical development. ......................... 4 3 2 1 N/M N/A
• Recognize practical and investigational strategies to maximize the clinical utility of endocrine therapy in the management of ER-positive breast cancer ........................................................... 4 3 2 1 N/M N/A
• Educate patients about the benefits and risks of bevacizumab in combination with evidence-based chemotherapeutic partners ........ 4 3 2 1 N/M N/A
• Critique the available data with multikinase inhibitors in the management of metastatic breast cancer ........................................ 4 3 2 1 N/M N/A
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• Define the role of the immune system in mediating the activity of cancer vaccine therapy ...................................................... 4 3 2 1 N/M N/A
• Explain the scientific rationale for selectively treating triple-negative and/or BRCA-deficient breast tumors with PARP inhibitors .......... 4 3 2 1 N/M N/A
Educational Assessment and Credit Form (continued)

What other practice changes will you make or consider making as a result of this activity?

What additional information or training do you need on the activity topics or other oncology-related topics?

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 TWO — Please tell us about the faculty 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>
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</tbody>
</table>
Educational Assessment and Credit Form (continued)

Please recommend additional faculty for future activities:

Other comments about the faculty 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: .........................