



ATLAS OF MOLECULAR ONCOLOGY

Critical Pathways in Breast Cancer Treatment

Faculty

Jenny C Chang, MD
Paul E Goss, MD, PhD
Kathy D Miller, MD
Lawrence N Shulman, MD
Dennis J Slamon, MD, PhD
Andrew Tutt, MB ChB, PhD

Editor

Neil Love, MD



Sponsored by Research To Practice.

Not an official event of the ASCO Annual Meeting. Not sponsored or endorsed by ASCO or The ASCO Cancer Foundation.

From the publishers of:

Breast Cancer[®]
U P D A T E

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 health-care 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.

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.

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

Post-test (continued)

6. BLP25 is a liposome-encapsulated vaccine consisting of a synthetic peptide derived from the MUC-1 antigen with potential antineoplastic activity.
- True
 - 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.
- HER2-positive
 - BRCA1-mutant
 - 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.
- One month
 - 4.5 months
 - 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 _____.
- Five percent
 - 26 percent
 - 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.
- True
 - False
11. The synthetic lethality of PARP inhibitors refers to _____.
- Unblocking all repair pathways in a damaged cell
 - Blocking a second repair pathway in a cell with a single blocked pathway
 - Repairing the BRCA mutation
 - 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?

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

.....

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
- Assess the scientific rationale for continuation of biologic therapy at the time of first disease progression 4 3 2 1 N/M N/A
- 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

4 = Excellent

3 = Good

2 = Adequate

1 = Suboptimal

Faculty	Knowledge of subject matter				Effectiveness as an educator			
Jenny C Chang, MD	4	3	2	1	4	3	2	1
Paul E Goss, MD, PhD	4	3	2	1	4	3	2	1
Kathy D Miller, MD	4	3	2	1	4	3	2	1
Lawrence N Shulman, MD	4	3	2	1	4	3	2	1
Dennis J Slamon, MD, PhD	4	3	2	1	4	3	2	1
Andrew Tutt, MB ChB, PhD	4	3	2	1	4	3	2	1

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:

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.

Educational Assessment and Credit Form (continued)

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

Signature: Date:

AMOBREAST10

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 CME.ResearchToPractice.com.

Copyright © 2010 Research To Practice. All rights reserved.

The compact disc, Internet content and accompanying printed material are protected by copyright. No part of this program may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording or utilizing any information storage and retrieval system, without written permission from the copyright owner.

The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

Participants have an implied responsibility to use the newly acquired information to

enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management.

Any procedures, medications or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patients' conditions and possible contraindications or dangers in use, review of any applicable manufacturer's product information and comparison with recommendations of other authorities.



ATLAS OF MOLECULAR ONCOLOGY

Copyright © 2010 Research To Practice.

This activity is supported by educational grants from
EMD Serono Inc and Genentech BioOncology.

Research To Practice®

Sponsored by Research To Practice.

Last review date: June 2010

Release date: June 2010

Expiration date: June 2011

Estimated time to complete: 2.5 hours