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Implications of Recent Clinical Research Data Sets in the Management of HER2-Positive Breast Cancer

A Breast Cancer Update
Journal Club

MODERATOR

Neil Love, MD

FACULTY

Mark D Pegram, MD

Charles L Vogel, MD

Sandra M Swain, MD

Antonio C Wolff, MD




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Implications of Recent Clinical Research Data Sets in the Management of HER2-Positive Breast Cancer

A Continuing Medical Education Program

OVERVIEW OF ACTIVITY

The human epidermal growth factor receptor gene (HER2) is amplified in 25 to 30 percent of patients with breast cancer (BC), and its presence marks an aggressive form of the disease, historically associated with significantly shortened disease-free and overall survival. Results from numerous ongoing trials lead to the continual emergence of new therapeutic agents, treatment strategies and diagnostic/prognostic tools for this BC phenotype. In order to offer optimal patient care — including the option of clinical trial participation — the practicing clinician must be well informed of these advances. Featuring information on the latest research developments along with expert perspectives, this CME program is designed to assist medical oncologists, hematologists and hematology-oncology fellows with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Assess novel technologies and HER2 diagnostic assays for the identification of patients likely to benefit from anti-HER2 treatment.
- Individualize the selection of evidence-based adjuvant trastuzumab regimens for patients with HER2-overexpressing BC.
- Apply the results of emerging research when prescribing systemic therapy for patients with HER2-positive metastatic breast cancer (mBC) who have previously been exposed to trastuzumab.
- When recommending initiation of trastuzumab or lapatinib, identify patients who may be at increased risk for treatment-associated cardiac toxicity.
- Explain the scientific rationale for dual molecular targeting as a means of enhancing therapeutic efficacy and overcoming acquired resistance to HER2-directed therapy.
- Evaluate the efficacy and safety of novel anti-HER2 directed therapies for the treatment of mBC.
- Recall the design and eligibility criteria for ongoing clinical trials evaluating novel anti-HER2 strategies, and counsel appropriately selected patients with BC about study participation.

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This program is supported by educational grants from Genentech BioOncology, GlaxoSmithKline and Monogram BioSciences Inc.

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CME INFORMATION

MODERATOR

Neil Love, MD
Editor, *Breast Cancer Update*
Research To Practice
Miami, Florida

FACULTY

Mark D Pegram, MD
Full Professor of Medicine
Director for the Translational Research Program, Braman Family Breast Cancer Research Institute, UM Sylvester Comprehensive Cancer Center
Miami, Florida

Sandra M Swain, MD
Medical Director, Washington Cancer Institute
Washington Hospital Center
Professor of Medicine
Georgetown University
Washington, DC

Charles L Vogel, MD
Senior Research Advisor
Aptium Oncology, Breast Cancer
Boca Raton Comprehensive Cancer Center
Boca Raton, Florida

Antonio C Wolff, MD
Associate Professor of Oncology
Breast Cancer Program
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
Baltimore, Maryland

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FACULTY — **Dr Wolff** 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 Pegram** — Advisory Committee: Amgen Inc, Genentech BioOncology, Genomic Health Inc, GlaxoSmithKline, Sanofi-Aventis; Consulting Agreements: Genentech BioOncology, GlaxoSmithKline, Sanofi-Aventis; Data Safety and Monitoring Board: Wyeth; Paid Research: Sanofi-Aventis; Speakers Bureau: Genentech BioOncology, Genomic Health Inc, GlaxoSmithKline, Sanofi-Aventis. **Dr Vogel** — Advisory Committee: Amgen Inc, AstraZeneca Pharmaceuticals LP, Biogen Idec, Bristol-Myers Squibb Company, EMD Serono Inc, Genentech BioOncology, GlaxoSmithKline, Monogram BioSciences Inc, Novartis Pharmaceuticals Corporation, Roche Laboratories Inc, Sanofi-Aventis; Consulting Agreement: Genentech BioOncology; Speakers Bureau: Amgen Inc, Bristol-Myers Squibb Company, Genomic Health Inc, GlaxoSmithKline, Roche Laboratories Inc, Sanofi-Aventis. **Dr Swain** — Paid Travel: Sanofi-Aventis.

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POST-TEST

Implications of Recent Clinical Research Data Sets in the Management of HER2-Positive Breast Cancer

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **Trastuzumab-DM1 (T-DM1) is an immunoconjugate combining trastuzumab with a highly potent _____ agent.**
   a. Antimicrotubule
   b. Alkylating
   c. Antimetabolite

2. **An independent review confirmed an overall response rate of approximately _____ with T-DM1 for patients with heavily pretreated HER2-positive metastatic breast cancer (mBC).**
   a. 75 percent
   b. 50 percent
   c. 25 percent
   d. 10 percent

3. **Pertuzumab is a second-generation humanized anti-HER2 monoclonal antibody that blocks dimerization between HER2 and other HER receptors.**
   a. True
   b. False

4. **What was the response rate with the combination of trastuzumab/pertuzumab for patients with HER2-positive mBC whose disease progressed during trastuzumab therapy?**
   a. 10 percent
   b. 24 percent
   c. 48 percent

5. **First-line lapatinib monotherapy for patients with HER2-positive mBC resulted in a _____ response rate.**
   a. 10 percent
   b. 24 percent
   c. 49 percent

6. **In a Phase II trial of first-line trastuzumab/bevacizumab in patients with HER2-positive mBC, the overall response rate was _____.**
   a. 10 percent
   b. 24 percent
   c. 48 percent

7. **The TAnDEM study and the EGF30008 trial demonstrated increased progression-free survival for postmenopausal patients with ER-positive, HER2-positive mBC who received _____ and anti-HER2 targeted agents.**
   a. Tamoxifen
   b. Fulvestrant
   c. Aromatase inhibitors

8. **In a Phase III study by von Minckwitz and colleagues, continuation of trastuzumab combined with capecitabine resulted in improvements in time to disease progression compared to capecitabine alone for patients with HER2-positive mBC progressing on trastuzumab.**
   a. True
   b. False

9. **In a randomized study, the combination of lapatinib and trastuzumab resulted in equivalent progression-free survival compared to lapatinib alone for patients with heavily pretreated HER2-positive mBC progressing on trastuzumab.**
   a. True
   b. False

10. **CLEOPATRA, a Phase III randomized trial, is evaluating docetaxel/trastuzumab with or without _____ as first-line therapy for HER2-positive mBC.**
    a. Lapatinib
    b. Pertuzumab
    c. T-DM1
    d. Neratinib
    e. None of the above

11. **The HERmark™ Breast Cancer Assay quantifies HER2 total protein and HER2 homodimer levels in formalin-fixed paraffin-embedded tissue.**
    a. True
    b. False

Post-test answer key: 1a, 2c, 3a, 4b, 5b, 6c, 7c, 8a, 9a, 10b, 11a

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Implications of Recent Clinical Research Data Sets in the Management of HER2-Positive Breast Cancer

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
HERmark assay for the quantification of HER2/HER3 and HER2 homodimers and outcomes for patients receiving trastuzumab	4 3 2 1	4 3 2 1
Efficacy and safety of T-DM1 in patients with heavily pretreated HER2-positive mBC	4 3 2 1	4 3 2 1
Efficacy of pertuzumab alone or in combination with trastuzumab in HER2-positive mBC	4 3 2 1	4 3 2 1
First-line letrozole with or without lapatinib in postmenopausal women with ER-positive mBC	4 3 2 1	4 3 2 1
Continuation of trastuzumab with lapatinib or chemotherapy beyond disease progression in HER2-positive mBC	4 3 2 1	4 3 2 1
Risk of recurrence and benefits of trastuzumab-based adjuvant therapy for small, node-negative, HER2-positive BC	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:.....

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:

- Assess novel technologies and HER2 diagnostic assays for the identification of patients likely to benefit from anti-HER2 treatment. . . . . 4 3 2 1 N/M N/A
- Individualize the selection of evidence-based adjuvant trastuzumab regimens for patients with HER2-overexpressing BC. . . . . 4 3 2 1 N/M N/A
- Apply the results of emerging research when prescribing systemic therapy for patients with HER2-positive metastatic breast cancer (mBC) who have previously been exposed to trastuzumab. . . . . 4 3 2 1 N/M N/A
- When recommending initiation of trastuzumab or lapatinib, identify patients who may be at increased risk for treatment-associated cardiac toxicity . . . . . 4 3 2 1 N/M N/A
- Explain the scientific rationale for dual molecular targeting as a means of enhancing therapeutic efficacy and overcoming acquired resistance to HER2-directed therapy. . . . . 4 3 2 1 N/M N/A
- Evaluate the efficacy and safety of novel anti-HER2 directed therapies for the treatment of mBC. . . . . 4 3 2 1 N/M N/A
- Recall the design and eligibility criteria for ongoing clinical trials evaluating novel anti-HER2 strategies, and counsel appropriately selected patients with BC about study participation. . . . . 4 3 2 1 N/M N/A

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 and moderator for this educational activity

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

Faculty	Knowledge of subject matter	Effectiveness as an educator
Mark D Pegram, MD	4 3 2 1	4 3 2 1
Charles L Vogel, MD	4 3 2 1	4 3 2 1
Sandra M Swain, MD	4 3 2 1	4 3 2 1
Antonio C Wolff, MD	4 3 2 1	4 3 2 1
Moderator	**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 moderator for this activity:

.....

REQUEST FOR CREDIT — Please print clearly

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

Professional Designation:

☐ MD ☐ DO ☐ PharmD ☐ NP ☐ RN ☐ PA ☐ Other .....

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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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HER2JC109

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Moderator	Neil Love, MD
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Contact Information	Neil Love, MD Research To Practice One Biscayne Tower 2 South Biscayne Boulevard, Suite 3600 Miami, FL 33131 Fax: (305) 377-9998 Email: DrNeilLove@ResearchToPractice.com
For CME/CNE Information	Email: CE@ResearchToPractice.com

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