

# Second Opinion

## *Clinical Investigators Provide Their Perspectives on Challenging Cases and Controversies in the Management of Metastatic Breast Cancer*

### CME INFORMATION

#### TARGET AUDIENCE

This activity is intended for medical oncologists and other healthcare providers involved in the treatment of breast cancer.

#### OVERVIEW OF ACTIVITY

Breast cancer (BC) remains the most frequently diagnosed cancer in women, and it is estimated that approximately 234,580 new cases will be identified in the United States in the year 2013 and 40,030 individuals will die from the disease. Advances in screening and prevention have resulted in a steady down-stage migration at the time of disease presentation, such that only 5% of women have identifiable distant metastases at primary diagnosis. Because of this, the number of individuals living with BC has increased substantially, as has the population “at risk” for metastatic or recurrent disease. Depending on the histological subtype, the initial stage of their disease at the time of diagnosis and the subsequent treatment strategy employed, approximately 20% to 80% of these women will develop a distant metastasis within 5 years of their BC diagnosis.

Historically, available treatment options offered little for patients with this incurable disease. However, with the introduction of more effective systemic therapies over the past 20 years, there has been a substantial improvement in clinical outcomes. While the diagnosis and treatment of this disease remains in many ways more advanced than for other solid cancers, challenging issues in the management of metastatic BC (mBC) continue to require refinement. Increasing emphasis is being placed on a “personalized medicine” approach that promises to more effectively identify specific treatments that will benefit the individual, based on specific patient and disease characteristics. In conjunction with this approach researchers are developing novel agents to target additional signaling pathways, with the aim of enhancing the efficacy of existing treatments or overcoming resistance/restoring sensitivity to endocrine therapy, chemotherapy or other biologics.

To assist medical oncologists and other allied BC professionals in keeping informed about these approved and developmental approaches, these proceedings from a case-based CME Grand Rounds presentation introduce the perspectives of 12 renowned investigators on a number of controversial clinical and research issues in the management of mBC.

#### LEARNING OBJECTIVES

- Compare and contrast expert perspectives on breast cancer treatment recommendations, and use this information to refine or validate your existing management strategies.
- Implement a clinical plan for the management of advanced HER2-positive breast cancer, incorporating existing and recently approved targeted treatments.
- Assimilate new clinical trial evidence into the therapeutic algorithm for advanced ER-positive postmenopausal breast cancer.
- Integrate recent clinical trial results into the management of metastatic breast cancer with no evidence of disease.
- Recall the results of pivotal trials introducing effective new breast cancer therapeutics, and identify their impact on existing treatment algorithms.
- Counsel appropriately selected patients with breast cancer about participation in ongoing clinical trials investigating novel therapeutic agents and strategies.

#### ACCREDITATION STATEMENT

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#### HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should watch the video, complete the Post-test with a score of 70% or better and fill out the Educational Assessment and Credit Form located at [ResearchToPractice.com/SecondOpinionBC13/CME](http://ResearchToPractice.com/SecondOpinionBC13/CME).

## CONTENT VALIDATION AND DISCLOSURES

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**Hardware/Software Requirements:**

A high-speed Internet connection  
A monitor set to 1280 x 1024 pixels or more  
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later  
Adobe Flash Player 10.2 plug-in or later  
Adobe Acrobat Reader  
(Optional) Sound card and speakers for audio

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## SELECT PUBLICATIONS

- 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](#).
- Baselga J et al. **Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer.** *N Engl J Med* 2012;366(6):520-9.
- Baselga J et al. **Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer.** *N Engl J Med* 2012;366(2):109-19.
- Bergh J et al. **FACT: An open-label randomized phase III study of fulvestrant and anastrozole in combination compared with anastrozole alone as first-line therapy for patients with receptor-positive postmenopausal breast cancer.** *J Clin Oncol* 30(16):1919-25.
- Chavez-MacGregor M et al. **S1207: Phase III randomized, placebo-controlled clinical trial evaluating the use of adjuvant endocrine therapy +/- one year of everolimus in patients with high-risk, hormone receptor-positive and HER2-neu negative breast cancer (NCT01674140).** San Antonio Breast Cancer Symposium 2012;[Abstract OT2-2-04](#).
- Datko F et al. **Phase II study of pertuzumab, trastuzumab, and weekly paclitaxel in patients with HER2-overexpressing metastatic breast cancer.** San Antonio Breast Cancer Symposium 2012;[Abstract P5-18-20](#).
- Ellis PA et al. **MARIANNE: A phase III, randomized study of trastuzumab-DM1 (T-DM1) with or without pertuzumab (P) compared with trastuzumab (H) plus taxane for first-line treatment of HER2-positive, progressive, or recurrent locally advanced or metastatic breast cancer (MBC).** *Proc ASCO* 2011;[Abstract TPS102](#).
- Finn RS et al. **Results of a randomized Phase 2 study of PD 0332991, a cyclin-dependent kinase (CDK) 4/6 inhibitor, in combination with letrozole vs letrozole alone for first-line treatment of ER-positive/HER2-negative advanced breast cancer.** San Antonio Breast Cancer Symposium 2012;[Abstract S1-6](#).
- LoRusso PM et al. **Trastuzumab emtansine: A unique antibody-drug conjugate in development for human epidermal growth factor receptor 2-positive cancer.** *Clin Cancer Res* 2011;17(20):6437-47.
- Mehta RS et al. **Combination anastrozole and fulvestrant in metastatic breast cancer.** *N Engl J Med* 2012;367(5):435-44.
- Mohd Shariq MS et al. **Overcoming resistance and restoring sensitivity to HER2-targeted therapies in breast cancer.** *Ann Oncol* 2012;23(12):3007-16.
- Olson EM et al. **Maximizing human epidermal growth factor receptor 2 inhibition: A new oncologic paradigm in the era of targeted therapy.** *J Clin Oncol* 2012;30(14):1712-4.
- O'Regan R et al. **Phase III, randomized, double-blind, placebo-controlled multicenter trial of daily everolimus plus weekly trastuzumab and vinorelbine in trastuzumab-resistant, advanced breast cancer (BOLERO-3).** *Proc ASCO* 2013;[Abstract 505](#).
- Swain SM et al. **Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): Overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study.** *Lancet Oncol* 2013;14(6):461-71.
- Swain SM et al. **Confirmatory overall survival (OS) analysis of CLEOPATRA: A randomized, double-blind, placebo-controlled Phase III study with pertuzumab (P), trastuzumab (T), and docetaxel (D) in patients (pts) with HER2-positive first-line (1L) metastatic breast cancer (MBC).** San Antonio Breast Cancer Symposium 2012;[Abstract P5-18-26](#).
- Verma S et al. **Trastuzumab emtansine for HER2-positive advanced breast cancer.** *N Engl J Med* 2012;367(19):1783-91.
- Von Minckwitz G et al. **Adjuvant Pertuzumab and Herceptin IN Initial TherapY in breast cancer: APHINITY (BIG 4-11/BO25126/TOC4939g).** San Antonio Breast Cancer Symposium 2011;[Abstract OT1-02-04](#).