Cases from the Community

Clinical Investigators Provide Their Perspectives on Actual Patients with Breast Cancer

CME Information

TARGET AUDIENCE

This program is intended for medical oncologists, hematology-oncology fellows and other allied healthcare professionals involved in the treatment of breast cancer (BC).

OVERVIEW OF ACTIVITY

BC remains the most frequently diagnosed cancer in women, and in 2015 in the United States alone the disease will culminate in an estimated 234,190 new cases and 40,730 deaths. The current clinical management of BC is multidisciplinary and includes surgical resection of local disease with or without radiation therapy and the treatment of systemic disease (micro- or macroscopic) with cytotoxic chemotherapy, endocrine therapy, biologic therapy or combinations of these approaches. The indication and utility of these local and systemic treatment options are largely based on a number of prognostic and predictive risk factors present within the patient or her tumor at the time of diagnosis. Increasingly, an emphasis is being placed on a "personalized medicine" approach that promises to more effectively identify specific treatments that will benefit individuals based on specific patient- and disease-related characteristics.

Several consensus- and evidence-based treatment guidelines are available and aim to assist clinicians with making BC management decisions in the face of this dynamic clinical and research environment, but despite the existence of these tools many areas of controversy persist within academic and community settings. By using the perspectives of leading BC clinical investigators regarding a number of cases presented by a panel of community-based oncologists as well as a review of key data sets that support this case-based discussion, this activity will assist the practicing oncologist in the development of evidence-based strategies for the treatment of BC.

LEARNING OBJECTIVES

- Appreciate the similarities and differences among existing genomic assays, and use this information to select appropriate platform(s) to assess risk and individualize therapy for patients with early BC (EBC).
- Individualize the selection of evidence-based neoadjuvant and adjuvant chemobiologic regimens for patients with HER2-overexpressing EBC.
- Implement a long-term clinical plan for the management of metastatic HER2-positive BC, incorporating existing, recently approved and investigational targeted treatments.
- Develop an evidence-based algorithm for the initial and long-term treatment of localized hormone receptor-positive pre- and postmenopausal BC.
- Establish an evidence-based algorithm for the treatment of hormone-sensitive advanced BC, including the use of endocrine, biologic and chemotherapeutic agents.
- Consider clinical data and patient preferences in the selection and sequencing of available chemotherapeutic agents in patients with HER2-negative metastatic BC (mBC), including the option of clinical trial participation.
- Recognize clinical investigator perspectives regarding the indications for BRCA mutation testing, and use this information to appropriately select patients with BC for this analysis.
- Appraise the rationale for and clinical data with investigational anti-PD-1 and/or anti-PD-L1 antibodies in patients with mBC.

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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/ASCOBreast15/CME.

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FACULTY — 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:

William J Gradishar, MD
Betsy Bramsen Professor of Breast Oncology
Professor of Medicine
Director, Maggie Daley Center for Women's Cancer Care
Robert H Lurie Comprehensive Cancer Center
Northwestern University Feinberg School of Medicine
Northwestern Memorial Hospital
Chicago, Illinois

No real or apparent conflicts of interest to disclose.

Joyce O'Shaughnessy, MD
Chair, Breast Cancer Research Program
Baylor-Charles A Sammons Cancer Center
Texas Oncology
US Oncology
Dallas, Texas

Consulting Agreements: Abbott Laboratories, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Celgene Corporation, Eisai Inc, Genentech BioOncology, GlaxoSmithKline, Lilly, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche Laboratories Inc, Sanofi, Takeda Oncology.

Ann H Partridge, MD, MPH
Director, Adult Survivorship Program
Founder and Director
Program for Young Women with Breast Cancer
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Advisory Committee: Pfizer Inc.

Hope S Rugo, MD
Professor of Medicine
Director, Breast Oncology and Clinical Trials Education
University of California, San Francisco
Helen Diller Family Comprehensive Cancer Center
San Francisco, California

Contracted Research: Amgen Inc, Eisai Inc, Genentech BioOncology, GlaxoSmithKline, Merck, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche Laboratories Inc; **Speakers Bureau:** Genomic Health Inc.

Ian E Smith, MD
Professor of Cancer Medicine
Head of the Breast Unit
The Royal Marsden Hospital and Institute of Cancer Research
London, United Kingdom

Advisory Committee: Pfizer Inc; Speakers Bureau: Eisai Inc.

CONSULTING ONCOLOGISTS — The following consulting oncologists (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process:

Patricia J Madej, MD
Illinois Cancer Specialists
Medical Director
Breast Care Center
Adventist Hinsdale and Adventist LaGrange Hospitals
Hinsdale, Illinois

No real or apparent conflicts of interest to disclose.

Steven W Papish, MD
Medical Director
Carol G Simon Cancer Center
Morristown Medical Center
Morristown, New Jersey

Speakers Bureau: bioTheranostics Inc, Genentech BioOncology, Genomic Health Inc, Novartis Pharmaceuticals Corporation, Pfizer Inc.

Estelamari Rodriguez, MD, MPH
Hematology-Oncology Attending
Mount Sinai Comprehensive Cancer Center
Miami Beach, Florida

Advisory Committee: Clovis Oncology.

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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

Ian E Smith, MD

Baselga J et al. **First results of the NeoALTTO trial (BIG 01-06/EGF 106903): A phase III, randomized, open label, neoadjuvant study of lapatinib, trastuzumab, and their combination plus paclitaxel in women with HER2-positive primary breast cancer.** San Antonio Breast Cancer Symposium 2010;**Abstract S3-3**.

Buzdar AU et al. **Significantly higher pathologic complete remission rate after neoadjuvant therapy with trastuzumab, paclitaxel, and epirubicin chemotherapy: Results of a randomized trial in human epidermal growth factor receptor 2-positive operable breast cancer.** *J Clin Oncol* 2005;23(16):3676-85.

Gianni L et al. **Five-year analysis of the phase II NeoSphere trial evaluating four cycles of neoadjuvant docetaxel (D) and/or trastuzumab (T) and/or pertuzumab (P).** *Proc ASCO* 2014;**Abstract 505**.

Gianni L et al. **Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): A randomised multicentre, open-label, Phase 2 trial.** *Lancet Oncol* 2012;13(1):25-32.

Gianni L et al. **Neoadjuvant chemotherapy with trastuzumab followed by adjuvant trastuzumab versus neoadjuvant chemotherapy alone, in patients with HER2-positive locally advanced breast cancer (the NOAH trial): A randomised controlled superiority trial with a parallel HER2-negative cohort.** *Lancet* 2010;375(9712):377-84.

Piccart-Gebhart M et al. **First results from the phase III ALTTO trial (BIG 2-06; NCCTG [Alliance] N063D) comparing one year of anti-HER2 therapy with lapatinib alone (L), trastuzumab alone (T), their sequence (T→L), or their combination (T+L) in the adjuvant treatment of HER2-positive early breast cancer (EBC).** *Proc ASCO* 2014;**Abstract LBA4**.

Joyce O'Shaughnessy, MD

Alba E et al. **A randomized phase II trial of platinum salts in basal-like breast cancer patients in the neoadjuvant setting. Results from the GEICAM/2006-03, multicenter study.** *Breast Cancer Res Treat* 2012;136(2):487-93.

Budd GT et al. **SWOG S0221: A phase III trial comparing chemotherapy schedules in high-risk early-stage breast cancer.** *J Clin Oncol* 2015;33(1):58-64.

Hoch U et al. **Nonclinical pharmacokinetics and activity of etirinotecan pegol (NKTR-102), a long-acting topoisomerase 1 inhibitor, in multiple cancer models.** *Cancer Chemother Pharmacol* 2014;74(6):1125-37.

Jameson GS et al. **A multicenter, phase I, dose-escalation study to assess the safety, tolerability, and pharmacokinetics of etirinotecan pegol in patients with refractory solid tumors.** *Clin Cancer Res* 2013;19(1):268-78.

Lehmann BD et al. **Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies.** *J Clin Invest* 2011;121(7):2750-67.

Nanda R et al. **A phase Ib study of pembrolizumab (MK-3475) in patients with advanced triple-negative breast cancer.** San Antonio Breast Cancer Symposium 2014;**Abstract S1-09**.

Nounou M et al. **Etirinotecan pegol accumulates in breast cancer brain metastases and prolongs survival in an experimental model of brain metastases of human triple negative breast cancer.** *Proc AACR* 2014.

Perez EA et al. **Phase III trial of etirinotecan pegol (EP) versus treatment of physician's choice (TPC) in patients (pts) with advanced breast cancer (aBC) whose disease has progressed following anthracycline (A), taxane (T) and capecitabine (C): The BEACON study.** *Proc ASCO* 2015;**Abstract 1001**.

Sikov WM et al. **Impact of the addition of carboplatin and/or bevacizumab to neoadjuvant once-per-week paclitaxel followed by dose-dense doxorubicin and cyclophosphamide on pathologic complete response rates in stage II to III triple-negative breast cancer: CALGB 40603 (Alliance).** *J Clin Oncol* 2015;33(1):13-21.

Sparano JA et al. **Ten year update of E1199: Phase III study of doxorubicin-cyclophosphamide followed by paclitaxel or docetaxel given every 3 weeks or weekly in patients with axillary node-positive or high-risk node-negative breast cancer.** San Antonio Breast Cancer Symposium 2014;**Abstract S3-03**.

Tamura K et al. **Randomized phase II study of weekly paclitaxel with or without carboplatin followed by cyclophosphamide/epirubicin/5-fluorouracil as neoadjuvant chemotherapy for stage II/IIIA HER2-negative breast cancer.** *Proc ASCO* 2014;**Abstract 1017**.

Traina T et al. **Results from a phase 2 study of enzalutamide (ENZA), an androgen receptor (AR) inhibitor, in advanced AR+ triple-negative breast cancer (TNBC).** *Proc ASCO* 2015;**Abstract 1003**.

Select Publications

Tutt A et al. **Oral poly(ADP-ribose) polymerase inhibitor olaparib in patients with BRCA1 or BRCA2 mutations and advanced breast cancer: A proof-of-concept trial.** *Lancet* 2010;376(9737):235-44.

Untch M et al. **A randomized phase III trial comparing neoadjuvant chemotherapy with weekly nanoparticle-based paclitaxel with solvent-based paclitaxel followed by anthracyline/cyclophosphamide for patients with early breast cancer (GeparSepto); GBG 69.** San Antonio Breast Cancer Symposium 2014;**Abstract PD2-6**.

von Minckwitz G et al. **Neoadjuvant carboplatin in patients with triple-negative and HER2-positive early breast cancer (GeparSixto; GBG 66): A randomised phase 2 trial.** *Lancet Oncol* 2014;15(7):747-56.

von Minckwitz G et al. **Pathological complete response (pCR) rates after carboplatin-containing neoadjuvant chemotherapy in patients with germline BRCA (gBRCA) mutation and triple-negative breast cancer (TNBC): Results from GeparSixto.** *Proc ASCO* 2014;**Abstract 1005**.

von Minckwitz G et al. **Prediction of pathological complete response (pCR) by homologous recombination deficiency (HRD) after carboplatin-containing neoadjuvant chemotherapy in patients with TNBC: Results from GeparSixto.** *Proc ASCO* 2014;**Abstract 1004**.

Hope S Rugo, MD

Ellis PA et al. **Phase III, randomized study of trastuzumab emtansine (T-DM1) ± pertuzumab (P) vs trastuzumab + taxane (HT) for first-line treatment of HER2-positive MBC: Primary results from the MARIANNE study.** *Proc ASCO* 2015;**Abstract 507**.

Hurvitz SA et al. **Trastuzumab emtansine (T-DM1) vs trastuzumab plus docetaxel (H+T) in previously-untreated HER2-positive metastatic breast cancer (MBC): Primary results of a randomized, multicenter, open-label Phase II study (TDM4450g/BO21976).** European Multidisciplinary Cancer Congress 2011;**Abstract 5001**.

Swain SM et al. **Pertuzumab, trastuzumab, and docetaxel in HER2-positive metastatic breast cancer.** *N Engl J Med* 2015;372(8):724-34.

Verma S et al. **Trastuzumab emtansine for HER2-positive advanced breast cancer.** *N Engl J Med* 2012;367(19):1783-91.

Ann H Partridge, MD, MPH

Albain KS et al. **Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, oestrogen-receptor-positive breast cancer on chemotherapy: A retrospective analysis of a randomised trial.** *Lancet Oncol* 2010;11(1):55-65.

Buyse M et al. **Validation and clinical utility of a 70-gene prognostic signature for women with node-negative breast cancer.** *J Natl Cancer Inst* 2006;98(17):1183-92.

Chang M et al. **Comparison of Onco*type* DX with multi-gene profiling assays, (eg, MammaPrint, PAM50) and other tests (eg, Adjuvant! Online, Ki-67 and IHC4) in early-stage breast cancer.** Cancer Care Ontario 2013;Recommendation Report MOAC-2.

Dowsett M et al. **Comparison of PAM50 risk of recurrence score with Onco*type* DX and IHC4 for predicting risk of distant recurrence after endocrine therapy.** *J Clin Oncol* 2013;31(22):2783-90.

Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Peto R et al. **Comparisons between different polychemotherapy regimens for early breast cancer: Meta-analyses of long-term outcome among 100,000 women in 123 randomised trials.** *Lancet* 2012;379(9814):432-44.

Francis PA et al. **Randomized comparison of adjuvant tamoxifen (T) plus ovarian function suppression (OFS) versus tamoxifen in premenopausal women with hormone receptor-positive (HR+) early breast cancer (BC): Analysis of the SOFT trial.** San Antonio Breast Cancer Symposium 2014;**Abstract S3-08**.

Paik S et al. **Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer.** *J Clin Oncol* 2006;24(23):3726-34.

Paik S et al. **A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer.** *N Engl J Med* 2004;351(27):2817-26.

Sestak I et al. **Factors predicting late recurrence for estrogen receptor-positive breast cancer.** *J Natl Cancer Inst* 2015;105(19):1504-11.

Sestak I et al. **Prediction of late distant recurrence after 5 years of endocrine treatment: A combined analysis of patients from the Austrian Breast and Colorectal Cancer Study Group 8 and Arimidex, Tamoxifen Alone or in Combination randomized trials using the PAM50 risk of recurrence score.** *J Clin Oncol* 2015;33(8):916-22.

Select Publications

William J Gradishar, MD

Finn RS et al. **The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): A randomised phase 2 study.** *Lancet Oncol* 2015;16(1):25-35.

Robertson JF et al. **Fulvestrant 500 mg versus anastrozole 1 mg for the first-line treatment of advanced breast cancer: Follow-up analysis from the randomized 'FIRST' study.** *Breast Cancer Res Treat* 2012;136(2):503-11.

Rugo HS et al. **Clinical performance of the DigniCap system, a scalp hypothermia system, in preventing chemotherapy-induced alopecia.** *Proc ASCO* 2015;**Abstract 9518**.

Turner NC et al. **Palbociclib in hormone-receptor-positive advanced breast cancer.** *N Engl J Med* 2015;373(3):209-19.