Beyond the Guidelines

Investigator Perspectives on Current Clinical Issues and Ongoing Research in the Management of Early and Advanced 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.

OVERVIEW OF ACTIVITY

Breast cancer remains the most frequently diagnosed cancer in women, and in 2017 in the United States alone the disease will culminate in an estimated 255,180 new cases and 41,070 deaths. The current clinical management of breast cancer 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 for and/or utility of these local and systemic treatment options are largely based on a number of prognostic and predictive risk factors present in the patient or tumor at the time of diagnosis. In fact, as the field of oncology is challenged to improve the precision with which it therapeutically targets malignant cells, biomarker-driven treatment algorithms have become the norm for many tumor types, particularly breast cancer. Although diagnosis and treatment remain in many ways more advanced for breast cancer than for other solid cancers, challenging issues in the basic management of this disease continue to require refinement.

Several consensus- and evidence-based treatment guidelines are available and aim to assist clinicians with making breast cancer management decisions in this dynamic clinical and research environment. However, in situations where multiple acceptable therapeutic options exist, such guidelines may not be particularly helpful at the time of decision-making. By exploring the perspectives of leading breast cancer clinical investigators regarding a number of clinical scenarios and a review of key data sets, this activity will assist medical oncologists, hematology-oncology fellows and other healthcare professionals in the development of evidence-based strategies for the treatment of breast cancer.

LEARNING OBJECTIVES

- Compare and contrast expert perspectives on breast cancer treatment recommendations, and use this information to refine or validate existing management strategies.
- Appreciate the similarities and differences among existing genomic assays, and use this information to select an appropriate platform or platforms to assess risk and individualize therapy for patients with hormone receptor-positive breast cancer in the neoadjuvant, adjuvant and extended-adjuvant settings.
- Individualize the selection of evidence-based neoadjuvant and adjuvant chemobiologic regimens for patients with HER2-overexpressing early breast cancer.
- Implement a clinical plan for the management of metastatic HER2-positive breast cancer, incorporating existing and emerging targeted treatments.
- Develop an evidence-based algorithm for the treatment of hormone-sensitive advanced breast cancer, including the use of endocrine, biologic and chemotherapeutic agents.
- Recall the results of pivotal trials introducing effective new breast cancer therapeutic agents, and identify their potential impact on existing treatment algorithms.
- Counsel appropriately selected patients with breast cancer about participation in ongoing clinical trials investigating novel therapeutic agents and strategies.

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Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2.75 Medical Knowledge MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialty: **medical oncology**.

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FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

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Advisory Committee and Consulting Agreements: Amgen Inc, AstraZeneca Pharmaceuticals LP, Genentech BioOncology, Novartis, Pfizer Inc, Roche Laboratories Inc.

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San Francisco, California

Contracted Research: Amgen Inc, Eisai Inc, Genentech BioOncology, GlaxoSmithKline, Lilly, MacroGenics Inc, Merck, Novartis, OBI Pharma Inc, Pfizer Inc, Roche Laboratories Inc.

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No relevant conflicts of interest to disclose.

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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

Eric P Winer, MD

Chan A et al. **Neratinib after trastuzumab-based adjuvant therapy in patients with HER2-positive breast cancer (ExteNET): A multicentre, randomised, double-blind, placebo-controlled, phase 3 trial.** *Lancet Oncol* 2016;17(3):367-77.

Chan A et al. **Neratinib after adjuvant chemotherapy and trastuzumab in HER2-positive early breast cancer: Primary analysis at 2 years of a phase 3, randomized, placebo-controlled trial (ExteNET).** *Proc ASCO* 2015;**Abstract 508**.

Tolaney SM et al. **Seven-year (yr) follow-up of adjuvant paclitaxel (T) and trastuzumab (H) (APT trial) for node-negative, HER2-positive breast cancer (BC).** *Proc ASCO* 2017;**Abstract 511**.

Julie R Gralow, MD

Bear HD et al. **Using the 21-gene assay from core needle biopsies to choose neoadjuvant therapy for breast cancer: A multi-center trial.** San Antonio Breast Cancer Symposium 2016;**Abstract P2-10-04**.

Cardoso F et al. **70-gene signature as an aid to treatment decisions in early-stage breast cancer.** *N Engl J Med* 2016;375(8):717-29.

Coates AS et al. **Tailoring therapies — Improving the management of early breast cancer: St Gallen International Expert Consensus on the primary therapy of early breast cancer 2015.** *Ann Oncol* 2015;26(8):1533-46.

Gluz O et al. **West German Study Group Phase III PlanB trial: First prospective outcome data for the 21-gene recurrence score assay and concordance of prognostic markers by central and local pathology assessment.** *J Clin Oncol* 2016;34(20):2341-9.

Harris LN et al. **Use of biomarkers to guide decisions on adjuvant systemic therapy for women with early-stage invasive breast cancer: American Society of Clinical Oncology clinical practice guideline.** *J Clin Oncol* 2016;34(10):1134-50.

Hudis C, Dickler M. **Increasing precision in adjuvant therapy for breast cancer.** *N Engl J Med* 2016;375(8):790-1.

Senkus E et al. **Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.** *Ann Oncol* 2015;26(Supp 5):v8-30.

Sparano JA et al. **Prospective validation of a 21-gene expression assay in breast cancer.** *N Engl J Med* 2015;373(21):2005-14.

Kimberly L Blackwell, MD

A phase III randomized, double-blind, placebo-controlled study of LEE011 or placebo in combination with tamoxifen and goserelin or a non-steroidal aromatase inhibitor (NSAI) and goserelin for the treatment of premenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer. NCT02278120

A randomized double-blind, placebo-controlled study of ribociclib in combination with fulvestrant for the treatment of men and postmenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer who have received no or only one line of prior endocrine treatment. NCT02422615

Cristofanilli M et al. **Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): Final analysis of the multicentre, double-blind, phase 3 randomised controlled trial.** *Lancet Oncol* 2016;17(4):425-39.

Finn RS et al. **Palbociclib and letrozole in advanced breast cancer.** *N Engl J Med* 2016;375(20):1925-36.

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.

Hortobagyi G et al. **Ribociclib as first-line therapy for HR-positive, advanced breast cancer.** *N Engl J Med* 2016;375(18):1738-48.

Juric D et al. **Ribociclib (LEE011) and letrozole in estrogen receptor-positive (ER+), HER2-negative (HER2–) advanced breast cancer (aBC): Phase Ib safety, preliminary efficacy and molecular analysis.** *Proc ASCO* 2016;**Abstract 568**.

O'Brien NA et al. **In vivo efficacy of combined targeting of CDK4/6, ER and PI3K signaling in ER+ breast cancer.** *Proc AACR* 2014;**Abstract 4756**.

Sledge GW et al. **MONARCH 2: Abemaciclib in combination with fulvestrant in patients with HR+/HER2- advanced breast cancer who progressed on endocrine therapy.** *Proc ASCO* 2017;**Abstract 1000**.

Turner NC et al. **Treatment postprogression in women with endocrine-resistant HR+/HER2- advanced breast cancer who received palbociclib plus fulvestrant in PALOMA-3.** San Antonio Breast Cancer Symposium 2016;**Abstract P4-22-06**.

Select Publications

Mark D Pegram, MD

Hanker AB et al. **An acquired HER2T798I gatekeeper mutation induces resistance to neratinib in a patient with HER2 mutant-driven breast cancer.** *Cancer Discov* 2017;7(6):575-85.

Johnston S et al. **Lapatinib combined with letrozole versus letrozole and placebo as first-line therapy for postmenopausal hormone receptor-positive metastatic breast cancer.** *J Clin Oncol* 2009;27(33):5538-46.

Pietras RJ et al. **HER-2 tyrosine kinase pathway targets estrogen receptor and promotes hormone-independent growth in human breast cancer cells.** *Oncogene* 1995;10(12):2435-46.

Rimawi M et al. **Primary analysis of PERTAIN: A randomized, two-arm, open-label, multicenter phase II trial assessing the efficacy and safety of pertuzumab given in combination with trastuzumab plus an aromatase inhibitor in first-line patients with HER2-positive and hormone receptor-positive metastatic or locally advanced breast cancer.** San Antonio Breast Cancer Symposium 2016;**Abstract S3-04**.

Rita Nanda, MD

de Bono J et al. **Phase I, dose-escalation, two-part trial of the PARP inhibitor talazoparib in patients with advanced germline BRCA1/2 mutations and selected sporadic cancers.** *Cancer Discov* 2017;7(6):620-9.

Gelmon KA et al. **Olaparib in patients with recurrent high-grade serous or poorly differentiated ovarian carcinoma or triple-negative breast cancer: A phase 2, multicentre, open-label, non-randomised study.** *Lancet Oncol* 2011;12(9):852-61.

Geyer CE et al. **Phase 3 study evaluating efficacy and safety of veliparib (V) plus carboplatin (Cb) or Cb in combination with standard neoadjuvant chemotherapy (NAC) in patients (pts) with early stage triple-negative breast cancer (TNBC).** *Proc ASCO* 2017;**Abstract 520**.

Kaufman B et al. **Olaparib monotherapy in patients with advanced cancer and a germline BRCA1/2 mutation.** *J Clin Oncol* 2015;33(3):244-50.

Lord CJ, Ashworth A. **PARP inhibitors: Synthetic lethality in the clinic.** *Science* 2017;355(6330):1152-8.

Robson M et al. **OlympiAD: Phase III trial of olaparib monotherapy versus chemotherapy for patients (pts) with HER2-negative metastatic breast cancer (mBC) and a germline BRCA mutation (gBRCAm).** *Proc ASCO* 2017;**Abstract LBA4**.

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.

Hope S Rugo, MD

Adams S et al. **Phase 2 study of pembrolizumab as first-line therapy for PD-L1–positive metastatic triple-negative breast cancer (mTNBC): Preliminary data from KEYNOTE-086 cohort B.** *Proc ASCO* 2017;**Abstract 1088**.

Cimino-Mathews A et al. **PD-L1 (B7-H1) expression and the immune tumor microenvironment in primary and metastatic breast carcinomas.** *Hum Pathol* 2016;47(1):52-63.

Cimino-Mathews A et al. **Immune targeting in breast cancer.** *Oncology (Williston Park)* 2015;29(5):375-85.

Di Leo A et al. **BELLE-3: A phase III study of buparlisib + fulvestrant in postmenopausal women with HR+, HER2–, aromatase inhibitor-treated, locally advanced or metastatic breast cancer, who progressed on or after mTOR inhibitor-based treatment.** San Antonio Breast Cancer Symposium 2016;**Abstract S4-07**.

Johnston SR et al. **Fulvestrant plus anastrozole or placebo versus exemestane alone after progression on non-steroidal aromatase inhibitors in postmenopausal patients with hormone-receptor-positive locally advanced or metastatic breast cancer (SoFEA): A composite, multicentre, phase 3 randomised trial.** *Lancet Oncol* 2013;14(10):989-98.

Ma C et al. **Circulating tumor DNA (ctDNA) sequencing for *HER2* mutation (*HER2*^{mut}) screening and response monitoring to neratinib in metastatic breast cancer (MBC).** *Proc AACR* 2017;**Abstract CT011**.

Nanda R et al. **Pembrolizumab plus standard neoadjuvant therapy for high-risk breast cancer (BC): Results from I-SPY 2.** *Proc ASCO* 2017;**Abstract 506**.

Nanda R et al. **Pembrolizumab in patients with advanced triple-negative breast cancer: Phase Ib KEYNOTE-012 Study.** *J Clin Oncol* 2016;34(21):2460-7.

Schmid P et al. **Atezolizumab in metastatic TNBC (mTNBC): Long-term clinical outcomes and biomarker analyses.** *Proc AACR* 2017;**Abstract 2986**.