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 remains the most frequently diagnosed cancer in women, and in 2014 in the United States alone the disease culminated in an estimated 232,670 new cases and 40,000 deaths. 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. Consequently, the number of individuals living with breast cancer has increased substantially, as has the population “at risk” for recurrent disease.

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 and/or utility of these local and systemic treatment options is largely based on a number of prognostic and predictive risk factors present within the patient or her 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, including breast cancer.

These proceedings from a CME symposium during the 37th annual San Antonio Breast Cancer Symposium explore the most significant therapeutic advances during the previous year by using the perspectives of leading breast cancer experts on challenging cases and questions submitted by clinicians in the community to frame a relevant discussion of how this information has aided in the refinement of current routine clinical practice and ongoing research. This CME activity will help medical oncologists integrate these findings into best-practice disease management strategies.

LEARNING OBJECTIVES
- Appreciate the similarities and differences between existing genomic assays, and use this information to select an appropriate platform or platforms to assess risk and individualize therapy for patients with invasive and noninvasive early breast cancer.
- Develop an evidence-based algorithm for the initial and long-term treatment of localized hormone receptor-positive pre- and postmenopausal breast cancer.
- Individualize the selection of evidence-based neoadjuvant and adjuvant chemobiologic regimens for patients with HER2-overexpressing early breast cancer.
- Implement a long-term clinical plan for the management of metastatic HER2-positive breast cancer, incorporating existing, recently approved and investigational targeted treatments.
- Develop an evidence-based algorithm for the treatment of advanced hormone receptor-positive breast cancer, including the use of endocrine, biologic and chemotherapeutic agents.
- Apply the results of current clinical research to the selection and sequencing of available therapeutics for patients with localized and advanced triple-negative breast cancer.
- Recall emerging research data with next-generation sequencing, and determine the clinical and/or research application for patients with metastatic breast cancer.
- Counsel appropriately selected patients about participation in ongoing breast cancer clinical research.

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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:

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MODERATOR — 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: AbbVie Inc, Amgen Inc, Astellas Scientific and Medical Affairs Inc, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, Bionetics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Corporation, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, Incyte Corporation, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Lilly, Medivation Inc, Merck, Myriad Genetic Laboratories Inc, Novartis Pharmaceuticals Corporation, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pharmacyclics Inc, Prometheus Laboratories Inc, Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Teva Oncology, Tokai Pharmaceuticals Inc and VisionGate Inc.

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This activity is supported by educational grants from AbbVie Inc, AstraZeneca Pharmaceuticals LP, Foundation Medicine, Genentech BioOncology, Genomic Health Inc and Lilly.

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

Last review date: April 2015
Expiration date: April 2016
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A Cancer Research UK phase II proof of principle trial of the activity of the PARP-1 inhibitor, AG-014699, in known carriers of a BRCA 1 or BRCA 2 mutation with locally advanced or metastatic breast or advanced ovarian cancer. NCT00664781

A Phase I/II study of CR011-vcMMAE in patients with locally advanced or metastatic breast cancer. NCT00704158

A phase I, open-label study to assess the safety and tolerability of KU-0059436 in combination with carboplatin, KU-0059436 in combination with a paclitaxel/carboplatin T/C doublet and KU-0059436 in combination with paclitaxel in the treatment of patients with advanced solid tumours. NCT00516724

A phase II study of neratinib in metastatic HER2 non-amplified but HER2 mutant breast cancer. NCT01670877

ABRAZO: A Phase 2, 2-stage, 2-cohort study of talazoparib (BMN 673), in locally advanced and/or metastatic breast cancer patients with BRCA mutation (ABRAZO study). NCT02034916

ABT-888 with cyclophosphamide in refractory BRCA-positive ovarian, primary peritoneal or ovarian high-grade serous carcinoma, fallopian tube cancer, triple-negative breast cancer, and low-grade non-Hodgkin's lymphoma. NCT01306032

An open-label, multicenter, phase 1/2 study of poly(ADP-ribose) polymerase (PARP) inhibitor E7449 as single agent in subjects with advanced solid tumors or with B-cell malignancies and in combination with temozolomide (TMZ) or with carboplatin and paclitaxel in subjects with advanced solid tumors. NCT01618136


EMBRACA: A study evaluating talazoparib (BMN 673), a PARP inhibitor, in advanced and/or metastatic breast cancer patients with BRCA mutation (EMBRACA study). NCT01945775

Evaluation of the efficacy of high throughput genome analysis as a therapeutic decision tool for patients with metastatic breast cancer. NCT02299999


METRIC: Study of glembatumumab vedotin (CDX-011) in patients with metastatic, gpNMB over-expressing, triple negative breast cancer (METRIC). NCT01997333

Muro K et al. A phase 1b study of pembrolizumab (Pembro; MK-3475) in patients (Pts) with advanced gastric cancer. Proc ESMO 2014; Abstract LBA15.


OlympiAD: Assessment of the efficacy and safety of olaparib monotherapy versus physicians choice chemotherapy in the treatment of metastatic breast cancer patients with germine BRCA1/2 mutations. NCT02000622

PARP inhibition for triple negative breast cancer (ER-/PR-/HER2-) with BRCA1/2 mutations. NCT01074970

Phase I study of the oral PI3kinase inhibitor BKM120 or BLY719 and the oral PARP inhibitor olaparib in patients with recurrent triple negative breast cancer or high grade serous ovarian cancer. NCT01623349

Phase I/II study of cediranib and olaparib in combination for treatment of recurrent papillary-serous ovarian, fallopian tube, or peritoneal cancer or for treatment of recurrent triple-negative breast cancer. NCT01116648
Phase II study of AZD2281 in patients with known BRCA mutation status or recurrent high grade ovarian cancer or patients with known BRCA mutation status/triple negative breast cancer. NCT00679783


The study evaluating efficacy and tolerability of veliparib in combination with temozolomide or in combination with carboplatin and paclitaxel versus placebo in subjects with BRCA1 and BRCA2 mutation and metastatic breast cancer. NCT01506609

Tutt A et al. The TNT trial: A randomized phase III trial of carboplatin (C) compared with docetaxel (D) for patients with metastatic or recurrent locally advanced triple negative or BRCA1/2 breast cancer (CRUK/07/012). San Antonio Breast Cancer Symposium 2014;Abstract S3-01.


Adam M Brufsky, MD, PhD
A phase III, randomized, open-label, multicenter study comparing GW572016 and capecitabine (XELODA) versus capecitabine in women with refractory advanced or metastatic breast cancer. NCT00078572


CLEOPATRA: A phase III, randomized, double-blind, placebo-controlled clinical trial to evaluate the efficacy and safety of pertuzumab + trastuzumab + docetaxel vs placebo + trastuzumab + docetaxel in previously untreated HER2-positive metastatic breast cancer (CLEOPATRA). NCT00567190

EMILIA: An open-label study of trastuzumab emtansine (T-DM1) vs capecitabine + lapatinib in patients with HER2-positive locally advanced or metastatic breast cancer (EMILIA). NCT00829166


Pivot X et al. CEREBEL (EGF111438): An open label randomized phase III study comparing the incidence of CNS metastases in patients (pts) with HER2+ metastatic breast cancer (MBC), treated with lapatinib plus capecitabine (LC) versus trastuzumab plus capecitabine (TC). Proc ESMO 2012;Abstract LBA11.


Swain S et al. Final overall survival (OS) analysis from the CLEOPATRA study of first-line (1L) pertuzumab (Ptz), trastuzumab (T), and docetaxel (D) in patients (pts) with HER2-positive metastatic breast cancer (MBC). Proc ESMO 2014;Abstract 3500_PR.

TH3RESA: A phase III randomized, multicenter, two arm, open-label trial to evaluate the efficacy of trastuzumab emtansine compared with treatment of physician’s choice in patients with HER2-positive metastatic breast cancer who have received at least two prior regimen of HER2 directed therapy. NCT01419197


Angelo Di Leo, MD, PhD


PALOMA-2: A randomized, multicenter, double-blind phase 3 study of PD-0332991 (oral CDK 4/6 inhibitor) plus letrozole versus placebo plus letrozole for the treatment of postmenopausal women with ER (+), HER2 (-) breast cancer who have not received any prior systemic anti cancer treatment for advanced disease. NCT01740427


Pestrin M et al. Molecular analysis of single circulating tumor cells (CTCS) isolated from metastatic breast cancer (MBC) patients (pts). Ann Oncol 2013;24(3).


Kathy D Miller, MD

Ach RA et al. Robust interlaboratory reproducibility of a gene expression signature measurement consistent with the needs of a new generation of diagnostic tools. BMC Genomics 2007;8:148.


Eric P Winer, MD

A study of Kadcyla (trastuzumab emtansine) plus Perjeta (pertuzumab) following anthracyclines in comparison with herceptin (trastuzumab) plus Perjeta and a taxane following anthracyclines as adjuvant therapy in patients with operable HER2-positive primary breast cancer. NCT01966471

APHINITY: A randomized multicenter, double-blind, placebo-controlled comparison of chemotherapy plus trastuzumab plus placebo versus chemotherapy plus trastuzumab plus pertuzumab as adjuvant therapy in patients with operable HER2-positive primary breast cancer. NCT01358877

ATEMPT: A randomized phase II study of trastuzumab emtansine (T-DM1) vs paclitaxel in combination with trastuzumab for Stage I HER2-positive breast cancer (ATEMPT trial). NCT01853748


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.

KAITLIN: A study of Kadcyla (trastuzumab emtansine) plus Perjeta (pertuzumab) following anthracyclines in comparison with Herceptin (trastuzumab) plus Perjeta and a taxane following anthracyclines as adjuvant therapy in patients with operable HER2-positive primary breast cancer. NCT01966471


Romond E et al. Trastuzumab plus adjuvant chemotherapy for HER2-positive breast cancer: Final planned joint analysis of overall survival (OS) from NSABP B-31 and NCCTG N9831. San Antonio Breast Cancer Symposium 2012; Abstract S5-5.
