The Practical Application of Research Advances and Emerging Data in the Management of Breast Cancer

CME Information

TARGET AUDIENCE

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

OVERVIEW OF ACTIVITY

BC remains the most frequently diagnosed cancer in women, and in 2015 it is estimated that the disease culminated in 234,190 new cases and 40,730 deaths in the United States alone. 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 BC has increased substantially, as has the population "at risk" for recurrent disease.

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/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, particularly BC.

These proceedings from a CME symposium during the 38th annual San Antonio Breast Cancer Symposium explore the most significant therapeutic advances during the previous year by using the perspectives of leading BC 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 early BC.
- Individualize the selection of evidence-based neoadjuvant and adjuvant chemobiologic regimens for patients with HER2-overexpressing early BC.
- Implement a long-term clinical plan for the management of metastatic HER2-positive BC, incorporating existing, recently approved and investigational targeted treatments.
- Apply the results of emerging research to the initial and long-term care of localized, hormone receptor-positive pre- and postmenopausal BC.
- Develop an evidence-based algorithm for the treatment of hormone-sensitive advanced BC, including the use of endocrine, biologic and chemotherapeutic agents.
- Recognize the recent FDA approval of palbociclib for patients with ER-positive metastatic BC (mBC), and discern how this agent can be optimally integrated into clinical practice.
- Consider clinical data and patient preferences in the selection and sequencing of available therapeutic agents for patients with ER/PR-negative, HER2-negative mBC, including the option of clinical trial participation.
- Appraise the rationale for and clinical data with investigational anti-PD-1 and/or anti-PD-L1 antibodies in patients with mBC.
- Counsel appropriately selected patients with BC about participation in ongoing clinical trials investigating novel therapeutic agents and strategies.

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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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Speakers Bureau: Celgene Corporation

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 Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, CTI BioPharma Corp, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, ImmunoGen Inc, Incyte Corporation, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Lilly, Medivation Inc, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis Pharmaceuticals Corporation, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pharmacyclics LLC, an AbbVie Company, 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 Astellas Pharma Global Development Inc/Medivation Inc, AstraZeneca Pharmaceuticals LP, bioTheranostics Inc, Celgene Corporation, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Lilly and Myriad Genetic Laboratories Inc.

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 2016

Expiration date: April 2017

Select Publications

Luca Gianni, MD

Baselga J et al. **Lapatinib with trastuzumab for HER2-positive early breast cancer (NeoALTTO): A randomised, open-label, multicentre, phase 3 trial.** *Lancet* 2012;379(9816):633-40.

Chan A et al. **Invasive disease-free survival benefit following neratinib as extended adjuvant therapy in centrally-confirmed HER2+ early-stage breast cancer: The ExteNET phase III randomized placebo-controlled trial.** *Proc ASCO* 2015;**Abstract 117**.

de Azambuja E et al. **Lapatinib with trastuzumab for HER2-positive early breast cancer (NeoALTTO): Survival outcomes of a randomised, open-label, multicentre, phase 3 trial and their association with pathological complete response.** *Lancet Oncol* 2014;15(10):1137-46.

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.

Goldhirsch A et al. **2 years versus 1 year of adjuvant trastuzumab for HER2-positive breast cancer (HERA): An open-label, randomised controlled trial.** *Lancet* 2013;382(9897):1021-8.

Harbeck N et al. **Efficacy of 12-weeks of neoadjuvant TDM1 with or without endocrine therapy in HER2-positive hormone-receptor-positive early breast cancer: WSG-ADAPT HER2+/HR+ phase II trial.** *Proc ASCO* 2015;**Abstract 506**.

Prowell TM, Pazdur R. **Pathological complete response and accelerated drug approval in early breast cancer.** *N Engl J Med* 2012;366(26):2438-41.

Clifford Hudis, MD

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.

Fan C et al. **Concordance among gene-expression-based predictors for breast cancer.** *N Engl J Med* 2006;355(6):560-9.

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.

Sanft T et al. **Prospective assessment of the decision-making impact of the Breast Cancer Index in recommending extended adjuvant endocrine therapy for patients with early-stage ER-positive breast cancer.** *Breast Cancer Res Treat* 2015;154(3):533-41.

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.

Zhang Y et al. **Breast Cancer Index identifies early-stage estrogen receptor-positive breast cancer patients at risk for early- and late-distant recurrence.** *Clin Cancer Res* 2013;19(15):4196-205.

Harold J Burstein, MD, PhD

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.

Finn RS et al. **PD 0332991, a selective cyclin D kinase 4/6 inhibitor, preferentially inhibits proliferation of luminal estrogen receptor-positive human breast cancer cell lines in vitro.** *Breast Cancer Res* 2009;11(5):R77.

Infante JR et al. **LEE011, a potent and selective CDK4/6 inhibitor, under preclinical and clinical investigation.** International Congress on Targeted Anticancer Therapies 2014;**Abstract O4.4**.

Migliaccio I et al. **Cyclin-dependent kinase 4/6 inhibitors in breast cancer therapy.** *Curr Opin Oncol* 2014;26(6):568-75.

Munster PN et al. **Phase Ib study of LEE011 and BYL719 in combination with letrozole in estrogen receptor-positive, HER2-negative breast cancer (ER+, HER2- BC)**. *Proc ASCO* 2014;**Abstract 533**.

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

Select Publications

Lisa A Carey, MD

Berry DA, Hudis CA. **Neoadjuvant therapy in breast cancer as a basis for drug approval.** *JAMA Oncol* 2015;1(7):875-6.

Burstein MD et al. **Comprehensive genomic analysis identifies novel subtypes and targets of triple-negative breast cancer.** *Clin Cancer Res* 2015;21(7):1688-98.

Dirix LY et al. **Avelumab (MSB0010718C), an anti-PD-L1 antibody, in patients with locally advanced or metastatic breast cancer: A phase Ib JAVELIN solid tumor trial.** San Antonio Breast Cancer Symposium 2015;**Abstract S1-04**.

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.

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**.

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**.

Kimberly L Blackwell, MD

Askoxylakis V et al. **Preclinical efficacy of ado-trastuzumab emtansine in the brain microenvironment.** *J Natl Cancer Inst* 2015;108(2).

Dinkel V et al. **ARRY-380, a potent, small molecule inhibitor of ErbB2, increases survival in intracranial ErbB2+ xenograft models in mice.** *Proc AACR* 2012;**Abstract 852**.

Freedman RA et al. **Translational Breast Cancer Research Consortium (TBCRC) 022: A phase II trial of neratinib for patients with human epidermal growth factor receptor 2-positive breast cancer and brain metastases.** *J Clin Oncol* 2016;34(9):945-52.

Kennecke H et al. **Metastatic behavior of breast cancer subtypes.** *J Clin Oncol* 2010;28(20):3271-7.

Krop IE et al. **Trastuzumab emtansine (T-DM1) versus lapatinib plus capecitabine in patients with HER2-positive metastatic breast cancer and central nervous system metastases: A retrospective, exploratory analysis in EMILIA.** *Ann Oncol* 2015;26(1):113-9.

Lin NU. **Better treatments needed for breast cancer brain metastases.** *Lancet Oncol* 2015;16(16):1583-4.

Lin NU et al. **Multicenter phase II study of lapatinib in patients with brain metastases from HER2-positive breast cancer.** *Clin Cancer Res* 2009;15(4):1452-9.

Ramakrishna N et al. **Recommendations on disease management for patients with advanced human epidermal growth factor receptor 2-positive breast cancer and brain metastases: American Society of Clinical Oncology clinical practice guideline.** *J Clin Oncol* 2014;32(19):2100-8.

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Tomasello G et al. **Brain metastases in HER2-positive breast cancer: The evolving role of lapatinib.** *Crit Rev Oncol Hematol* 2010;75(2):110-21.