Consensus or Controversy? Clinical Investigators Provide Perspectives on Practical Issues and Ongoing Research Related to the Management of Breast Cancer

CME Information

TARGET AUDIENCE

This program is intended for medical oncologists, hematologyoncology 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 2018 in the United States alone the disease will culminate in an estimated 268,670 new cases and 41,400 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 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 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. 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. In conjunction with this approach researchers are actively attempting to develop novel agents and immunotherapeutic strategies, with the aim of generating additional benefit, enhancing the efficacy of existing treatments or overcoming resistance to endocrine therapy, chemotherapy or biologic therapy. As such, the pace of change in the field of breast medical oncology has been rapid, and it is expected that a plethora of new data will continuously be disseminated requiring ongoing efforts to keep medical professionals informed.

These video proceedings from a CME symposium held during the 2018 ASCO Annual Meeting feature renowned breast cancer clinical investigators weighing in on challenging questions and cases from a panel of community-based general oncologists and reviewing relevant data. By exploring the perspectives of leading breast cancer clinical investigators regarding a number of clinical scenarios along with 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

- Consider published data to guide the use of biomarkers and genomic classifiers to assess risk and customize therapy for patients with hormone receptor-positive breast cancer in the neoadjuvant, adjuvant and extended adjuvant settings.
- Appraise available and emerging research evidence to individualize the selection and duration of neoadjuvant, adjuvant and/or extended adjuvant therapy 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 and investigational targeted treatments.
- Develop an evidence-based algorithm for the treatment of advanced hormone receptor-positive pre- and postmeno-pausal breast cancer, including endocrine, biologic and chemotherapeutic agents.
- Consider published research and patient preferences in the selection and sequencing of available and investigational therapeutic agents for metastatic ER/PR-negative, HER2-negative breast cancer.
- Appreciate the recent FDA approval of olaparib for patients with HER2-negative metastatic breast cancer harboring a germline BRCA mutation, and discern how this agent can be appropriately and safely integrated into routine clinical practice.
- Develop an understanding of the mechanisms of action, available data and potential clinical roles of investigational compounds in preparation for their potential introduction into future clinical practice.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Research To Practice designates this enduring material for a maximum of 2.75 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AMERICAN BOARD OF INTERNAL MEDICINE (ABIM) — MAINTENANCE OF CERTIFICATION (MOC)

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**.

Personal information and data sharing: Research To Practice aggregates deidentified user data for program-use analysis, program development, activity planning and site improvement. We may provide aggregate and deidentified data to third parties, including commercial supporters. We do not share or sell personally identifiable information to any unaffiliated third parties or commercial supporters. Please see our privacy policy at **ResearchToPractice.com/Privacy-Policy** for more information.

HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should review the CME information, watch the video, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located at **ResearchToPractice.com/ASCOBreast18/CME**.

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-theart education. We assess conflicts of interest with faculty, planners and managers of CME activities. Conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

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

Harold J Burstein, MD, PhD

Associate Professor of Medicine Harvard Medical School Breast Oncology Center Dana-Farber Cancer Institute Boston, Massachusetts

No relevant conflicts of interest to disclose.

Angelo Di Leo, MD, PhD

Head of the Sandro Pitigliani Department of Medical Oncology Hospital of Prato Istituto Toscano Tumori Prato, Italy Advisory Committee: AstraZeneca Pharmaceuticals LP, Celgene Corporation, Daiichi Sankyo Inc, Genomic Health Inc, Lilly, Novartis, Pfizer Inc, Roche Laboratories Inc; Consulting Agreements: Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Celgene Corporation, Eisai Inc, Genentech, Genomic Health Inc, Lilly, Novartis, Pfizer Inc, Roche Laboratories Inc; Contracted Research: AstraZeneca Pharmaceuticals LP, Novartis, Pfizer Inc.

Sara A Hurvitz, MD

Associate Professor of Medicine Director, Breast Oncology Program, Division of Hematology/Oncology University of California, Los Angeles Medical Director, Jonsson Comprehensive Cancer Center Clinical Research Unit Los Angeles, California Co-Director, Santa Monica-UCLA Outpatient Oncology Practices Santa Monica, California

Contracted Research: Amgen Inc, Bayer HealthCare Pharmaceuticals, BioMarin, Boehringer Ingelheim Pharmaceuticals Inc, Cascadian Therapeutics, Dignitana, Genentech, GlaxoSmithKline, Lilly, Medivation Inc, a Pfizer Company, Merrimack Pharmaceuticals Inc, Novartis, OBI Pharma Inc, Pfizer Inc, Puma Biotechnology Inc, Roche Laboratories Inc, Seattle Genetics; **Paid Travel:** Bayer HealthCare Pharmaceuticals, Lilly, Novartis, OBI Pharma Inc.

Mark Robson, MD

Clinic Director, Clinical Genetics Service Associate Attending Physician, Clinical Genetics and Breast Cancer Medicine Associate Member, Memorial Sloan Kettering Cancer Center Associate Professor of Medicine, Weill Medical College of Cornell University New York, New York

Advisory Committee, Consulting Agreement and Contracted Research: AstraZeneca Pharmaceuticals LP.

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: Eisai Inc, Genentech, Lilly, MacroGenics Inc, Merck, Novartis, OBI Pharma Inc, Pfizer Inc, Plexxikon Inc, Roche Laboratories Inc; **Paid Travel:** Lilly, Mylan NV, Puma Biotechnology Inc.

George W Sledge Jr, MD

Professor of Medicine Chief, Division of Oncology Department of Medicine Stanford University School of Medicine Stanford, California

Advisory Committee: Syndax Pharmaceuticals Inc, Taiho Oncology Inc; Contracted Research: Genentech.

MODERATOR — **Dr Love** is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma - A member of the AstraZeneca Group, Adaptive Biotechnologies, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma 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, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech, Genomic Health Inc, Gilead Sciences Inc, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Kite Pharma Inc, Lexicon Pharmaceuticals Inc, Lilly, Medivation Inc, a Pfizer Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro Inc, Teva Oncology and Tokai Pharmaceuticals Inc.

RESEARCH TO PRACTICE CME PLANNING COMMITTEE MEMBERS, STAFF AND REVIEWERS — Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

This educational activity contains discussion of published and/ or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

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

Hardware/Software Requirements:

A high-speed Internet connection A monitor set to 1280 x 1024 pixels or more Internet Explorer 11 or later, Firefox 56 or later, Chrome 61 or later, Safari 11 or later, Opera 48 or later Adobe Flash Player 27 plug-in or later Adobe Acrobat Reader (Optional) Sound card and speakers for audio

Release date: August 2018

Expiration date: August 2019

Select Publications

Sara A Hurvitz, MD

Chan A et al; ExteNET Study Group. 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.

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.

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

Huober JB et al. Survival outcomes of the NeoALTTO study: Updated results of a randomized multicenter phase III neoadjuvant trial. *Proc ASCO* 2017; Abstract 512.

Martin M et al. Neratinib after trastuzumab-based adjuvant therapy in HER2-positive breast cancer (ExteNET): 5-year analysis of a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol* 2017;18(12):1688-700.

Moreno-Aspitia A et al. Updated 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 \rightarrow L) or their combination (L+T) in the adjuvant treatment of HER2-positive early breast cancer. *Proc ASCO* 2017;Abstract 502.

Perez EA et al. Trastuzumab plus adjuvant chemotherapy for human epidermal growth factor receptor 2-positive breast cancer: Planned joint analysis of overall survival from NSABP B-31 and NCCTG N9831. *J Clin Oncol* 2014;32(33):3744-52.

Slamon D et al; Breast Cancer International Research Group. Adjuvant trastuzumab in HER2-positive breast cancer. N Engl J Med 2011;365(14):1273-83.

Von Minckwitz G et al. APHINITY trial (BIG 4-11): A randomized comparison of chemotherapy (C) plus trastuzumab (T) plus placebo (Pla) versus chemotherapy plus trastuzumab (T) plus pertuzumab (P) as adjuvant therapy in patients (pts) with HER2-positive early breast cancer (EBC). *Proc ASCO* 2017;Abstract LBA500.

Harold J Burstein, MD, PhD

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

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.

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.

Sparano JA et al. Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. *N Engl J Med* 2018; [Epub ahead of print].

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

Sparano JA, Paik S. Development of the 21-gene assay and its application in clinical practice and clinical trials. *J Clin Oncol* 2008;26(5):721-8.

Angelo Di Leo, MD, PhD

Bachelot T et al. Abemaciclib for the treatment of brain metastases secondary to hormone receptor positive breast cancer. San Antonio Breast Cancer Symposium 2017; AbstractP1-17-03.

Baselga J et al. Phase III study of taselisib (GDC-0032) + fulvestrant (FULV) v FULV in patients (pts) with estrogen receptor (ER)-positive, PIK3CA-mutant (MUT), locally advanced or metastatic breast cancer (MBC): Primary analysis from SANDPIPER. ASCO 2018;Abstract LBA1006.

Baselga J et al. Buparlisib plus fulvestrant versus placebo plus fulvestrant in postmenopausal, hormone receptor-positive, HER2-negative, advanced breast cancer (BELLE-2): A randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol* 2017;18(7):904-16.

Bonechi M et al. Plasma thymidine kinase-1 activity predicts outcome in patients with hormone receptor positive and HER2 negative metastatic breast cancer treated with endocrine therapy. *Oncotarget* 2018;9(23):16389-99.

Select Publications

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.

Di Leo A et al. Buparlisib plus fulvestrant in postmenopausal women with hormone-receptor-positive, HER2-negative, advanced breast cancer progressing on or after mTOR inhibition (BELLE-3): A randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol* 2018;19(1):87-100.

Di Leo A et al. MONARCH 3: Abemaciclib as initial therapy for patients with HR+/HER2- advanced breast cancer. *Proc ESMO* 2017; Abstract 2360_PR.

Finn RS et al. Overall survival results from the randomized phase II study of palbociclib (P) in combination with letrozole (L) vs letrozole alone for frontline treatment of ER+/HER2- advanced breast cancer (PALOMA-1; TRIO-18). *Proc ASCO* 2017;Abstract 1001.

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

Hortobagyi G et al. Updated results from MONALEESA-2, a phase 3 trial of first-line ribociclib + letrozole in hormone receptor-positive (HR+), HER2-negative (HER2–), advanced breast cancer (ABC). *Proc ASCO* 2017;Abstract 1038.

Sledge GW et al. MONARCH 2: Abemaciclib in combination with fulvestrant in women with HR+/HER2- advanced breast cancer who had progressed while receiving endocrine therapy. *J Clin Oncol* 2017;35(25):2875-84.

George W Sledge Jr, MD

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.

Freedman R et al. TBCRC 022: Phase II trial of neratinib + capecitabine for patients (Pts) with human epidermal growth factor receptor 2 (HER2+) breast cancer brain metastases (BCBM). *Proc ASCO* 2017; Abstract 1005.

Gianna L et al. Neoadjuvant treatment with trastuzumab and pertuzumab plus palbociclib and fulvestrant in HER2-positive, ER-positive breast cancer (NA-PHER2): An exploratory, open-label, phase 2 study. *Lancet Oncol* 2018;19(2):249-56.

Goel S et al. Overcoming therapeutic resistance in HER2-positive breast cancers with CDK4/6 inhibitors. *Cancer Cell* 2016;29(3):255-69.

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.

Kaufman B et al. Trastuzumab plus anastrozole versus anastrozole alone for the treatment of postmenopausal women with human epidermal growth factor receptor 2-positive, hormone receptor-positive metastatic breast cancer: Results from the randomized phase III TAnDEM study. *J Clin Oncol* 2009;27(33):5529-37.

Kodack DP et al. The brain microenvironment mediates resistance in luminal breast cancer to PI3K inhibition through HER3 activation. *Sci Transl Med* 2017;9(391):eaal4682.

Lin N et al. Breast cancer in the central nervous system: Multidisciplinary considerations and management. *Am Soc Clin Oncol Educ Book* 2017;37:45-56.

Petrelli F et al. The efficacy of lapatinib and capecitabine in HER-2 positive breast cancer with brain metastases: A systematic review and pooled analysis. *Eur J Cancer* 2017;84:141-8.

Mark Robson, MD

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

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

Han HS et al. Efficacy and tolerability of veliparib (V; ABT-888) in combination with carboplatin (C) and paclitaxel (P) vs placebo (Plc)+C/P in patients (pts) with *BRCA1* or *BRCA2* mutations and metastatic breast cancer: A randomized, phase 2 study. San Antonio Breast Cancer Symposium 2016; Abstract S2-05.

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.

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.

Select Publications

Robson M et al. **Olaparib for metastatic breast cancer in patients with a germline BRCA mutation.** *N Engl J Med* 2017;377(6):523-33.

Hope S Rugo, MD

Dirix LY et al. Avelumab, an anti-PD-L1 antibody, in patients with locally advanced or metastatic breast cancer: A phase 1b JAVELIN solid tumor study. *Breast Cancer Res Treat* 2018;167(3):671-86.

Emens LA et al. Inhibition of PD-L1 by MPDL3280A leads to clinical activity in patients with metastatic triple-negative breast cancer (TNBC). *Proc AACR* 2015; Abstract 2859.

Kok M et al. Adaptive phase II randomized trial of nivolumab after induction treatment in triple negative breast cancer (TONIC trial): Final response data stage I and first translational data. ASCO 2018;Abstract 1012.

Loi S et al. Relationship between tumor infiltrating lymphocyte (TIL) levels and response to pembrolizumab (pembro) in metastatic triple-negative breast cancer (mTNBC): Results from KEYNOTE-086. *Proc ESMO* 2017;Abstract LBA13.

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.

Postow MA et al. **Immune-related adverse events associated with immune checkpoint blockade.** *N Engl J Med* 2018;378(2):158-68.

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

Slomovitz BM, Coleman RL. The PI3K/AKT/mTOR pathway as a therapeutic target in endometrial cancer. *Clin Cancer Res* 2012;18(21):5856-64.

Tolaney S et al. Updated efficacy, safety, & PD-L1 status of patients with HR+, HER2- metastatic breast cancer administered abemaciclib plus pembrolizumab. *Proc ASCO* 2018; Abstract 1059.

Vinayak S et al. TOPACIO/Keynote-162: Niraparib + pembrolizumab in patients (pts) with metastatic triple-negative breast cancer (TNBC), a phase 2 trial. *Proc ASCO* 2018; Abstract 1011.