Cancer Conference Update

A Multimedia Review of Key Breast Cancer Presentations from the 2016 San Antonio Breast Cancer Symposium and the 2017 American Society of Clinical Oncology Annual Meeting

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 2017 in the United States alone the disease will culminate in an estimated 255,180 new cases and 41,070 deaths. Advances in screening and prevention have resulted in a steady down-stage migration at the time of disease presentation, such that only about 5% of women have identifiable distant metastases with 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 available local and systemic treatment options is largely based on a number of prognostic and predictive risk factors present in the patient or the 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, biomarkerdriven treatment algorithms have become the "norm" for many tumor types, particularly breast cancer.

Several consensus- and evidence-based treatment guidelines are available and aim to assist clinicians with making breast cancer management decisions in the face of this dynamic environment. But despite the existence of these tools, many areas of controversy persist within academic and community settings. By providing information on the latest clinical developments in the context of expert perspectives, this activity assists medical oncologists, hematologists and hematologyoncology fellows with the formulation of evidence-based and current therapeutic strategies in the management of breast cancer, which in turn facilitates optimal patient care.

LEARNING OBJECTIVES

- Appraise recently published clinical research data and adapt current breast cancer diagnostic and management approaches on the basis of practice-changing findings.
- Appreciate the similarities and differences between existing genomic assays, and use this information to select the appropriate platform 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-positive breast cancer.
- Develop an understanding of the mechanisms of action, available research data and ongoing trials of approved and investigational CDK4/6 inhibitors and other novel therapies under investigation in the management of advanced breast cancer.
- Consider clinical data and patient preferences in the selection and sequencing of available therapeutic agents for patients with newly diagnosed and metastatic triple-negative breast cancer.
- Counsel appropriately selected patients with breast cancer about participation in ongoing clinical trials investigating novel therapeutic agents and strategies.

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 3 *AMA PRA Category* 1 *Credits*TM. 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 3 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 slide and video components. To receive credit, the participant should review the slide presentations, 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/CACUBreast17/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:

Kimberly L Blackwell, MD

Professor of Medicine Director, Breast Cancer Program Duke Cancer Institute Durham, North Carolina

Advisory Committee: Advaxis Inc, Bayer HealthCare Pharmaceuticals, Eisai Inc, MacroGenics Inc, Merck, Novartis, Pfizer Inc, Pierian Biosciences, Syndax Pharmaceuticals Inc; Consulting Agreements: Celgene Corporation, Coherus Biosciences, G1 Therapeutics, Genentech BioOncology, Lilly, Puma Biotechnology Inc, Sandoz, Novartis, Pfizer Inc, Roche Laboratories Inc; Contracted Research: Celgene Corporation, Genentech BioOncology, Novartis, Pfizer Inc.

Karen A Gelmon, MD

Professor, Medicine Head, Division of Medical Oncology University of British Columbia Medical Oncologist, BC Cancer Agency Vancouver Cancer Centre Vancouver, Canada

Advisory Committee: AstraZeneca Pharmaceuticals LP, Lilly, Merck, Novartis, Pfizer Inc.

Ian E Krop, MD, PhD

Director of Clinical Research Breast Oncology Center Dana-Farber Cancer Institute Assistant Professor of Medicine Harvard Medical School Boston, Massachusetts

Advisory Committee: Genentech BioOncology, Roche Laboratories Inc, Seattle Genetics; Contracted Research: Roche Laboratories Inc.

Kathy D Miller, MD

Co-Director, IU Simon Cancer Center Breast Cancer Program Ballvé-Lantero Scholar in Oncology Professor of Medicine Division of Hematology/Oncology Indiana University Melvin and Bren Simon Cancer Center Indianapolis, Indiana

Contracted Research: Astellas Pharma Global Development Inc, Genentech BioOncology, Medivation Inc, a Pfizer Company, Merrimack Pharmaceuticals Inc, Novartis, Pfizer Inc, Taiho Oncology Inc; **Data Monitoring Committee:** ImClone Systems, a wholly owned subsidiary of Eli Lilly and Company, Merck.

Rita Nanda, MD

Co-Director, Breast Medical Oncology Associate Professor of Medicine Section of Hematology/Oncology The University of Chicago Chicago, Illinois

Advisory Committee: Celgene Corporation, Pfizer Inc, Syndax Pharmaceuticals Inc, Puma Biotechnology Inc; Contracted Research: Celgene Corporation, Genentech BioOncology, Merck.

Sara Tolaney, MD, MPH

Department of Medical Oncology Dana-Farber Cancer Institute Assistant Professor in Medicine Harvard Medical School Boston, Massachusetts

Contracted Research: Genentech BioOncology, Lilly, Merck, Novartis, Pfizer Inc.

EDITOR — **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, Acerta Pharma, 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 BioOncology, 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, 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 STAFF AND EXTERNAL

REVIEWERS — The scientific staff and 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 Foundation Medicine, Lilly and Novartis.

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:** October 2017

Expiration date: October 2018

Video References

Adams S et al. Phase 2 study of pembrolizumab (pembro) monotherapy for previously treated metastatic triple-negative breast cancer (mTNBC): KEYNOTE-086 cohort A. *Proc ASCO* 2017; Abstract 1008.

Bardia A et al. TRINITI-1: Ribociclib + everolimus (EVE) + exemestane (EXE) triplet combination in men or postmenopausal women with HR+, HER2– advanced breast cancer (ABC) following progression on a cyclin-dependent kinase (CDK) 4/6 inhibitor. San Antonio Breast Cancer Symposium 2016; Abstract OT2-01-05.

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

Blok EJ et al. Optimal duration of extended letrozole treatment after 5 years of adjuvant endocrine therapy; results of the randomized phase III IDEAL trial (BOOG 2006-05). San Antonio Breast Cancer Symposium 2016; Abstract S1-04.

Blum JL et al. Anthracyclines in early breast cancer: The ABC trials-USOR 06-090, NSABP B-46-I/USOR 07132, and NSABP B-49 (NRG Oncology). J Clin Oncol 2017; [Epub ahead of print].

Coleman RE et al. A phase 2 randomized, double-blind, placebo-controlled trial of endocrine therapy ± radium-223 dichloride in HER2-negative, hormone receptor–positive breast cancer patients with bone metastases. San Antonio Breast Cancer Symposium 2016;Abstract OT1-04-04.

Dieras V et al. Phase 2 study of abemaciclib plus tamoxifen or abemaciclib alone in women with previously treated hormone receptor-positive (HR+), HER2- metastatic breast cancer. San Antonio Breast Cancer Symposium 2016; Abstract OT2-01-08.

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**.

Fasching PA et al. **RIBECCA** — A phase IIIb, multi-center, open label study for women with estrogen receptor positive locally advanced or metastatic breast cancer treated with ribociclib (LEE011) in combination with letrozole. San Antonio Breast Cancer Symposium 2016;Abstract OT2-01-18.

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.

Freedman RA 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.

Gradishar WJ et al. Phase III study of lapatinib (L) plus trastuzumab (T) and aromatase inhibitor (AI) vs T+AI vs L+AI in postmenopausal women (PMW) with HER2+, HR+ metastatic breast cancer (MBC): ALTERNATIVE. *Proc ASCO* 2017; Abstract 1004.

Hurvitz S et al. Biological effects of abemaciclib in a phase 2 neoadjuvant study for postmenopausal patients with HR+, HER2- breast cancer. San Antonio Breast Cancer Symposium 2016; Abstract S4-06.

Jones VE et al. Evaluation of miracle mouthwash (MMW) plus hydrocortisone or prednisolone mouth rinses as prophylaxis for everolimus-associated stomatitis: Results of a randomized phase II study. San Antonio Breast Cancer Symposium 2016;Abstract P4-16-01.

Kornblum NS et al. PrECOG 0102: A randomized, double-blind, phase II trial of fulvestrant plus everolimus or placebo in post-menopausal women with hormone receptor (HR)-positive, HER2-negative metastatic breast cancer (MBC) resistant to aromatase inhibitor (AI) therapy. San Antonio Breast Cancer Symposium 2016;Abstract S1-02.

Kuijer A et al. Impact of 70-gene signature use on adjuvant chemotherapy decisions in patients with estrogen receptorpositive early breast cancer: Results of a prospective cohort study. *J Clin Oncol* 2017;[Epub ahead of print].

Malorni L et al. A phase II trial of the CDK4/6 inhibitor palbociclib (P) as single agent or in combination with the same endocrine therapy (ET) received prior to disease progression, in patients (pts) with hormone receptor positive (HR+) HER2 negative (HER2–) metastatic breast cancer (mBC) (TREnd trial). *Proc ASCO* 2017;Abstract 1002.

Mamounas EP et al. A randomized, double-blinded, placebo-controlled clinical trial of extended adjuvant endocrine therapy (tx) with letrozole (L) in postmenopausal women with hormone-receptor (+) breast cancer (BC) who have completed previous adjuvant tx with an aromatase inhibitor (AI): Results from NRG Oncology/NSABP B-42. San Antonio Breast Cancer Symposium 2016;Abstract S1-05.

Video References

Masuda N et al. Adjuvant capecitabine for breast cancer after preoperative chemotherapy. *N Engl J Med* 2017;376(22):2147-59.

Miller KD. Questioning our APHINITY for more. N Engl J Med 2017;377(2):186-7.

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. **KEYNOTE-012: Long-lasting responses in a phase lb study of pembrolizumab for metastatic triple-negative breast cancer (mTNBC).** San Antonio Breast Cancer Symposium 2016; Abstract P6-10-03.

Nangia JR et al. Scalp cooling alopecia prevention trial (SCALP) for patients with early stage breast cancer. San Antonio Breast Cancer Symposium 2016; Abstract S5-02.

O'Shaughnessy J et al. First-line ribociclib plus letrozole in patients with de novo HR+, HER2– advanced breast cancer (ABC): A subgroup analysis of the MONALEESA-2 trial. San Antonio Breast Cancer Symposium 2016; Abstract P4-22-05.

Raska P et al. Detecting high mutational load ER+ breast cancer patients through Foundation One cancer gene panel mutations. San Antonio Breast Cancer Symposium 2016; Abstract P6-09-22.

Rimawi MF et al. A phase III trial evaluating pCR in patients with HR+, HER2-positive breast cancer treated with neoadjuvant docetaxel, carboplatin, trastuzumab, and pertuzumab (TCHP) +/- estrogen deprivation: NRG Oncology/NSABP B-52. San Antonio Breast Cancer Symposium 2016; Abstract S3-06.

Rimawi MF 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.

Robson M et al. **Olaparib for metastatic breast cancer in patients with a germline BRCA mutation.** *N Engl J Med* 2017;[Epub ahead of print].

Robson ME 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.

Ross JS et al. Comprehensive genomic profiling of 8,654 breast carcinoma reveals therapeutically targetable molecular subtypes beyond those defined by hormone-receptor expression. San Antonio Breast Cancer Symposium 2016;Abstract P1-05-08.

Rugo HS et al. A phase 2 randomized, double-blind, placebo-controlled trial of radium-223 dichloride with exemestane and everolimus in patients with HER2-negative, hormone receptor–positive breast cancer and bone metastases. San Antonio Breast Cancer Symposium 2016; Abstract OT1-04-05.

Rugo H et al. A phase 2 study of abemaciclib plus pembrolizumab for patients with hormone receptor positive (HR+), HER2 negative (HER2-) metastatic breast cancer (MBC). San Antonio Breast Cancer Symposium 2016; Abstract OT2-01-07.

Sestak I et al. Comprehensive comparison of prognostic signatures for breast cancer in TransATAC. San Antonio Breast Cancer Symposium 2016; Abstract S6-05.

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;[Epub ahead of print].

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.

Spoerke JM et al. The complete spectrum of ESR1 mutations from 7590 BC tumor samples. San Antonio Breast Cancer Symposium 2016; Abstract P6-07-08.

Tjan-Heihnen VC et al. First results from the multicenter phase III DATA study comparing 3 versus 6 years of anastrozole after 2-3 years of tamoxifen in postmenopausal women with hormone receptor-positive early breast cancer. San Antonio Breast Cancer Symposium 2016; Abstract S1-03.

Tolaney S et al. Phase 1b/2 study to evaluate eribulin mesylate in combination with pembrolizumab in patients with metastatic triple-negative breast cancer. San Antonio Breast Cancer Symposium 2016; Abstract P5-15-02.

Tolaney SM et al. **Ribociclib + fulvestrant in postmenopausal women with HR+, HER2– advanced breast cancer (ABC).** San Antonio Breast Cancer Symposium 2016;**Abstract P4-22-12**.

Turner NC et al. Final results of a phase 2 study of talazoparib (TALA) following platinum or multiple cytotoxic regimens in advanced breast cancer patients (pts) with germline BRCA1/2 mutations (ABRAZO). *Proc ASCO* 2017; Abstract 1007.

Video References

Villanueva C et al. Stomatitis in patients treated with first-line everolimus (EVE) plus letrozole (LET): Results from BOLERO-4 trial. San Antonio Breast Cancer Symposium 2016; Abstract P2-11-08.

von Minckwitz G et al. Adjuvant pertuzumab and trastuzumab in early HER2-positive breast cancer. N Engl J Med 2017;377(2):122-31.

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.

Wander SA et al. Blocking the cycle: Cyclin-dependent kinase 4/6 inhibitors in metastatic, hormone receptor-positive breast cancer. *J Clin Oncol* 2017;[Epub ahead of print].

Yuan Y et al. Synergistic suppression of triple negative breast cancer with the combination of PI3K inhibitor (alpelisib, BYL719) and CDK inhibitor (ribociclib, LEE011). San Antonio Breast Cancer Symposium 2016; Abstract P3-03-15.