Cases from the Community Investigators Provide Their Perspectives on the Practice Implications of Emerging Clinical Research

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, breast cancer surgeons, radiation oncologists and other healthcare professionals involved in the diagnosis and treatment of breast cancer (BC).

OVERVIEW OF ACTIVITY

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. 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. The pace of change in the field of breast medical oncology has been rapid, creating an important need for education about the unique mechanisms of action, toxicities and effectiveness of novel agents to properly prepare clinicians for their appropriate use (or potential use) in clinical practice. Several consensus- and evidence-based treatment guidelines are available and aim to assist clinicians with making BC management decisions in the face of this dynamic clinical and research environment, but despite the existence of these tools many areas of controversy persist within academic and community settings.

These proceedings from a CME symposium during the 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 find answers to the individualized questions and concerns that they frequently encounter and in turn provide high-quality cancer care.

LEARNING OBJECTIVES

- Consider available data and the use of biomarkers and genomic assays to assess risk and individualize therapy for patients with hormone receptor-positive BC 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 BC.
- Implement a long-term clinical plan for the management of metastatic HER2-positive BC, incorporating existing and investigational targeted treatments.
- Recognize the FDA approval of palbociclib for patients with ER-positive metastatic BC, and discern how its availability affects the selection and sequence of therapy for these individuals.
- Develop an understanding of the mechanisms of action, available research data and ongoing trials of investigational CDK4/6 inhibitors and other novel therapies under development for the management of advanced ER-positive BC.
- Consider clinical data and patient preferences in the selection and sequencing of available therapeutic agents for patients with newly diagnosed and metastatic ER/ PR-negative, HER2-negative BC.
- Recall available guideline recommendations regarding the indications for BRCA mutation testing in BC, and use the results of this analysis to inform protocol and nonprotocol treatment decision-making for patients.
- Identify ongoing trials of other investigational approaches in BC, and obtain consent and refer patients for study participation.

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*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 enables the participant to earn up to 2.75 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 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/SanAntonioBC16/Video/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.

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 Pharmaceutical Inc, Boehringer Ingelheim Pharmaceuticals Inc, Dignitana, Genentech BioOncology, GlaxoSmithKline, Lilly, Novartis Pharmaceuticals Corporation, OBI Pharma Inc, Pfizer Inc, Puma Biotechnology Inc.

Joyce O'Shaughnessy, MD

Chair, Breast Cancer Research Program Baylor Charles A Sammons Cancer Center Texas Oncology US Oncology Dallas, Texas

Consulting Agreements: AstraZeneca Pharmaceuticals LP, Celgene Corporation, Eisai Inc, Genentech BioOncology, Lilly, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche Laboratories Inc, Sanofi Genzyme, Takeda Oncology.

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 BioOncology, GlaxoSmithKline, Lilly, MacroGenics Inc, Merck, Novartis Pharmaceuticals Corporation, Pfizer Inc, Plexxikon Inc, Roche Laboratories Inc; **Speakers Bureau:** Genomic Health Inc.

Ian E Smith, MD

Professor of Cancer Medicine The Royal Marsden Foundation Trust and Institute of Cancer Research London and Surrey United Kingdom

Advisory Committee: Eisai Inc, Pierre Fabre, Seattle Genetics.

Sandra M Swain, MD

Associate Dean for Research Development Professor of Medicine Georgetown University Medical Center Washington, DC

Advisory Committee: Genentech BioOncology, Lilly, Roche Laboratories Inc; Consulting Agreements: Genentech BioOncology, Lilly, Pieris Pharmaceuticals Inc, Roche Laboratories Inc; Contracted Research: Genentech BioOncology, Lilly, Merrimack Pharmaceuticals Inc, Pfizer Inc, Puma Biotechnology Inc, Roche Laboratories Inc; Travel: Genentech BioOncology, Roche Laboratories Inc. **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, Acerta Pharma, Agendia 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, Daiichi Sankyo Inc, 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, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Lilly, Medivation Inc, a Pfizer Company, 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, 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, Tokai Pharmaceuticals Inc and VisionGate 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 AbbVie Inc, Agendia Inc, Astellas Pharma Global Development Inc/ Medivation Inc, a Pfizer Company, AstraZeneca Pharmaceuticals LP, bioTheranostics Inc, Celgene Corporation, Genentech BioOncology, Genomic Health Inc, Lilly and Tesaro 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: March 2017

Expiration date: March 2018

Sara A Hurvitz, 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.

Carey LA et al. Molecular heterogeneity and response to neoadjuvant human epidermal growth factor receptor 2 targeting in CALGB 40601, a randomized phase III trial of paclitaxel plus trastuzumab with or without lapatinib. *J Clin Oncol* 2016;34(6):542-9.

Caudle AS, Hunt KK. The neoadjuvant approach in breast cancer treatment: It is not just about chemotherapy anymore. *Curr Opin Obstet Gynecol* 2011;23(1):31-6.

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.

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.

Gianni L et al. Treatment with trastuzumab for 1 year after adjuvant chemotherapy in patients with HER2-positive early breast cancer: A 4-year follow-up of a randomised controlled trial. *Lancet Oncol* 2011;12(3):236-44.

Guarneri V et al. Preoperative chemotherapy plus trastuzumab, lapatinib, or both in human epidermal growth factor receptor **2-positive operable breast cancer: Results of the randomized phase II CHER-LOB study.** *J Clin Oncol* 2012;30(16):1989-95.

Hurvitz SA et al. Final analysis of a phase II 3-arm randomized trial of neoadjuvant trastuzumab or lapatinib or the combination of trastuzumab and lapatinib, followed by six cycles of docetaxel and carboplatin with trastuzumab and/or lapatinib in patients with HER2+ breast cancer (TRIO-US B07). San Antonio Breast Cancer Symposium 2013;Abstract S1-02.

Kaufmann M et al. Recommendations from an international expert panel on the use of neoadjuvant (primary) systemic treatment of operable breast cancer: An update. *J Clin Oncol* 2006;24(12):1940-9.

Montagna E et al. Pathological complete response after preoperative systemic therapy and outcome: Relevance of clinical and biologic baseline features. *Breast Cancer Res Treat* 2010;124(3):689-99.

Musolino A et al. Multifactorial central nervous system recurrence susceptibility in patients with HER2-positive breast cancer: Epidemiological and clinical data from a population-based cancer registry study. *Cancer* 2011;117(9):1837-46.

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.

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.

Robidoux A et al. Lapatinib as a component of neoadjuvant therapy for HER2-positive operable breast cancer (NSABP protocol **B-41):** An open-label, randomised phase 3 trial. *Lancet Oncol* 2013;14(12):1183-92.

Schneeweiss A et al. Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: A randomized phase II cardiac safety study (TRYPHAENA). *Ann Oncol* 2013;24(9):2278-84.

Schneeweiss A et al. Neoadjuvant pertuzumab and trastuzumab concurrent or sequential with an anthracycline-containing or concurrent with an anthracycline-free standard regimen: A randomized phase II study (TRYPHAENA). San Antonio Breast Cancer Symposium 2011; Abstract S5-6.

Slamon DJ et al. Ten year follow-up of BCIRG-006 comparing doxorubicin plus cyclophosphamide followed by docetaxel (AC \rightarrow T) with doxorubicin plus cyclophosphamide followed by docetaxel and trastuzumab (AC \rightarrow TH) with docetaxel, carboplatin and trastuzumab (TCH) in HER2+ early breast cancer. San Antonio Breast Cancer Symposium 2015; Abstract S5-04.

Von Minckwitz G et al. Correlation of various pathologic complete response (pCR) definitions with long-term outcome and the prognostic value of pCR in various breast cancer subtypes: Results from the German neoadjuvant meta-analysis. *Proc ASCO* 2011; Abstract 1028.

Hope S Rugo, MD

Cardosa 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.

Dubsky P et al. The EndoPredict score provides prognostic information on late distant metastases in ER+/HER2- breast cancer patients. *Br J Cancer* 2013;109(12):2959-64.

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.

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.

Sgroi DC et al. Prediction of late disease recurrence and extended adjuvant letrozole benefit by the HOXB13/IL17BR biomarker. J Natl Cancer Inst 2013;105(14):1036-42.

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

Harold J Burstein, MD, PhD

Barroso-Sousa R et al. Clinical development of the CDK4/6 inhibitors ribociclib and abemaciclib in breast cancer. Breast Care (Basel) 2016;11(3):167-73.

Bergh J et al. FACT: An open-label randomized phase III study of fulvestrant and anastrozole in combination compared with anastrozole alone as first-line therapy for patients with receptor-positive postmenopausal breast cancer. *J Clin Oncol* 2012;30(16):1919-25.

Dickler M et al. MONARCH1: Results from a phase II study of abemaciclib, a CDK4 and CDK6 inhibitor, as monotherapy, in patients with HR+/HER2- breast cancer, after chemotherapy for advanced disease. *Proc ASCO* 2016; Abstract 510.

Ellis MJ et al. FALCON: A phase III randomised trial of fulvestrant 500 mg vs anastrozole for hormone receptor-positive advanced breast cancer. *Proc ESMO* 2016; Abstract LBA14_PR.

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

Finn RS et al. Targeting the cyclin-dependent kinases (CDK) 4/6 in estrogen receptor-positive breast cancers. *Breast Cancer Res* 2016;18(1):17.

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.

Fribbens C et al. Plasma ESR1 mutations and the treatment of estrogen receptor-positive advanced breast cancer. *J Clin Oncol* 2016;34(25):2961-8.

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

Jeselsohn R et al. Emergence of constitutively active estrogen receptor- α mutations in pretreated advanced estrogen receptor-positive breast cancer. *Clin Cancer Res* 2014;20(7):1757-67.

O'Leary B et al. Treating cancer with selective CDK4/6 inhibitors. Nat Rev Clin Oncol 2016;13(7):417-30.

Mehta RS et al. Combination anastrozole and fulvestrant in metastatic breast cancer. N Engl J Med 2012;367(5):435-44.

Rugo HS et al. Endocrine therapy for hormone receptor-positive metastatic breast cancer: American Society of Clinical Oncology guideline. *J Clin Oncol* 2016;34(25):3069-103.

Schiavon G et al. Analysis of ESR1 mutation in circulating tumor DNA demonstrates evolution during therapy for metastatic breast cancer. *Sci Transl Med* 2015;7(313):313.

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

Sandra M Swain, MD

Arpino G 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.

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.

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.

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.

Harbeck N et al. Final analysis of WSG-ADAPT HER2+/HR+ phase II trial: Efficacy, safety, and predictive markers for 12-weeks of neoadjuvant TDM1 with or without endocrine therapy versus trastuzumab + endocrine therapy in HER2-positive hormone-receptor-positive early breast cancer. San Antonio Breast Cancer Symposium 2015;Abstract S5-03.

Loibl S et al. PIK3CA mutations are associated with reduced pathological complete response rates in primary HER2-positive breast cancer: Pooled analysis of 967 patients from five prospective trials investigating lapatinib and trastuzumab. *Ann Oncol* 2016;27(8):1519-25.

Rimawi MF et al. **TBCRC023: A randomized multicenter phase II neoadjuvant trial of lapatinib plus trastuzumab, with endcorine therapy and without chemotherapy, for 12 vs 24 weeks in patients with HER2 overexpressing breast cancer.** San Antonio Breast Cancer Symposium 2014; Abstract S6-02.

Robidoux A et al. Lapatinib as a component of neoadjuvant therapy for HER2-positive operable breast cancer (NSABP protocol **B-41)**: An open-label, randomised phase 3 trial. *Lancet Oncol* 2013;14(12):1183-92.

Schettini F et al. Hormone receptor/human epidermal growth factor receptor 2-positive breast cancer: Where we are now and where we are going. *Cancer Treat Rev* 2016;46:20-6.

Schneeweiss A et al. Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: A randomized phase II cardiac safety study (TRYPHAENA). *Ann Oncol* 2013;24(9):2278-84.

Slamon DJ et al. Predictive biomarkers of everolimus efficacy in HER2+ advanced breast cancer: Combined exploratory analysis from BOLERO-1 and BOLERO-3. *Proc ASCO* 2015; Abstract 512.

Untch M et al. *Nab*-paclitaxel versus solvent-based paclitaxel in neoadjuvant chemotherapy for early breast cancer (Gepar-Septo-GBG 69): A randomised, phase 3 trial. *Lancet Oncol* 2016;17(3):345-56.

Urruticoechea A et al. PHEREXA: A phase III study of trastuzumab (H) + capecitabine (X) \pm pertuzumab (P) for patients (pts) who progressed during/after one line of H-based therapy in the HER2-positive metastatic breast cancer (MBC) setting. *Proc* ASCO 2016; Abstract 504.

Joyce O'Shaughnessy, MD

Bayraktar S et al. Outcome of metastatic breast cancer in selected women with or without deleterious BRCA mutations. *Clin Exp Metastasis* 2013;30(5):631-42.

Bryant HE et al. Specific killing of BRCA2-deficient tumours with inhibitors of poly(ADP-ribose) polymerase. *Nature* 2005;434(7035):913-7.

Farmer H et al. Targeting the DNA repair defect in BRCA mutant cells as a therapeutic strategy. *Nature* 2005;434(7035): 917-21.

McCabe N et al. Deficiency in the repair of DNA damage by homologous recombination and sensitivity to poly(ADP-ribose) polymerase inhibition. *Cancer Res* 2006;66(16):8109-15.

McLornan DP et al. Applying synthetic lethality for the selective targeting of cancer. N Engl J Med 2014;371(18):1725-35.

Mirza MR et al. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. *N Engl J Med* 2016;375(22): 2154-64.

Rugo HS et al. Adaptive randomization of veliparib-carboplatin treatment in breast cancer. N Engl J Med 2016;375(1):23-34.

Somlo F et al. Phase II trial of single agent PARP inhibitor ABT-888 (veliparib [vel]) followed by postprogression therapy of vel with carboplatin (carb) in patients (pts) with stage BRCA-associated metastatic breast cancer (MBC): California Cancer Consortium trial PHII-96. *Proc ASCO* 2014;Abstract 1021.

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.

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.

Ian E Smith, MD

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

Cortes J et al. Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): A phase 3 open-label randomised study. *Lancet* 2011;377(9769):914-23.

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.

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.

Gianni L et al. ETNA (Evaluating Treatment with Neoadjuvant Abraxane) randomized phase III study comparing neoadjuvant *nab*-paclitaxel (*nab*-P) versus paclitaxel (P) both followed by anthracycline regimens in women with HER2-negative high-risk breast cancer: A MICHELANGO study. *Proc ASCO* 2016;Abstract 502.

Gucalp A et al. Phase II trial of bicalutamide in patients with androgen receptor-positive, estrogen receptor-negative metastatic Breast Cancer. *Clin Cancer Res* 2013;19(19):5505-12.

Joensuu H et al. Adjuvant capesitabine in combination with docetaxel (T), epirubicin (E), and cyclophosphamide (C) in the treatment of early breast cancer (BC): 10-year survival results from the randomized FinXX trial. *Proc ASCO* 2016, Abstract 1001.

Lehmann BD et al. Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies. *J Clin Invest* 2011;121(7):2750-67.

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**.

Partridge AH et al. Chemotherapy and targeted therapy for women with human epidermal growth factor receptor 2-negative (or unknown) advanced breast cancer: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol* 2014;32(29):3307-29.

Rugo HS et al. Randomized phase III trial of paclitaxel once per week compared with nanoparticle albumin-bound *nab*-paclitaxel once per week or ixabepilone with bevacizumab as first-line chemotherapy for locally recurrent or metastatic breast cancer: CALGB 40502/NCCTG N063H (Alliance). *J Clin Oncol* 2015;33(21):2361-9.

Traina TA 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.

Untch M et al. *Nab*-paclitaxel versus solvent-based paclitaxel in neoadjuvant chemotherapy for early breast cancer (Gepar-Septo-GBG 69): A randomised, phase 3 trial. *Lancet Oncol* 2016;17(3):345-56.

Yardley DA et al. **EMERGE: A randomized phase II study of the antibody-drug conjugate glembatumumab vedotin in advanced glycoprotein NMB-expressing breast cancer.** *J Clin Oncol* 2015;33(14):1609-19.