Year in Review

On Demand — Significance and Relevance of Recent Data Sets and Publications in the Management of Breast Cancer

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, hematologists, hematology-oncology fellows and other 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. Although the diagnosis and treatment of breast cancer remain, in many ways, more advanced than in other solid tumors, challenging issues in the basic management of this disease continue to require refinement. 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 patient- and disease-related characteristics. In conjunction with this approach, researchers are developing novel agents and immunotherapeutic strategies with the aim of enhancing the efficacy of existing treatments and overcoming resistance or restoring sensitivity to endocrine therapy, chemotherapy or biologic agents. In order to offer optimal patient care — including the option of clinical trial participation — the practicing cancer clinician must be well informed of these advances.

This special CME activity aims to bridge the gap between research and patient care by presenting a one-on-one discussion with leading breast cancer investigator Dr Hope S Rugo reviewing the year's most important presentations and publications and summarizing their potential impact on current and future treatment algorithms.

LEARNING OBJECTIVES

- Discuss the clinical relevance of recent pivotal breast cancer research results, as published in peer-reviewed journals and/or presented at major oncology conferences.
- 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.
- Implement a long-term clinical plan for the management of metastatic HER2-positive breast cancer.
- Develop an evidence-based algorithm for the treatment of hormone-sensitive advanced breast cancer, including the use of endocrine, biologic and chemotherapeutic agents.
- Recall emerging efficacy and safety data with the use of PARP inhibitors in patients with metastatic breast cancer harboring a germline BRCA mutation, and consider the potential diagnostic and therapeutic implications of these findings on protocol and off-protocol care.
- Appraise the rationale for and clinical data with investigational anti-PD-1/PD-L1 antibodies in patients with metastatic breast cancer.
- Counsel appropriately selected patients with breast cancer about participation in ongoing clinical trials evaluating other novel therapeutic agents and strategies.

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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**.

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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/YIROnDemand18/Breast/CME**.

CONTENT VALIDATION AND DISCLOSURES

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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:

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.

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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

Last review date: September 2018

Expiration date: September 2019

Select Publications

A phase Ib/II, open-label, multicenter, randomized umbrella study evaluating the efficacy and safety of multiple immuno-therapy-based treatment combinations in patients with metastatic triple-negative breast cancer (Morpheus-TNBC). NCT03424005

A phase III randomized double-blind, placebo controlled study of alpelisib in combination with fulvestrant for men and postmenopausal women with hormone receptor positive, HER2-negative advanced breast cancer which progressed on or after aromatase inhibitor treatment. NCT02437318

A randomised, double-blind, parallel group, placebo-controlled multi-centre phase III study to assess the efficacy and safety of olaparib versus placebo as adjuvant treatment in patients with gBRCA1/2 mutations and high risk HER2-negative primary breast cancer who have completed definitive local treatment and neoadjuvant or adjuvant chemotherapy. NCT02032823

A randomized, multicenter, open-label, Phase II trial to evaluate the efficacy and safety of palbociclib in combination with fulvestrant or letrozole in patients with HER2 negative, ER+ metastatic breast cancer. NCT02491983

A randomized, open-label, phase 3 study of abemaciclib combined with standard adjuvant endocrine therapy versus standard adjuvant endocrine therapy alone in patients with high risk, node positive, early stage, hormone receptor positive, human epidermal receptor 2 negative, breast cancer. NCT03155997

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.** *Proc AACR* 2017;**Abstract OT2-01-05**.

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.** *Proc ASCO* 2018;**Abstract LBA1006**.

Baselga J et al. **SANDPIPER: Phase III study of the PI3-kinase (PI3K) inhibitor taselisib (GDC-0032) plus fulvestrant in patients (pts) with estrogen receptor (ER)-positive, HER2-negative locally advanced or metastatic breast cancer (BC) enriched for pts with PIK3CA-mutant tumors.** *Proc ASCO* 2017;**Abstract TPS1119**.

Business Wire. **Phase III IMpassion130 study showed Genentech's TECENTRIQ plus Abraxane significantly reduced the risk of disease worsening or death in people with metastatic or locally advanced triple negative breast cancer** [press release]. July 2, 2018. Available at: **https://www.businesswire.com/news/home/20180701005088/en/Phase-III-IMpassion130-Study-Showed-Genentech's-TECENTRIQ**.

Chandarlapaty S et al. **Prevalence of ESR1 mutations in cell-free DNA and outcomes in metastatic breast cancer: A secondary analysis of the BOLERO-2 clinical trial.** *JAMA Oncol* 2016;2(10):1310-5.

Curigliano G et al. **De-escalating and escalating treatments for early-stage breast cancer: The St Gallen International Expert Consensus Conference on the primary therapy of early breast cancer 2017.** *Ann Oncol* 2018;[Epub ahead of print].

Denduluri N et al. **Selection of optimal adjuvant chemotherapy and targeted therapy for early breast cancer: ASCO clinical practice guideline focused update.** *J Clin Oncol* 2018;36(23):2433-43.

Early Breast Cancer Trialists' Collaborative Group (EBCTCG). **Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: Meta-analysis of individual patient data from ten randomised trials.** *Lancet Oncol* 2018;19(1):27-39.

Francis PA et al. **Tailoring adjuvant endocrine therapy for premenopausal breast cancer.** *N Engl J Med* 2018;379(2):122-37.

GlobeNewswire. **TRIO awarded NATALEE study, largest single phase III breast cancer clinical trial in its history** [press release]. July 9, 2018. Available at: **https://globenewswire.com/news-release/2018/07/09/1534927/0/en/TRIO-Awarded-NATALEE-Study-Largest-Single-Phase-III-Breast-Cancer-Clinical-Trial-in-its-History.html**.

Gnant M et al. **A prospective randomized multi-center phase-III trial of additional 2 versus additional 5 years of anastrozole after initial 5 years of adjuvant endocrine therapy — results from 3,484 postmenopausal women in the ABCSG-16 trial.** San Antonio Breast Cancer Symposium 2017;**Abstract GS3-01**.

Hortobagyi GN et al. **Correlative analysis of genetic alterations and everolimus benefit in hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer: Results from BOLERO-2.** *J Clin Oncol* 2016;34(5):419-26.

Hurvitz S et al. **Ribociclib in combination with everolimus and exemestane in men and postmenopausal women with HR+/HER2– advanced breast cancer following progression on a CDK4/6 inhibitor: Safety, tolerability, and pharmacokinetic results from Phase 1 of TRINITI-1 study.** *Proc AACR* 2017;**Abstract CT110**.

Select Publications

Ibrahim E et al. **Effects of adding budesonide or colestipol to loperamide prophylaxis on neratinib-associated diarrhea in patients (pts) with HER2+ early-stage breast cancer (eBC): The CONTROL trial.** *Proc AACR* 2017;**Abstract CT128**.

I-SPY 2 trial (investigation of serial studies to predict your therapeutic response with imaging and molecular analysis 2). NCT01042379

Jerusalem GHM et al. **Everolimus (EVE) + exemestane (EXE) vs EVE alone or capecitabine (CAP) for estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (ABC): BOLERO-6, an open-label phase 2 study.** *Proc ASCO* 2018;**Abstract 1005**.

Jerusalem G et al. **Everolimus plus exemestane vs everolimus or capecitabine monotherapy for estrogen receptor-positive, HER2-negative advanced breast cancer: The BOLERO-6 randomized clinical trial.** *JAMA Oncol* 2018;[Epub ahead of print].

Johnston SRD et al. **Phase III, randomized study of dual human epidermal growth factor receptor 2 (HER2) blockade with lapatinib plus trastuzumab in combination with an aromatase inhibitor in postmenopausal women with HER2-positive, hormone receptor-positive metastatic breast cancer: ALTERNATIVE.** *J Clin Oncol* 2018;36(8):741-8.

Kornblum N et al. **Randomized phase II trial of fulvestrant plus everolimus or placebo in postmenopausal women with hormone receptor-positive, human epidermal growth factor receptor 2-negative metastatic breast cancer resistant to aromatase inhibitor therapy: Results of PrE0102.** *J Clin Oncol* 2018;36(16):1556-63.

Krop I et al. **Results from a randomized placebo-controlled phase 2 trial evaluating exemestane ± enzalutamide in patients with hormone receptor–positive breast cancer.** San Antonio Breast Cancer Symposium 2017;**Abstract GS4-07**.

Lippman ME. **Endocrine adjuvant therapy for localized breast cancer.** *N Engl J Med* 2018;379(2):193-4.

Litton J et al. **EMBRACA: A phase 3 trial comparing talazoparib, an oral PARP inhibitor, to physician's choice of therapy in patients with advanced breast cancer and a germline *BRCA* mutation.** San Antonio Breast Cancer Symposium 2017;**Abstract GS6-07**.

Loi S et al. **Phase Ib/II study evaluating safety and efficacy of pembrolizumab and trastuzumab in patients with trastuzumab-resistant HER2-positive metastatic breast cancer: Results from the PANACEA (IBCSG 45-13/BIG 4-13/KEYNOTE-014) study.** San Antonio Breast Cancer Symposium 2017;**Abstract GS2-06**.

Martin M et al; ExteNET Study Group. **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.

Moynahan ME et al. **Correlation between PIK3CA mutations in cell-free DNA and everolimus efficacy in HR$^+$, HER2$^-$ advanced breast cancer: Results from BOLERO-2.** *Br J Cancer* 2017;116(6):726-30.

Neven P et al. **Abemaciclib for pre/perimenopausal women with HR+, HER2- advanced breast cancer.** *Proc ASCO* 2018;**Abstract 1002**.

Pagani O et al. **Randomized comparison of adjuvant aromatase inhibitor exemestane (E) plus ovarian function suppression (OFS) vs tamoxifen (T) plus OFS in premenopausal women with hormone receptor positive (HR+) early breast cancer (BC): Update of the combined TEXT and SOFT trials.** San Antonio Breast Cancer Symposium 2017;**Abstract GS4-02**.

Palbociclib after CDK and endocrine therapy (PACE): A randomized phase II study of fulvestrant, palbociclib, and avelumab for endocrine pre-treated ER+/HER2- metastatic breast cancer. NCT03147287

Palbociclib Collaborative Adjuvant Study: A randomized phase III trial of palbociclib with standard adjuvant endocrine therapy versus standard adjuvant endocrine therapy alone for hormone receptor positive (HR+) / human epidermal growth factor receptor 2 (HER2)-negative early breast cancer. NCT02513394

Pan H et al; EBCTCG. **20-year risks of breast-cancer recurrence after stopping endocrine therapy at 5 years.** *N Engl J Med* 2017;377(19):1836-46.

Phase III study evaluating palbociclib (PD-0332991), a cyclin-dependent kinase (CDK) 4/6 inhibitor in patients with hormone-receptor-positive, HER2-normal primary breast cancer with high relapse risk after neoadjuvant chemotherapy. NCT01864746

Regan MM et al. **Absolute improvements in freedom from distant recurrence with adjuvant endocrine therapies for premenopausal women with hormone receptor-positive (HR+) HER2-negative breast cancer (BC): Results from TEXT and SOFT.** *Proc ASCO* 2018;**Abstract 503**.

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.

Select Publications

Royce M et al. **Everolimus plus endocrine therapy for postmenopausal women with estrogen receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer: A clinical trial.** *JAMA Oncol* 2018;4(7):977-84.

Rugo HS et al. **Palbociclib (PAL) + letrozole (LET) as first-line therapy in estrogen receptor–positive (ER+)/human epidermal growth factor receptor 2–negative (HER2–) advanced breast cancer (ABC): Efficacy and safety updates with longer follow-up across patient subgroups.** San Antonio Breast Cancer Symposium 2017;**Abstract P5-21-03**.

Rugo HS et al. **Prevention of everolimus-related stomatitis in women with hormone receptor-positive, HER2-negative metastatic breast cancer using dexamethasone mouthwash (SWISH): A single-arm, phase 2 trial.** *Lancet Oncol* 2017;18(5):654-62.

Slamon DJ et al. **Phase III randomized study of ribociclib and fulvestrant in hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer: MONALEESA-3.** *J Clin Oncol* 2018;36(24):2465-72.

Slamon DJ et al. **Ribociclib (RIB) + fulvestrant (FUL) in postmenopausal women with hormone receptor-positive (HR+), HER2-negative (HER2–) advanced breast cancer (ABC): Results from MONALEESA-3.** *Proc ASCO* 2018;**Abstract 1000**.

Sparano JA et al. **Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer.** *N Engl J Med* 2018;379(2):111-21.

Tolaney SM 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**.

Tolaney SM 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 2017;**Abstract PD6-13**.

Tripathy D et al. **Ribociclib plus endocrine therapy for premenopausal women with hormone-receptor-positive, advanced breast cancer (MONALEESA-7): A randomised phase 3 trial.** *Lancet Oncol* 2018;19(7):904-15.

Tripathy D et al. **First-line ribociclib vs placebo with goserelin and tamoxifen or a non-steroidal aromatase inhibitor in premenopausal women with hormone receptor-positive, HER2-negative advanced breast cancer: Results from the randomized phase III MONALEESA-7 trial.** San Antonio Breast Cancer Symposium 2017;**Abstract GS2-05**.

Turner NC et al. **Genetic landscape of resistance to CDK4/6 inhibition in circulating tumor DNA (ctDNA) analysis of the PALOMA3 trial of palbociclib and fulvestrant versus placebo and fulvestrant.** *Proc ASCO* 2018;**Abstract 1001**.

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**.

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

Yee D et al. **Pathological complete response predicts event-free and distant disease-free survival in the I-SPY2 trial.** San Antonio Breast Cancer Symposium 2017;**Abstract GS3-08**.