Visiting Professors

Clinical Investigators Provide Their Perspectives on Current Cases and Emerging Research in the Management of Breast Cancer

CME Information

TARGET AUDIENCE

This activity is intended for medical, radiation and surgical oncologists and other healthcare professionals involved in the treatment of breast cancer.

OVERVIEW OF ACTIVITY

Each year nearly 1.4 million women are newly diagnosed with breast cancer, making it the most prevalent diagnosis among women and the second most common cancer in both sexes worldwide. Equally relevant, more than 450,000 patients will die due to this disease. As such, breast cancer has a tremendous global impact and has become the subject of extensive ongoing clinical research. For this reason, the clinical management of breast cancer is frequently in a state of evolution, necessitating rapid and consistent clinician access to emerging data sets of relevance to the continuous delivery of quality care.

By providing access to the latest research developments and expert perspectives, these proceedings from an international case-based CME symposium held at the 2014 ESMO Annual Meeting in Madrid, Spain aim to assist medical oncologists, breast surgeons and other healthcare providers as they attempt to formulate optimal disease management strategies in the face of a constantly evolving body of knowledge.

LEARNING OBJECTIVES

- Appropriately use existing and emerging biomarkers to assess risk and individualize therapy for patients with invasive 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 adjuvant trastuzumab regimens for patients with HER2-overexpressing breast cancer.
- Implement a long-term clinical plan for the management of metastatic HER2-positive breast cancer, incorporating existing, recently approved and investigational targeted treatments.
- Formulate individualized approaches to neoadjuvant therapy for patients with ER-positive, HER2-negative disease and those with advanced triple-negative breast cancer.
- Develop an evidence-based approach to clinical decision-making for patients with discordant assay results for ER or HER2.
- Counsel appropriately selected patients about participation in ongoing clinical trials.

ACCREDITATION STATEMENT

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CREDIT DESIGNATION STATEMENT

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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 75% or better and fill out the Educational Assessment and Credit Form located at ResearchToPractice.com/ESMOBreast14/CME.

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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

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Select Publications

Hope S Rugo, MD

A Phase III, randomized clinical trial of standard adjuvant endocrine therapy +/- chemotherapy in patients with 1-3 positive nodes, hormone receptor-positive and HER2-negative breast cancer with Recurrence Score (RS) of 25 or less. RxPONDER: A clinical trial Rx for positive node, endocrine responsive breast cancer. NCT01272037

Albain KS et al. **Adjuvant chemotherapy and timing of tamoxifen in postmenopausal patients with endocrine-responsive, node-positive breast cancer: A phase 3, open-label, randomised controlled trial.** *Lancet* 2009;374(9707):2055-63.

Bartlett JM et al. **Mammostrat as a tool to stratify breast cancer patients at risk of recurrence during endocrine therapy.** *Breast Cancer Res* 2010;12(4):R47.

Buyse M et al. **Validation and clinical utility of a 70-gene prognostic signature for women with node-negative breast cancer.** *J Natl Cancer Inst* 2006;98(17):1183-92.

Cuzick J et al. **Prognostic value of a combined estrogen receptor, progesterone receptor, Ki-67, and human epidermal growth factor receptor 2 immunohistochemical score and comparison with the Genomic Health recurrence score in early breast cancer.** *J Clin Oncol* 2011;29(32):4273-8.

De Laurentiis M et al. **The effect of physician's characteristics on adjuvant chemotherapy (CT) decisions for early stage HR+, HER2- breast cancer (BC) patients (pts).** *Proc ESMO* 2014;**Abstract 261PD**.

Drukker CA et al. **A prospective evaluation of a breast cancer prognosis signature in the observational RASTER study.** *Int J Cancer* 2013;133(4):929-36.

Gnant M et al. **Predicting distant recurrence in receptor-positive breast cancer patients with limited clinicopathological risk: Using the PAM50 Risk of Recurrence score in 1478 postmenopausal patients of the ABCSG-8 trial treated with adjuvant endocrine therapy alone.** *Ann Oncol* 2014;25(2):339-45.

Knauer M et al. **The predictive value of the 70-gene signature for adjuvant chemotherapy in early breast cancer.** *Breast Cancer Res Treat* 2010;120(3):655-61.

MINDACT (microarray in node-negative and 1 to 3 positive lymph node disease may avoid chemotherapy): A prospective, randomized study comparing the 70-gene signature with the common clinical-pathological criteria in selecting patients for adjuvant chemotherapy in breast cancer with 0 to 3 positive nodes. NCT00433589

Nielsen TO et al. **A comparison of PAM50 intrinsic subtyping with immunohistochemistry and clinical prognostic factors in tamoxifen-treated estrogen receptor-positive breast cancer.** *Clin Cancer Res* 2010;16(21):5222-32.

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.

Parker JS et al. **Supervised risk predictor of breast cancer based on intrinsic subtypes.** *J Clin Oncol* 2009;27(8):1160-7.

Program for the assessment of clinical cancer tests (PACCT-1): Trial assigning individualized options for treatment: The TAILORx trial. NCT00310180

Shivers SC et al. **Direct comparison of risk classification between MammaPrint®, Onco*type* DX® and Mammostrat® assays in patients with early stage breast cancer.** San Antonio Breast Cancer Symposium 2013;**Abstract P6-06-02**.

Javier Cortes, MD, PhD

A multicenter randomized Phase III study comparing 6 versus 12 months of trastuzumab in combination with dose dense docetaxel following FE75C as adjuvant treatment of women with axillary lymph node positive breast cancer over-expressing HER2. NCT00615602

A Phase III trials program exploring the integration of bevacizumab, everolimus (RAD001), and lapatinib into current neoadjuvant chemotherapy regimes for primary breast cancer. NCT00567554

A randomised, multi-centre, open-label, Phase III study of adjuvant lapatinib, trastuzumab, their sequence and their combination in patients with HER2/ErbB2 positive primary breast cancer. NCT00490139

A randomized Phase II study of trastuzumab emtansine (T-DM1) vs paclitaxel in combination with trastuzumab for Stage I HER2-positive breast cancer (ATEMPT trial). NCT01853748

A randomized Phase III study comparing trastuzumab plus docetaxel (HT) followed by 5-FU, epirubicin, and cyclophosphamide (FEC) to the same regimen followed by single-agent trastuzumab as adjuvant treatments for early breast cancer. NCT00593697

Select Publications

A randomized Phase III trial of neoadjuvant therapy for patients with palpable and operable HER2-positive breast cancer comparing the combination of trastuzumab plus lapatinib to trastuzumab and to lapatinib administered with weekly paclitaxel following AC accompanied by correlative science studies to identify predictors of pathologic complete response. NCT00486668

A study of trastuzumab-DM1 plus pertuzumab versus trastuzumab [Herceptin] plus a taxane in patients with metastatic breast cancer. NCT01120184

APHINITY trial: A randomized multicenter, double-blind, placebo-controlled comparison of chemotherapy plus trastuzumab plus placebo versus chemotherapy plus trastuzumab plus pertuzumab as adjuvant therapy in patients with operable HER2-positive primary breast cancer. NCT01358877

Baselga J et al. **Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer.** *N Engl J Med* 2012;366(2):109-19.

Baselga J et al. **First results of the NeoALTTO trial (BIG 01-06/EGF 106903): A phase III, randomized, open label, neoadjuvant study of lapatinib, trastuzumab, and their combination plus paclitaxel in women with HER 2-positive primary breast cancer.** San Antonio Breast Cancer Symposium 2010;**Abstract S3-3**.

Chang JCN et al. **TBCRC 006: A multicenter phase II study of neoadjuvant lapatinib and trastuzumab in patients with HER2-overexpressing breast cancer.** *Proc ASCO* 2011;**Abstract 505**.

Earl HM et al. **PERSEPHONE: Duration of trastuzumab with chemotherapy in women with HER2-positive early breast cancer — Six versus twelve months.** *Proc ASCO* 2013;**Abstract TPS667**.

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.

Gianni L et al. **Neoadjuvant pertuzumab (P) and trastuzumab (H): Antitumor and safety analysis of a randomized phase II study ('NeoSphere').** San Antonio Breast Cancer Symposium 2010;**Abstract S3-2**.

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.

Goldhirsch A et al. **Personalizing the treatment of women with early breast cancer: Highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013.** *Ann Oncol* 2013;24(9):2206-23.

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.

Ismael G et al. **Subcutaneous versus intravenous administration of (neo)adjuvant trastuzumab in patients with HER2-positive, clinical stage I-III breast cancer (HannaH study): A phase 3, open-label, multicentre, randomised trial.** *Lancet Oncol* 2012;13(9):869-78.

Krop IE et al. **Trastuzumab emtansine versus treatment of physician's choice for pretreated HER2-positive advanced breast cancer (TH3RESA): A randomised, open-label, Phase 3 trial.** *Lancet Oncol* 2014;15(7):689-99.

National Comprehensive Cancer Network (NCCN®). **NCCN clinical practice guidelines in oncology.** Breast cancer — Version 3.2014. Available at: **http://www.nccn.org/professionals/physician_gls/f_guidelines.asp**.

Perez EA et al. **Four-year follow-up of trastuzumab plus adjuvant chemotherapy for operable human epidermal growth factor receptor 2-positive breast cancer: Joint analysis of data from NCCTG N9831 and NSABP B-31.** *J Clin Oncol* 2011;29(25):3366-73.

Perez EA et al. **Sequential versus concurrent trastuzumab in adjuvant chemotherapy for breast cancer.** *J Clin Oncol* 2011;29(34):4491-7.

Piccart-Gebhart MJ et al. **Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer.** *N Engl J Med* 2005;353(16):1659-72.

Pivot X et al. **6 months versus 12 months of adjuvant trastuzumab for patients with HER2-positive early breast cancer (PHARE): A randomised Phase 3 trial.** *Lancet Oncol* 2013;14(8):741-8.

Randomized, double-blind, placebo-controlled Phase II trial of fulvestrant (Faslodex) plus everolimus in post-menopausal patients with hormone-receptor positive metastatic breast cancer resistant to aromatase inhibitor therapy. NCT01797120

Romond EH et al. **Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer.** *N Engl J Med* 2005;353(16):1673-84.

Select Publications

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

Senkus E et al. **Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.** *Ann Oncol* 2013;24(Suppl 6):vi7-23.

Short-HER: Multicentric randomised Phase III trial of 2 different adjuvant chemotherapy regimens plus 3 vs 12 months of trastuzumab in HER2 positive breast cancer patients. NCT00629278

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

Slamon D et al. **BCIRG 006: 2nd interim analysis phase III randomized trial comparing cyclophosphamide followed by docetaxel (AC → T) with doxorubicin and cyclophosphamide followed by docetaxel and trastuzumab (AC → TH) with docetaxel, carboplatin and trastuzumab (TCH) in Her2neu positive early breast cancer patients.** San Antonio Breast Cancer Symposium 2006. No abstract available.

Slamon DJ et al. **Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2.** *N Engl J Med* 2001;344(11):783-92.

Smith I et al. **2-year follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: A randomised controlled trial.** *Lancet* 2007;369(9555):29-36.

Swain S et al. **Final overall survival (OS) analysis from the CLEOPATRA study of first-line (1L) pertuzumab (Ptz), trastuzumab (T), and docetaxel (D) in patients (pts) with HER2-positive metastatic breast cancer (MBC).** *Proc ESMO* 2014;**Abstract 350O_PR**.

Tolaney SM et al. **A phase II study of adjuvant paclitaxel (T) and trastuzumab (H) (APT trial) for node-negative, HER2-positive breast cancer (BC).** San Antonio Breast Cancer Symposium 2013;**Abstract S1-04**.

Verma S et al. **Trastuzumab emtansine for HER2-positive advanced breast cancer.** *N Engl J Med* 2012;367(19):1783-91.

John Crown, BCh, BAO, BSc, MD, MBA

Akashi-Tanaka S et al. **21-gene expression profile assay on core needle biopsies predicts responses to neoadjuvant endocrine therapy in breast cancer patients.** *Breast* 2009;18(3):171-4.

Chang JC et al. **Gene expression patterns in formalin-fixed, paraffin-embedded core biopsies predict docetaxel chemosensitivity in breast cancer patients.** *Breast Cancer Res Treat* 2008;108(2):233-40.

Chen XS et al. **Both carboplatin and bevacizumab improve pathological complete remission rate in neoadjuvant treatment of triple negative breast cancer: A meta-analysis.** *PLoS One* 2014;9(9):e108405.

Gianni L et al. **Gene expression profiles in paraffin-embedded core biopsy tissue predict response to chemotherapy in women with locally advanced breast cancer.** *J Clin Oncol* 2005;23(29):7265-77.

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.

Rugo HS et al. **Veliparib/carboplatin plus standard neoadjuvant therapy for high-risk breast cancer: First efficacy results from the I-SPY 2 trial.** San Antonio Breast Cancer Symposium 2013;**Abstract S5-02**.

Sikov WM et al. **Impact of the addition of carboplatin (Cb) and/or bevacizumab (B) to neoadjuvant weekly paclitaxel (P) followed by dose-dense AC on pathologic complete response (pCR) rates in triple-negative breast cancer (TNBC): CALGB 40603 (Alliance).** San Antonio Breast Cancer Symposium 2013;**Abstract S5-01**.

Angelo Di Leo, MD, PhD

Chang HJ et al. **Discordant human epidermal growth factor receptor 2 and hormone receptor status in primary and metastatic breast cancer and response to trastuzumab.** *Jpn J Clin Oncol* 2011;41(5):593-9.

Fabi A et al. **HER2 protein and gene variation between primary and metastatic breast cancer: Significance and impact on patient care.** *Clin Cancer Res* 2011;17(7):2055-64.

Turner NH, Di Leo A. **HER2 discordance between primary and metastatic breast cancer: Assessing the clinical impact.** *Cancer Treat Rev* 2013;39(8):947-57.