ENDOCRINE TREATMENT OF METASTATIC BREAST CANCER: NEW ADVANCES; PATIENT EDUCATION IMPLICATIONS

An Interactive Grand Rounds Series for Nurses

CNE Information

TARGET AUDIENCE

This activity is intended for oncology nurses, nurse practitioners, clinical nurse specialists and other healthcare providers involved in the treatment of ER-positive metastatic breast cancer (mBC).

OVERVIEW OF ACTIVITY

Among the widely acknowledged BC phenotypes, ER-positive disease, which represents approximately 63% of cases, is perhaps the most nuanced with regard to therapeutic decision-making in the advanced disease setting. Specifically, improved understanding of the mechanisms by which breast tumors develop resistance to endocrine therapy has led to the appreciation that several other biologic pathways may be implicated in this process and has in turn fostered a spate of clinical research designed to evaluate novel therapies with inhibitory activity against these potential targets. Significantly, the results of these efforts have now been actualized in the clinic as over the past several years the FDA has granted approval to several unique treatments that, when combined with hormonal therapy (or in some instances on their own), have been shown to enhance efficacy over endocrine intervention alone. Importantly, although the availability of these therapies undoubtedly provides immense benefit to patients, the many related issues (eg, sequencing, side effects) have increased the demands placed on clinicians and created additional areas of uncertainty.

Although medical oncologists have been routinely responsible for counseling patients with regard to therapeutic decision-making, oncology nurses play an integral role in the successful delivery of systemic anticancer therapy and the preservation of patient physical and psychosocial well-being. This video presentation uses a review of recent relevant publications and presentations to assist oncology nurses involved in the treatment of ER-positive mBC with the formulation of optimal therapeutic and supportive care strategies.

PURPOSE STATEMENT

By providing information on the latest research developments in the context of expert perspectives, this CNE activity will assist oncology nurses, nurse practitioners and clinical nurse specialists with the formulation of state-of-the-art clinical management strategies to facilitate optimal care of patients with ER-positive mBC.

LEARNING OBJECTIVES

- Describe the influence of estrogen and/or progesterone receptor positivity on long-term outcomes and the selection of systemic therapy for patients with advanced BC.
- Discuss the benefits and risks associated with existing and recently approved systemic therapies used in the evidence-based treatment of ER-positive mBC, including endocrine agents, chemotherapy regimens and biologic treatments.
- Recognize the FDA-endorsed indications for the commercially available CDK4/6 inhibitors, and discern how these agents can be optimally employed in the nonresearch care of patients with mBC.
- Educate patients regarding the unique side effects associated with CDK4/6 inhibitors, and develop preventive and emergent strategies to reduce or ameliorate these toxicities.
- Understand the biologic rationale for therapeutically targeting the mTOR pathway in patients with ER-positive mBC, and educate patients regarding the FDA-endorsed role and unique side effects associated with everolimus.
- Appreciate the detrimental effect of poor adherence to treatment, identify and monitor potential causes of this phenomenon and develop a plan to effectively assess and support compliance for patients receiving oral anticancer therapies.
- Identify opportunities to enhance communication and facilitate ongoing dialogue between the oncology nurse and patients with mBC to optimize clinical and quality-of-life outcomes.

ACCREDITATION STATEMENT

Research To Practice (RTP) is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

CREDIT DESIGNATION STATEMENTS

This educational activity for 1.3 contact hours is provided by RTP during the period of July 2019 through July 2020.

This activity is awarded 1.3 ANCC pharmacotherapeutic contact hours.

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The program content has been reviewed by the Oncology Nursing Certification Corporation (ONCC) and is acceptable for recertification points. To review certification qualifications, please visit **ResearchToPractice.com/GrandRoundsNursesBC19/ILNA**.

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FOR SUCCESSFUL COMPLETION

This is a video CNE program. To receive credit, participants should read the learning objectives and faculty disclosures, 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/GrandRoundsNursesBC19/CNE**.

CONTENT VALIDATION AND DISCLOSURES

RTP is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess conflicts of interest with faculty, planners and managers of CNE 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 reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

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

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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: July 2019

Expiration date: July 2020

Select Publications

André F et al. **Alpelisib (ALP) + fulvestrant (FUL) for advanced breast cancer (ABC): Results of the phase 3 SOLAR-1 trial.** *Proc ESMO* 2018;**Abstract LBA3_PR**.

Bachelot T et al. **Abemaciclib for the treatment of brain metastases secondary to hormone receptor positive breast cancer.** San Antonio Breast Cancer Symposium 2017;**Abstract P1-17-03**.

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

Baselga J et al. **Everolimus in postmenopausal hormone-receptor–positive advanced breast cancer.** *N Engl J Med* 2012;366(6):520-9.

Brufsky AM, Dickler MN. **Estrogen receptor-positive breast cancer: Exploiting signaling pathways implicated in endocrine resistance.** *Oncologist* 2018;23(5):528-39.

Brufsky AM. **Long-term management of patients with hormone receptor-positive metastatic breast cancer: Concepts for sequential and combination endocrine-based therapies.** *Cancer Treat Rev* 2017;59:22-32.

Cawley M et al. **Current trends in managing oral mucositis.** *Clin J Oncol Nurs* 2005;9(5):584-92.

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.

Clatot F et al. **Kinetics, prognostic and predictive values of ESR1 circulating mutations in metastatic breast cancer patients progressing on aromatase inhibitor.** *Oncotarget* 2016;7(46):74448-59.

Cortés J et al. **The next era of treatment for hormone receptor-positive, HER2-negative advanced breast cancer: Triplet combination-based endocrine therapies.** *Cancer Treat Rev* 2017;61:53-60.

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.

de Oliveira MA et al. **Clinical presentation and management of mTOR inhibitor-associated stomatitis.** *Oral Oncol* 2011;47(10):998-1003.

Dickler MN et al. **MONARCH 1, a phase II study of abemaciclib, a CDK4 and CDK6 inhibitor, as a single agent, in patients with refractory HR+/HER2- metastatic breast cancer.** *Clin Cancer Res* 2017;23(17):5218-24.

Fanning SW et al. **Estrogen receptor alpha somatic mutations Y537S and D538G confer breast cancer endocrine resistance by stabilizing the activating function-2 binding conformation.** *Elife* 2016;5:e12792.

Ferté C et al. **Natural history, management and pharmacokinetics of everolimus-induced-oral ulcers: Insights into compliance issues.** *Eur J Cancer* 2011;47(15):2249-55.

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

Goetz MP et al. **MONARCH 3: Abemaciclib as initial therapy for advanced breast cancer.** *J Clin Oncol* 2017;35(32):3638-46.

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

Hurvitz SA et al. **Phase III MONALEESA-7 trial of premenopausal patients with HR+/HER2– advanced breast cancer (ABC) treated with endocrine therapy ± ribociclib: Overall survival (OS) results.** *Proc ASCO* 2019;**Abstract LBA1008**.

Johnston S et al. **MONARCH 3 final PFS: A randomized study of abemaciclib as initial therapy for advanced breast cancer.** *NPJ Breast Cancer* 2019;5:5.

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.

Metzger-Filho O et al. **PATINA: A randomized open label phase III trial to evaluate the efficacy and safety of palbociclib + anti HER2 therapy + endocrine therapy vs anti HER2 therapy + endocrine therapy after induction treatment for hormone receptor positive, HER2 positive metastatic breast cancer.** San Antonio Breast Cancer Symposium 2017;**Abstract OT3-05-07**.

Miaskowski C et al. **Adherence to oral endocrine therapy for breast cancer: A nursing perspective.** *Clin J Oncol Nurs* 2008;12(2):213-21.

Select Publications

O'Leary B et al. **Genomic markers of early progression on fulvestrant with or without palbociclib for ER+ advanced breast cancer in the PALOMA-3 trial.** *Proc ASCO* 2019;**Abstract 1010**.

Park Y et al. **A randomized phase II study of palbociclib plus exemestane with GNRH agonist versus capecitabine in premenopausal women with hormone receptor-positive metastatic breast cancer (KCSG-BR 15-10, NCT02592746).** *Proc ASCO* 2019;**Abstract 1007**.

Raghavendra A et al. **Determinants of weight gain during adjuvant endocrine therapy and association of such weight gain with recurrence in long-term breast cancer survivors.** *Clin Breast Cancer* 2018;18(1):e7-13.

Razavi P et al. **Molecular profiling of ER+ metastatic breast cancers to reveal association of genomic alterations with acquired resistance to CDK4/6 inhibitors.** *Proc ASCO* 2019;**Abstract 1009**.

Ross DS et al. **Immunohistochemical analysis of estrogen receptor in breast cancer with ESR1 mutations detected by hybrid capture-based next-generation sequencing.** *Mod Pathol* 2019;32(1):81-7.

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.

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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**.

Sledge GW Jr 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.

Spoerke JM et al. **Heterogeneity and clinical significance of ESR1 mutations in ER-positive metastatic breast cancer patients receiving fulvestrant.** *Nat Comm* 2016;7:11579.

Stockler M et al. **Systematic reviews of chemotherapy and endocrine therapy in metastatic breast cancer.** *Cancer Treat Rev* 2000;26(3):151-68.

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.

Toy W et al. **Activating ESR1 mutations differentially affect the efficacy of ER antagonists.** *Cancer Discov* 2017;7(3):277-87.

Toy W et al. **ESR1 ligand-binding domain mutations in hormone-resistant breast cancer.** *Nat Genet* 2013;45(12):1439-45.

Turner NC et al. **Efficacy of palbociclib plus fulvestrant (P+F) in patients (pts) with metastatic breast cancer (MBC) and ESR1 mutations (mus) in circulating tumor DNA (ctDNA).** *Proc ASCO* 2016;**Abstract 512**.

Yardley DA et al. **Everolimus plus exemestane in postmenopausal patients with HR(+) breast cancer: BOLERO-2 final progression-free survival analysis.** *Adv Ther* 2013;30(10):870-84.

Younus J, Kligman L. **Management of aromatase inhibitor-induced arthralgia.** *Curr Oncol* 2010;17(1):87-90.