Addressing Current Questions and Emerging Considerations with the Use of PARP Inhibitors in the Management of Ovarian Cancer

Audio Interview

CME Information

TARGET AUDIENCE

This activity is intended for gynecologic oncologists, medical oncologists, gynecologists and other healthcare providers involved in the treatment of gynecologic cancers.

OVERVIEW OF ACTIVITY

Epithelial ovarian cancer accounts for approximately 90% of malignant ovarian neoplasms, and this makes it the leading cause of death from gynecologic cancer in the United States. The most significant recent development in ovarian cancer has been the introduction of poly(ADP-ribose) polymerase (PARP) inhibitors into the therapeutic milieu. Originally developed for and active in cancers with homologous recombination (HR) deficiencies — such as those harboring BRCA1 or BRCA2 mutations — PARP inhibitors have also demonstrated activity in the estimated 50% of ovarian cancer without BRCA1/2 gene mutations but deficient in other DNA repair genes. Evidence also suggests that PARP inhibitors may be active in cancers deficient in signaling pathways that mitigate DNA repair or, in combination with DNA-damaging agents, independent of DNA repair dysfunction. These and other important advances in the collective understanding of PARP inhibition as a mechanism to combat the development and progression of ovarian cancer have led to the FDA approval of multiple PARP inhibitors as maintenance therapy and as monotherapy for relapsed disease. The availability of PARP inhibitors has significant ramifications for practicing oncologists, who need to confront a variety of practical issues with regard to the safe and effective use of these agents.

This CME program was developed from a postmeeting interview with a leading gynecologic oncology investigator conducted after a satellite symposium held during the 2019 Society of Gynecologic Oncology Annual Meeting on Women's Cancer and features discussion on the use of PARP inhibitors in the management of ovarian cancer. This activity is designed to assist medical oncologists, gynecologic oncologists and other healthcare providers to gain a better understanding of emerging considerations for clinical decision-making and patient care.

LEARNING OBJECTIVES

- Appraise available clinical trial data with and FDA indications for the use of various PARP inhibitors as maintenance therapy for recurrent, platinum-sensitive ovarian cancer, and develop strategies to identify patients for whom this approach might be appropriate.
- Identify patients with multiregimen-refractory ovarian cancer who may be appropriate candidates for a PARP inhibitor, and safely integrate PARP inhibitors into nonresearch therapy.
- Recognize the toxicities associated with PARP inhibitors commonly used in the care of patients with ovarian cancer, and offer supportive management strategies to minimize and/or ameliorate these side effects.
- Recall the biologic rationale for and ongoing research efforts evaluating the role of PARP inhibitors in combination with other agents, and refer appropriate patients for clinical trial participation.

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Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.25 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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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: June 2019

Expiration date: June 2020

Select Publications

Burger RA et al. **Final overall survival (OS) analysis of an international randomized trial evaluating bevacizumab (BEV) in the primary treatment of advanced ovarian cancer: A NRG oncology/Gynecologic Oncology Group (GOG) study.** *Proc ASCO* 2018;**Abstract 5517.**

Burger RA et al. **Incorporation of bevacizumab in the primary treatment of ovarian cancer.** *N Engl J Med* 2011;365(26):2473-83.

Coleman RL et al. **Rucaparib maintenance treatment for recurrent ovarian carcinoma after response to platinum therapy (ARIEL3): A randomised, double-blind, placebo-controlled, phase 3 trial.** *Lancet* 2017;390(10106):1949-61.

Dougherty BA et al. **Biological and clinical evidence for somatic mutations in BRCA1 and BRCA2 as predictive markers for olaparib response in high-grade serous ovarian cancers in the maintenance setting.** *Oncotarget* 2017;8(27):43653-61.

Essel KG et al. **PARPi after PARPi in epithelial ovarian cancer.** *Proc SGO* 2019;**Abstract 7**.

Fabbro M et al. **Efficacy and safety of niraparib as maintenance treatment in older patients (≥ 70 years) with recurrent ovarian cancer: Results from the ENGOT-OV16/NOVA trial.** *Gynecol Oncol* 2019;152(3):560-7.

Friedlander M et al. **Long-term efficacy, tolerability and overall survival in patients with platinum-sensitive, recurrent high-grade serous ovarian cancer treated with maintenance olaparib capsules following response to chemotherapy.** *Br J Cancer* 2018;119(9):1075-85.

González Martín A et al. **Exploratory outcome analyses according to stage and/or residual disease in the ICON7 trial of carboplatin and paclitaxel with or without bevacizumab for newly diagnosed ovarian cancer.** *Gynecol Oncol* 2019;152(1):53-60.

Jorge S et al. **Simultaneous clinical testing for germline and somatic mutations in ovarian carcinoma (OC): Mutation rate and impact on therapeutic decisions.** *Proc SGO* 2019;**Abstract 6**.

Kwon JS et al. **Costs and benefits of tumor testing for *BRCA* mutations in high-grade serous ovarian cancer as a triage for confirmatory genetic testing.** *Proc SGO* 2019;Abstract 5.

Ledermann JA et al. **The effect of age on efficacy and safety outcomes with rucaparib: A post hoc exploratory analysis of ARIEL3, a phase III, randomized, placebo-controlled maintenance study in patients with recurrent ovarian carcinoma.** *Proc SGO* 2019;**Abstract 4**.

Lheureux S et al. **Long-term responders on olaparib maintenance in high-grade serous ovarian cancer: Clinical and molecular characterization.** *Clin Cancer Res* 2017;23(15):4086-94.

Liu JF et al. **Overall survival and updated progression-free survival outcomes in a randomized phase 2 study of combination cediranib and olaparib versus olaparib in relapsed platinum-sensitive ovarian cancer.** *Ann Oncol* 2019;[Epub ahead of print].

Liu JF et al. **Combination cediranib and olaparib versus olaparib alone for women with recurrent platinum-sensitive ovarian cancer: A randomised phase 2 study.** *Lancet Oncol* 2014;15(11):1207-14.

Lowe ES et al. **SOLO3: A randomized phase III trial of olaparib versus chemotherapy in platinum-sensitive relapsed ovarian cancer patients with a germline *BRCA1/2* mutation (g*BRCA*m).** *Proc ASCO* 2016;**Abstract TPS5598**.

Matulonis UA et al. **Baseline platelet count and body weight as predictors of early dose modification in the quadra trial of niraparib monotherapy for the treatment of heavily pretreated (≥4th line), advanced, recurrent high-grade serous ovarian cancer.** *Proc SGO* 2019;**Abstract 2**.

Matulonis UA et al. **Time without symptoms or toxicity in patients with recurrent ovarian cancer receiving niraparib maintenance treatment versus placebo: A TWIST analysis of the ENGOT24-OV16/NOVA trial.** *Proc SGO* 2019;**Abstract 1**.

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

Monk BJ et al. **A prospective evaluation of tolerability of niraparib dosing based upon baseline body weight and platelet count: Blinded pooled interim safety data from the ENGOT-OV26/PRIMA study.** *Proc SGO* 2019;**Abstract 3**.

Moore KN et al. **Niraparib monotherapy for late-line treatment of ovarian cancer (QUADRA): A multicentre, open-label, single-arm, phase 2 trial.** *Lancet Oncol* 2019;[Epub ahead of print].

Moore K et al. **Maintenance olaparib in patients with newly diagnosed advanced ovarian cancer.** *N Engl J Med* 2018;379(26):2495-505.

Moore KN et al. **The poly (ADP ribose) polymerase inhibitor niraparib: Management of toxicities.** *Gynecol Oncol* 2018;149(1):214-20.

Select Publications

Oza AM et al. **Standard chemotherapy with or without bevacizumab for women with newly diagnosed ovarian cancer (ICON7): Overall survival results of a phase 3 randomised trial.** *Lancet Oncol* 2015;16(8):928-36.

Pujade-Lauraine E et al. **Olaparib tablets as maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT-Ov21): A double-blind, randomised, placebo-controlled, phase 3 trial.** *Lancet Oncol* 2017;18(9):1274-84.

Pujade-Lauraine E et al. **OReO/ENGOT Ov-38: A Phase IIIb trial of olaparib maintenance retreatment in patients with epithelial ovarian cancer.** *Proc ESMO* 2017;**Abstract 987TiP**.

Ray-Coquard I et al. **PAOLA-1: An ENGOT/GCIG phase III trial of olaparib versus placebo combined with bevacizumab as maintenance treatment in patients with advanced ovarian cancer following first-line platinum-based chemotherapy plus bevacizumab.** *Proc ASCO* 2016;**Abstract TPS5607**.