Breakfast with the Investigators

Exploring the Role of PARP Inhibition in the Management of Ovarian Cancer

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, gynecologic oncologists and other healthcare providers involved in the treatment of ovarian cancer (OC).

OVERVIEW OF ACTIVITY

Epithelial OC 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 OC has been the introduction of PARP inhibitors into the therapeutic milieu. Important advances in the collective understanding of PARP inhibition as a mechanism to combat the development and progression of OC have led to the FDA approval of multiple PARP inhibitors in a number of clinical settings. 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.

These video proceedings from a CME symposium held during the 2019 ASCO Annual Meeting feature discussions with leading researchers with an expertise in OC regarding actual cases from their practices and the published data that drive clinical decision-making for patients in those and diverse other situations. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist medical oncologists, gynecologic oncologists and other healthcare providers with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Appraise guideline recommendations, consensus statements and clinical investigator perspectives regarding the indications for and selection of genetic testing platforms in OC, and use the results of these assessments to guide long-term treatment planning, including clinical trial accrual.
- Recognize the recent FDA approval of olaparib as maintenance therapy after first-line platinum-based chemotherapy for patients with advanced OC and a deleterious or suspected deleterious BRCA germline or somatic mutation, and consider how the availability of this strategy affects current therapeutic algorithms.
- Appreciate available clinical trial data with and approved indications for the use of FDA-endorsed PARP inhibitors for patients with platinum-sensitive and multiregimen-refractory OC in order to appropriately integrate these agents into routine clinical practice.
- Recognize the toxicities associated with PARP inhibitors commonly used in the care of patients with OC, and offer supportive management strategies to minimize or ameliorate these side effects.
- Develop an understanding of the mechanisms of action of, available data with and potential clinical roles for other investigational PARP inhibitors in preparation for their possible introduction into future clinical practice.
- Recall the biologic rationale for and ongoing research efforts evaluating the role of PARP inhibitors in combination with chemotherapy, targeted therapy or immunotherapy, and refer appropriate patients for clinical trial participation.

ACCREDITATION STATEMENT

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CREDIT DESIGNATION STATEMENT

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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 their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

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MODERATOR — **Dr Love** is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech, Genmab, Genomic Health Inc, Gilead Sciences Inc, Guardant Health, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Kite Pharma Inc, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seattle Genetics, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, Teva Oncology, Tokai Pharmaceuticals Inc and Tolero Pharmaceuticals.

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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

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Expiration date: July 2020

Select Publications

Aghajanian C et al. **Evaluation of rucaparib in platinum-sensitive recurrent ovarian carcinoma (rOC) in patients (pts) with or without residual bulky disease at baseline in the ARIEL3 study.** *Proc ASCO* 2018;**Abstract 5537**.

Berek JS et al. **Safety and dose modification for patients receiving niraparib.** *Ann Oncol* 2018;29(8):1784-92.

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.

De Bono J et al. **Phase I, dose-escalation, two-part trial of the PARP inhibitor talazoparib in patients with advanced germline BRCA1/2 mutations and selected sporadic cancers.** *Cancer Discov* 2017;7(6):620-9.

Domchek SM et al. **Efficacy and safety of olaparib monotherapy in germline BRCA1/2 mutation carriers with advanced ovarian cancer and three or more lines of prior therapy.** *Gynecol Oncol* 2016;140(2):199-203.

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

González-Martín A et al. **A prospective evaluation of tolerability of niraparib dosing based upon baseline body weight (wt) and platelet (plt) count: Blinded pooled interim safety data from the PRIMA study.** *Proc ESMO* 2018;**Abstract 941PD**.

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**.

Kaufman B et al. **Olaparib monotherapy in patients with advanced cancer and a germline BRCA1/2 mutation.** *J Clin Oncol* 2015;33(3):244-50.

Konstantinopoulos P et al. **TOPACIO/Keynote-162 (NCT02657889): A phase 1/2 study of niraparib + pembrolizumab in patients (pts) with advanced triple-negative breast cancer or recurrent ovarian cancer (ROC) — Results from ROC cohort.** *Proc ASCO* 2018;**Abstract 106**.

Konstantinopoulos PA et al. **Homologous recombination deficiency: Exploiting the fundamental vulnerability of ovarian cancer.** *Cancer Discov* 2015;5(11):1137-54.

Kristeleit R et al. **A phase I-II study of the oral PARP inhibitor rucaparib in patients with germline BRCA1/2-mutated ovarian carcinoma or other solid tumors.** *Clin Cancer Res* 2017;23(15):4095-106.

Ledermann JA et al. **ARIEL3: A phase 3, randomised, double-blind study of rucaparib vs placebo following response to platinum-based chemotherapy for recurrent ovarian carcinoma (OC).** *Proc ESMO* 2017;**Abstract LBA40_PR**.

Ledermann J et al. **Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer: A preplanned retrospective analysis of outcomes by BRCA status in a randomised phase 2 trial.** *Lancet Oncol* 2014;15(8):852-61.

Ledermann J et al. **Olaparib maintenance therapy in platinum-sensitive relapsed ovarian cancer.** *N Engl J Med* 2012;366(15):1382-92.

Lim JSJ, Tan DSP. **Understanding resistance mechanisms and expanding the therapeutic utility of PARP inhibitors.** *Cancers (Basel)* 2017;9(8):pii:E109.

Lord R et al. **Safety and dose modification for patients with low body weight receiving niraparib in the ENGOT-OV16/NOVA phase III trial.** *Proc SGO* 2018;**Abstract 20**.

Mirza M et al. **Combination of niraparib and bevacizumab versus niraparib alone as treatment of recurrent platinum-sensitive ovarian cancer. A randomized controlled chemotherapy-free study — NSGO-AVANOVA2/ENGOT-OV24.** *Proc ASCO* 2019;**Abstract 5505**.

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;20(5):636-48.

Moore KN 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. **SOLO1 and SOLO2: Randomized phase III trials of olaparib in patients (pts) with ovarian cancer and a BRCA1/2 mutation (BRCAm).** *Proc ASCO* 2014;**Abstract TPS5616**.

Select Publications

Norquist BM et al. **Inherited mutations in women with ovarian carcinoma.** *JAMA Oncol* 2016;2(4):482-90.

Ohmoto A, Yachida S. **Current status of poly(ADP-ribose) polymerase inhibitors and future directions.** *Onco Targets Ther* 2017;10:5195-208.

Oza AM et al. **Antitumor activity and safety of the PARP inhibitor rucaparib in patients with high-grade ovarian carcinoma and a germline or somatic BRCA1 or BRCA2 mutation: Integrated analysis of data from Study 10 and ARIEL2.** *Gynecol Oncol* 2017;147(2):267-75.

Penson RT et al. **Olaparib monotherapy versus (vs) chemotherapy for germline BRCA-mutated (gBRCAm) platinum-sensitive relapsed ovarian cancer (PSR OC) patients (pts): Phase III SOLO3 trial.** *Proc ASCO* 2019;**Abstract 5506**.

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.

Steffensen KD et al. **Veliparib monotherapy to patients with BRCA germ line mutation and platinum-resistant or partially platinum-sensitive relapse of epithelial ovarian cancer: A phase I/II study.** *Int J Gynecol Cancer* 2017;27(9):1842-9.

Swisher EM et al. **Rucaparib in relapsed, platinum-sensitive high-grade ovarian carcinoma (ARIEL2 Part 1): An international, multicentre, open-label, phase 2 trial.** *Lancet Oncol* 2017;18(1):75-87.

Vergote I et al. **Current perspectives on recommendations for BRCA genetic testing in ovarian cancer patients.** *Eur J Cancer* 2016;69:127-34.

Walsh T et al. **Mutations in 12 genes for inherited ovarian, fallopian tube, and peritoneal carcinoma identified by massively parallel sequencing.** *Proc Natl Acad Sci USA* 2011;108(44):18032-7.