Dissecting the Decision:
Investigators Discuss PARP Inhibition in the Management of Ovarian Cancer

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

The American Cancer Society estimates that in 2017, 22,440 new cases of ovarian cancer (OC) will be diagnosed in the United States and 14,080 individuals will die of the disease. For this reason significant financial and intellectual resources have been invested over the past few decades in attempts to better understand the natural history of the disease, identify genetic and other factors responsible for its proliferation and develop novel therapies with the potential to significantly improve outcomes for patients, ultimately culminating in — among other things — a number of clinical trials attempting to document the efficacy of various PARP inhibitors across multiple rational OC populations. Given the significant number of clinical and research questions created by the introduction of PARP inhibitors in the OC treatment milieu and the rapidly expanding database surrounding PARP inhibition in general, clinicians must be aware of emerging data and available protocols so that they may effectively counsel their patients.

These video proceedings from a CME symposium held during the Society of Gynecologic Oncology's 2017 Annual Meeting on Women's Cancer feature discussions with leading researchers with an expertise in gynecologic oncology. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist gynecologic oncologists, medical oncologists, gynecologists and other healthcare providers with the formulation of up-to-date clinical management strategies for OC.

LEARNING OBJECTIVES

- Consider available guidelines and consensus statements in the development of evidence-based approaches to genetic screening for patients with OC.
- Examine clinical investigator perspectives to assist healthcare professionals in the selection of a validated genetic testing platform(s) for patients with OC, and use the results from these assessments to guide treatment planning.
- Appraise the efficacy and safety of approved and investigational PARP inhibitors as monotherapy for patients with BRCA-mutant advanced OC, and employ this information in the formulation of protocol and nonprotocol treatment recommendations for these individuals.
- Evaluate emerging Phase III evidence supporting the potential use of PARP inhibition as maintenance therapy for patients with recurrent, platinum-sensitive OC.
- Educate patients about the potential side effects associated with approved and investigational PARP inhibitors, and provide preventive and emergent strategies to reduce or ameliorate these toxicities.

ACCREDITATION STATEMENT

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CREDIT DESIGNATION STATEMENT

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AMERICAN BOARD OF INTERNAL MEDICINE (ABIM) — MAINTENANCE OF CERTIFICATION (MOC)

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.75 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, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma, Adaptive Biotechnologies, Agendia Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, CTI BioPharma Corp, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Kite Pharma Inc, Lexicon Pharmaceuticals Inc, Lilly, Medivation Inc, a Pfizer Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro Inc, Teva Oncology and Tokai Pharmaceuticals 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 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

Richard T Penson, MD, MRCP

Alsop K et al. **BRCA mutation frequency and patterns of treatment response in BRCA mutation-positive women with ovarian cancer: A report from the Australian Ovarian Cancer Study Group.** *J Clin Oncol* 2012;30(21):2654-63.

Bowtell DD et al. **The genesis and evolution of high-grade serous ovarian cancer.** *Nat Rev Cancer* 2010;10(11):803-8.

Cancer Genome Atlas Research Network. **Integrated genomic analyses of ovarian carcinoma.** *Nature* 2011;474(7353):609-15.

King MC et al. **Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2.** *Science* 2003; 302(5645):643-6.

Pennington KP, Swisher EM. **Hereditary ovarian cancer: Beyond the usual suspects.** *Gynecol Oncol* 2012;124(2):347-53.

Rebbeck TR et al. **Prophylactic oophorectomy in carriers of BRCA1 or BRCA2 mutations.** *N Engl J Med* 2002; 346(21):1616-22.

Ursula A Matulonis, MD

Coleman RL et al. **A phase II evaluation of the potent, highly selective PARP inhibitor veliparib in the treatment of persistent or recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer in patients who carry a germline BRCA1 or BRCA2 mutation — An NRG Oncology/Gynecologic Oncology Group study.** *Gyn Onc* 2015;137(3):386-91.

Jones P et al. **Niraparib: A poly(ADP-ribose) polymerase (PARP) inhibitor for the treatment of tumors with defective homologous recombination.** *J of Med Chem* 2015;58(8):3302-14.

Matulonis UA et al. **Olaparib monotherapy in patients with advanced relapsed ovarian cancer and a germline BRCA1/2 mutation: A multistudy analysis of response rates and safety.** *Ann Oncol* 2016;27(6):1013-9.

Sandhu SK et al. **The poly(ADP-ribose) polymerase inhibitor niraparib (MK4827) in BRCA mutation carriers and patients with sporadic cancer: A phase 1 dose-escalation trial.** *Lancet Oncol* 2013;14(9):882-92.

Stover DG et al. **The role of proliferation in determining response to neoadjuvant chemotherapy in breast cancer: A gene expression-based meta-analysis.** *Clin Cancer Res* 2016;22(24):6039-50.

Jonathan A Ledermann, MD

Gelmon KA et al. **Olaparib in patients with recurrent high-grade serous or poorly differentiated ovarian carcinoma or triple-negative breast cancer: A phase 2, multicentre, open-label, non-randomised study.** *Lancet Oncol* 2011;12(9):852-61.

Ledermann J et al. **Overall survival in patients with platinum-sensitive recurrent serous ovarian cancer receiving olaparib maintenance monotherapy: An updated analysis from a randomised, placebo-controlled, double-blind, phase 2 trial.** *Lancet Oncol* 2016;17(11):1579-89.

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.

Mirza MR et al. **A randomized, double-blind phase 3 trial of maintenance therapy with niraparib vs placebo in patients with platinum-sensitive recurrent ovarian cancer (ENGOT-OV16/NOVA trial).** *Proc ESMO* 2016;**Abstract LBA3_PR**.

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

Robert L Coleman, MD

Bryant HE et al. **Specific killing of BRCA2-deficient tumours with inhibitors of poly(ADP-ribose) polymerase.** *Nature* 2005;434(7035):913-7.

Farmer H et al. **Targeting the DNA repair defect in BRCA mutant cells as a therapeutic strategy.** *Nature* 2005; 434(7035):917-21.

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.

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.