Addressing Current Questions and Controversies:

PARP Inhibition in the Management of Ovarian and Other Gynecologic Cancers

(Part 1 of a 2-Part Series)

CME Information

TARGET AUDIENCE

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

OVERVIEW OF ACTIVITY

Gynecologic cancers are comprised of 5 primary cancers affecting the ovaries, uterine corpus (endometrial cancer), uterine cervix (cervical cancer), vulva and vagina. In 2016, it is estimated that approximately 105,890 new cases of gynecologic cancer will be documented in the United States and 30,890 individuals will succumb to these diseases. Of this diverse yet related group of tumors, ovarian cancer (OC) has continually been the most lethal, and for this reason significant resources have been invested over the past decade to try to identify genetic and other factors responsible for its proliferation. This emphasis proved fruitful with the introduction of PARP inhibitors into the investigational and clinical milieu.

However, the recent availability of these agents mandates that treating physicians attain confidence and competence in identifying patients appropriate for treatment and requires that clinicians be aware of emerging data and available protocols so that they may effectively counsel their patients in this regard. These video proceedings from a CME symposium held during the Society of Gynecologic Oncology's 2016 Annual Meeting on Women's Cancer feature discussions with leading researchers with an expertise in gynecologic oncology regarding actual patient cases and related clinical research findings. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist gynecologic oncologists and other healthcare providers with the formulation of up-to-date clinical management strategies for various gynecologic cancers.

LEARNING OBJECTIVES

- Use available guidelines and consensus statements to develop an evidence-based algorithm for conducting genetic screening for patients with gynecologic cancers.
- Consider clinical investigator perspectives to assist healthcare professionals in the selection of a validated genetic testing platform or platforms for patients with gynecologic cancers, and use this information to guide treatment planning for these individuals and their immediate family members.
- Understand the rationale for the investigation of PARP inhibition as monotherapy or in combination with other novel agents for patients with BRCA-mutant and BRCA wild-type advanced OC, and use this information to inform protocol and clinical treatment options for these individuals.
- Appreciate the recent approval of olaparib for patients with highly refractory advanced OC, and safely integrate this agent into the clinical care of appropriate individuals.
- Develop an understanding of the emerging efficacy data and toxicity profiles of investigational PARP inhibitors to effectively prioritize clinical trial opportunities for appropriate patients with gynecologic cancers.

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 enables the participant to earn up to 1.25 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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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 80% or better and fill out the Educational Assessment and Credit Form located at **ResearchToPractice.com/GynOnc16/PARP/CME**.

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (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 CME 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 physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

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No relevant conflicts of interest to disclose.

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No relevant conflicts of interest to disclose.

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, Agendia Inc, Amgen 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, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, ImmunoGen Inc, Incyte Corporation, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Lilly, Medivation Inc, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis Pharmaceuticals Corporation, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Teva Oncology, Tokai Pharmaceuticals Inc and VisionGate 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

Kathleen Moore, MD

Barrow E et al. **Cumulative lifetime incidence of extracolonic cancers in Lynch syndrome: A report of 121 families with proven mutations.** *Clin Genet* 2009;75(2):141-9.

Koornstra JJ et al. **Management of extracolonic tumours in patients with Lynch syndrome.** *Lancet Oncol* 2009;10(4):400-8.

Loveday C et al. **Germline mutations in RAD51D confer susceptibility to ovarian cancer.** *Nat Genet* 2011;43(9):879-82.

Lu KH et al. **American Society of Clinical Oncology expert statement: Collection and use of a cancer family history for oncology providers.** *J Clin Oncol* 2014;32(8):833-40.

Meindl A et al. **Germline mutations in breast and ovarian cancer pedigrees establish RAD51C as a human cancer susceptibility gene.** *Nat Genet* 2010;42(5):410-4.

Pelttari LM et al. **A Finnish founder mutation in RAD51D: Analysis in breast, ovarian, prostate, and colorectal cancer.** *J Med Genet* 2012;49(7):429-32.

Rafnar T et al. **Mutations in BRIP1 confer high risk of ovarian cancer.** *Nat Genet* 2011;43(11):1104-7.

Rich TA et al. **Hereditary breast cancer syndromes and genetic testing.** *J Surg Oncol* 2015;111(1):66-80.

Stadler ZK et al. **Cancer genomics and inherited risk.** *J Clin Oncol* 2014;32(7):687-98.

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.

Ursula A Matulonis, MD

Audeh MW et al. **Oral poly(ADP-ribose) polymerase inhibitor olaparib in patients with BRCA1 or BRCA2 mutations and recurrent ovarian cancer: A proof-of-concept trial.** *Lancet* 2010;376(9737):245-51.

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.

Kaye SB et al. **Phase II, open-label, randomized, multicenter study comparing the efficacy and safety of olaparib, a poly (ADP-ribose) polymerase inhibitor, and pegylated liposomal doxorubicin in patients with BRCA1 or BRCA2 mutations and recurrent ovarian cancer.** *J Clin Oncol* 2012;30(4):372-9.

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.

Amit M Oza, MD

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

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.** *Gynecol Oncol* 2015;137(3):386-91.

Kristeleit R et al. **Final results of ARIEL2 (Part 1): A Phase 2 trial to prospectively identify ovarian cancer (OC) responders to rucaparib using tumor genetic analysis.** *Proc ECCO* 2015;**Abstract 2700**.

Wang ZC et al; Australian Ovarian Cancer Study Group. **Profiles of genomic instability in high-grade serous ovarian cancer predict treatment outcome.** *Clin Cancer Res* 2012;18(20):5806-15.

Elizabeth M Swisher, MD

Audeh MW et al. **Oral poly(ADP-ribose) polymerase inhibitor olaparib in patients with BRCA1 or BRCA2 mutations and recurrent ovarian cancer: A proof-of-concept trial.** *Lancet* 2010;376(9737):245-51.

Bouwman P, Jonkers J. **Molecular pathways: How can BRCA-mutated tumors become resistant to PARP inhibitors?** *Clin Cancer Res* 2014;20(3):540-7.

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.

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.

Select Publications

Kunos C et al. **A phase I-II evaluation of veliparib (NSC #737664), topotecan, and filgrastim or pegfilgrastim in the treatment of persistent or recurrent carcinoma of the uterine cervix: An NRG Oncology/Gynecologic Oncology Group study.** *Int J Gynecol Cancer* 2015;25(3):484-92.

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.

Lee JM et al. **Phase I/Ib study of olaparib and carboplatin in BRCA1 or BRCA2 mutation-associated breast or ovarian cancer with biomarker analyses.** *J Natl Cancer Inst* 2014;106(6):dju089.

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.

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.

Thaker PH et al. **A limited access phase I trial of paclitaxel, cisplatin and ABT-888 in the treatment of advanced, persistent, or recurrent carcinoma of the cervix: An NRG/GOG study.** *Proc ASCO* 2015;**Abstract 5600**.