

# Data + Perspectives

## Biologic Basis and Available Clinical Research Underlying the Protocol and Nonresearch Use of PARP Inhibition in Patients with Ovarian and Breast Cancer

### CME Information

#### TARGET AUDIENCE

This activity is intended for medical oncologists, hematologists, surgeons, radiation oncologists, oncology nurses and other healthcare professionals involved in basic, translational and clinical cancer research or treatment.

#### OVERVIEW OF ACTIVITY

Over the past 2 decades, the oncology community has witnessed a significant transformation in the way clinicians think about the diagnosis and treatment of cancer. During this time, a shift has occurred from a “one-size-fits-all” approach to one in which therapeutic decision-making is routinely informed by the presence of molecular alterations and/or relevant biomarkers. Given that one tumor type may share a number of biologic similarities with another, it is not surprising that researchers have attempted to apply knowledge and therapeutic understanding across multiple diseases, yielding a growing body of evidence illustrating that a single therapy can provide benefit for patients with the same genetic abnormality but an entirely different disease. Although it has long been established that women with a BRCA1/2 mutation are at higher risk of developing breast and ovarian cancer, it was not until recently that the therapeutic significance of these abnormalities was documented. Specifically, it has now been established that patients with these diseases and a BRCA1/2 mutation are sensitive to treatment with a PARP inhibitor. In addition, the efficacy of these agents may not be restricted to this population, and a number of strategies have been explored to select patients without these mutations who may still benefit. This new understanding has created an array of clinical, translational and practical questions across the oncology research and care continuum.

These video proceedings from a CME symposium held during the 2018 AACR Annual Meeting feature discussions with leading ovarian and breast cancer researchers regarding actual patient cases and related clinical research findings. By providing information on important developments, this activity will assist medical oncologists and other healthcare professionals to address existing management uncertainties and determine the current and future roles of PARP inhibition in these diseases.

#### LEARNING OBJECTIVES

- Appraise available guideline recommendations and consensus statements regarding the indications and evidence-based modalities for genetic testing in ovarian and breast cancer, and use the results of these assessments to guide long-term treatment planning, including clinical trial recruitment.
- Understand the biologic rationale for the investigation of PARP inhibition for ovarian and breast cancer, and use this insight to inform protocol and nonresearch therapy and future clinical trial design.
- Appreciate available clinical trial data with FDA-approved PARP inhibitors for ovarian cancer to safely integrate these agents into routine clinical care.
- Appreciate the recent FDA approval of olaparib for patients with HER2-negative metastatic breast cancer harboring a germline BRCA mutation, and discern how this agent can be appropriately and safely integrated into routine clinical practice.
- Recognize the toxicities associated with PARP inhibitors commonly used in the treatment of breast and ovarian cancer, and offer supportive management strategies to minimize and/or ameliorate these side effects.
- Describe mechanisms of acquired tumor resistance to PARP inhibitors, and identify investigational therapeutic opportunities to circumvent this process.
- Develop an understanding of the mechanisms of action, available data and potential clinical roles of other investigational PARP inhibitors in preparation for their possible availability.

#### ACCREDITATION STATEMENT

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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, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Bodesix 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, administered by Janssen Scientific Affairs LLC, 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,

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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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## Select Publications

### Ursula A Matulonis, MD

- Bouwman P et al. Molecular pathways: **How can BRCA-mutated tumors become resistant to PARP inhibitors?** *Clin Can Res* 2014;20(3):540-7.
- Coleman RL et al; ARIEL3 Investigators. **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.
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- Ledermann JA 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.
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### Mark Robson, MD

- Domchek SM et al. **An open-label, multitumor, phase II basket study of olaparib and durvalumab (MEDIOLA): Results in germline BRCA-mutated (gBRCAm) HER2-negative metastatic breast cancer (MBC).** San Antonio Breast Cancer Symposium 2017;Abstract PD6-11.
- 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.
- Lord CJ, Ashworth A. **PARP inhibitors: Synthetic lethality in the clinic.** *Science* 2017;355(6330):1152-8.
- Robson M et al. **Olaparib for metastatic breast cancer in patients with a germline BRCA mutation.** *N Engl J Med* 2017;377(6):523-33.
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### Kathleen Moore, MD

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### Andrew Tutt, MB ChB, PhD

- Ashworth A. **A synthetic lethal therapeutic approach: Poly(ADP) ribose polymerase inhibitors for the treatment of cancers deficient in DNA double-strand break repair.** *J Clin Oncol* 2008;26(22):3785-90.
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