

PARP Inhibition in Four Common Cancers: Biology, Clinical Research Database and Therapeutic Strategy

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, hematologists, surgeons, radiation oncologists 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 and approach the diagnosis and treatment of a variety of solid tumors and hematologic cancers. 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 cancer may share a number of biologic similarities with another and that abnormalities found in one disease may be present in others, it is not surprising that attempts are underway to apply knowledge and therapeutic understanding across multiple diseases. This rational approach to clinical research has now yielded a growing body of evidence illustrating that a single targeted therapy can provide demonstrable benefit for patients with the same identified genetic abnormality regardless of the type of cancer. One of the most compelling recent examples of this phenomenon has been the documentation of the efficacy of PARP inhibitors in patients with multiple solid tumors.

This CME program developed from the proceedings of a CME symposium held during the 2019 AACR Annual Meeting features video slide presentations given by leading investigators in ovarian, breast, pancreatic and prostate cancer regarding the underlying biology and current research database in support of the use of PARP inhibitors as a therapeutic strategy. By providing information on important developments, this CME activity will assist medical oncologists and other healthcare professionals to address existing management uncertainties and determine the clinical role of PARP inhibition in these diseases.

LEARNING OBJECTIVES

- Consider the correlation between BRCA1/2 mutations and the development of hereditary cancers, and counsel patients with these genetic abnormalities regarding their long-term outlook and therapeutic options.
- Appraise available guideline recommendations 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 accrual.
- Describe the rationale for testing patients with metastatic prostate cancer or pancreatic adenocarcinoma for mutations in homology-directed DNA repair predisposition genes, and advise individuals found to harbor these genetic abnormalities about participation in clinical trials evaluating PARP inhibitors.
- Appreciate available clinical trial data with FDA-approved PARP inhibitors for patients with ovarian cancer to safely integrate these agents into routine clinical care.
- Evaluate the recent FDA approvals of olaparib and talazoparib for patients with HER2-negative metastatic breast cancer harboring a germline BRCA mutation, and discern how these agents can be appropriately and safely integrated into routine clinical practice.
- Assess the pharmacologic, pharmacodynamic and pharmacokinetic similarities and differences among the commercially available and investigational PARP inhibitors to better understand the activity and toxicities associated with these agents.

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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 Medical Knowledge MOC point in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC

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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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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

Neil Love, MD

LaFargue CJ et al. **Exploring and comparing adverse events between PARP inhibitors.** *Lancet Oncol* 2019;20(1):e15-8.

Kathleen Moore, MD

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

Melinda Telli, MD

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Litton JK et al. **Talazoparib in patients with advanced breast cancer and a germline BRCA mutation.** *N Engl J Med* 2018;379(8):753-63.

McLornan DP et al. **Applying synthetic lethality for the selective targeting of cancer.** *N Engl J Med* 2014;371(18):1725-35.

Robson ME et al. **OlympiAD final overall survival and tolerability results: Olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER2-negative metastatic breast cancer.** *Ann Oncol* 2019;[Epub ahead of print].

Robson ME 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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Michael Pishvaian, MD, PhD

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- Witkiewicz AK et al. **Whole-exome sequencing of pancreatic cancer defines genetic diversity and therapeutic targets.** *Nat Commun* 2015;6:3744.
- Emmanuel S Antonarakis, MD**
- Abida W et al. **Preliminary results from TRITON2: A phase 2 study of rucaparib in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) associated with homologous recombination repair (HRR) gene alterations.** *Proc ESMO* 2018;Abstract 793PD.
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- Smith MR et al. **Phase II study of niraparib in patients with metastatic castration-resistant prostate cancer (mCRPC) and biallelic DNA-repair gene defects (DRD): Preliminary results of GALAHAD.** Genitourinary Cancers Symposium 2019;Abstract 202.
- Yu EY et al. **Keynote-365 cohort a: Pembrolizumab (pembro) plus olaparib in docetaxel-pretreated patients (pts) with metastatic castrate-resistant prostate cancer (mCRPC).** Genitourinary Cancers Symposium 2019;Abstract 145.