# Consensus or Controversy?

## Clinical Investigators Provide Perspectives on the Current and Future Management of Prostate Cancer

## CME Information

### TARGET AUDIENCE

This activity has been designed to meet the educational needs of medical and radiation oncologists, urologists and other allied healthcare professionals involved in the treatment of prostate cancer (PC).

### OVERVIEW OF ACTIVITY

Cancers of the genitourinary (GU) system affect hundreds of thousands of individuals within the United States each year and account for more than one fourth of all newly diagnosed human cancers. Although GU cancers are a diverse array of distinct diseases, tumors of the prostate are among the most prevalent and are therefore the topic of extensive ongoing clinical research. As such, the clinical management of both early and more advanced presentations of this disease is constantly evolving, necessitating rapid and consistent access to learning opportunities for clinicians who provide care for these patients. This CME program was developed from the proceedings of a satellite symposium held during the 2019 Genitourinary Cancers Symposium. It provides the perspectives and experiences of PC-specific experts to gain a better understanding of new management strategies and lingering clinical controversies facing the GU cancer community. This activity will help medical oncologists and other allied healthcare professionals to find answers to the individualized questions and concerns they frequently encounter and to in turn provide high-quality cancer care.

### LEARNING OBJECTIVES

- Appraise recent data on diagnostic and therapeutic advances in PC, and integrate this information, as appropriate, into current clinical care.
- Explore the published research database supporting the recent FDA approvals of secondary hormonal agents in the management of nonmetastatic PC, and consider this information in the discussion of nonresearch treatment options for these patients.
- Evaluate available data on the use of cytotoxic and secondary hormonal therapy in the setting of hormone-sensitive metastatic PC to effectively design treatment plans for appropriate individuals.
- Apply evidence-based research findings in the determination of best-practice selection and sequencing of available local and systemic treatment modalities for patients with metastatic PC.
- Describe the rationale for testing patients with metastatic PC for BRCA1/2 or ATM mutations, and advise individuals found to harbor these genetic abnormalities about participation in clinical trials evaluating the role of a PARP inhibitor.
- Recall the design of ongoing research studies evaluating other novel agents and strategies for PC, and counsel appropriate patients about availability and participation.

### ACCREDITATION STATEMENT

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Penn State College of Medicine and Research To Practice. Penn State College of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

For questions about CME credit, either email continuinged@pennstatehealth.psu.edu or call (717) 531-6483 and reference course number G6435-19-T.

### CREDIT DESIGNATION STATEMENT

Penn State College of Medicine designates this enduring material for a maximum of 1 *AMA PRA Category 1 Credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

### HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should review the CME information, 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/GUCancers19/Video/CME**.

### CONTENT VALIDATION AND DISCLOSURES

It is the policy of Research To Practice and Penn State College of Medicine to ensure balance, independence, objectivity and scientific rigor in all their educational programs. All faculty, planners and managers participating in this activity are required to disclose any relevant financial relationship(s)

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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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**Advisory Committee and Consulting Agreements:** Amgen Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Clovis Oncology, Dendreon Pharmaceuticals Inc, ESSA Pharma Inc, Janssen Biotech Inc, Medivation Inc, a Pfizer Company, Merck, Sanofi Genzyme; **Contracted Research:** AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Dendreon Pharmaceuticals Inc, Genentech, Janssen Biotech Inc, Johnson & Johnson Pharmaceuticals, Merck, Novartis, Sanofi Genzyme, Tokai Pharmaceuticals; **Other Remunerated Activities:** Co-inventor of a biomarker licensed to QIAGEN.

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**Consulting Agreements:** Bayer HealthCare Pharmaceuticals, Pfizer Inc, Sanofi Genzyme; **Contracted Research:** Bayer HealthCare Pharmaceuticals, Exelixis Inc, Genentech, Janssen Biotech Inc, Medivation Inc, a Pfizer Company, Roche Laboratories Inc, Sanofi Genzyme; **Honoraria:** Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Janssen Biotech Inc, Sanofi Genzyme.

**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, Merck, Merrimack Pharmaceuticals

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**PENN STATE COLLEGE OF MEDICINE** — Faculty and staff involved in the development and review of this activity have disclosed no relevant financial relationships.

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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

**Last review date:** April 2019

**Expiration date:** April 2020

## Select Publications


### Matthew R Smith, MD, PhD

Fizazi K et al. **ARAMIS: Efficacy and safety of darolutamide in nonmetastatic castration-resistant prostate cancer (nmCRPC).** Genitourinary Cancers Symposium 2019;**Abstract 140**.

Gartrell BA, Saad F. **Managing bone metastases and reducing skeletal related events in prostate cancer.** *Nat Rev Clin Oncol* 2014;11(6):335-45.

Hussain M et al. **Enzalutamide in men with nonmetastatic, castration-resistant prostate cancer.** *N Engl J Med* 2018;378(26):2465-74.

Hussain M et al. **PROSPER: A phase 3, randomized, double-blind, placebo (PBO)-controlled study of enzalutamide (ENZA) in men with nonmetastatic castration-resistant prostate cancer (M0 CRPC).** Genitourinary Cancers Symposium 2018;**Abstract 3**.

Scher HI et al. **Prevalence of prostate cancer clinical states and mortality in the United States: Estimates using a dynamic progression model.** *PLoS One* 2015;10(10);e0139440.

Smith MR et al. **Apalutamide treatment and metastasis-free survival in prostate cancer.** *N Eng J Med* 2018; 378(15):1408-18.

Smith MR et al. **Denosumab and bone metastasis-free survival in men with nonmetastatic castration-resistant prostate cancer: Exploratory analyses by baseline prostate-specific antigen doubling time.** *J Clin Oncol* 2013;31(30):3800-6.

Smith MR et al. **Natural history of rising serum prostate-specific antigen in men with castrate nonmetastatic prostate cancer.** *J Clin Oncol* 2005; 23(13):2918-25.

Zurth C et al. **Higher blood–brain barrier penetration of [$^{14}$C]apalutamide and [$^{14}$C]enzalutamide compared to [$^{14}$C]darolutamide in rats using whole-body autoradiography.** Genitourinary Cancers Symposium 2019;**Abstract 156**.

### Cora N Sternberg, MD

Armstrong AJ et al. **Phase 3 study of androgen deprivation therapy (ADT) with enzalutamide (ENZA) or placebo (PBO) in metastatic hormone-sensitive prostate cancer (mHSPC): The ARCHES trial.** Genitourinary Cancers Symposium 2019;**Abstract 687**.

Fizazi K et al. **ARAMIS: Efficacy and safety of darolutamide in nonmetastatic castration-resistant prostate cancer (nmCRPC).** Genitourinary Cancers Symposium 2019;**Abstract 140**.

Fizazi K et al. **Abiraterone plus prednisone in metastatic, castration-sensitive prostate cancer.** *N Engl J Med* 2017;377(4):352-60.

James ND et al. **Abiraterone for prostate cancer not previously treated with hormone therapy.** *N Engl J Med* 2017;377(4):338-51.

James ND et al. **Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): Survival results from an adaptive, multiarm, multistage, platform randomised controlled trial.** *Lancet* 2016;387(10024):1163-77.

Kyriakopoulos CE et al. **Chemohormonal therapy in metastatic hormone-sensitive prostate cancer: Long-term survival analysis of the randomized phase III E3805 CHAARTED trial.** *J Clin Oncol* 2018;36(11):1080-7.

Vale CL et al. **Addition of docetaxel or bisphosphonates to standard of care in men with localised or metastatic, hormone-sensitive prostate cancer: A systematic review and meta-analyses of aggregate data.** *Lancet Oncol* 2016;17(2):243-56.

### Howard I Scher, MD

Antonarakis ES et al. **AR-V7 and resistance to enzalutamide and abiraterone in prostate cancer.** *N Engl J Med* 2014;371(11):1028-38.

Antonarakis ES et al. **Androgen receptor splice variant 7 and efficacy of taxane chemotherapy in patients with metastatic castration-resistant prostate cancer.** *JAMA Oncol* 2015;1(5):582-91.

Armenia J et al. **The long tail of oncogenic drivers in prostate cancer.** *Nat Genet* 2018;50(5):645-51.

Scher HI et al. **Nuclear-specific AR-V7 protein localization is necessary to guide treatment selection in metastatic castration-resistant prostate cancer.** *Eur Urol* 201771(6):874-82.

Scher HI et al. **Trial design and objectives for castration-resistant prostate cancer: Updated recommendations from the Prostate Cancer Clinical Trials Working Group 3.** *J Clin Oncol* 2016;34(12):1402-18.

Sharma P et al. **Initial results from a phase II study of nivolumab (NIVO) plus ipilimumab (IPI) for the treatment of metastatic castration-resistant prostate cancer (mCRPC; CheckMate 650).** Genitourinary Cancers Symposium 2019;**Abstract 142**.

## Select Publications


Watson PA et al. **Emerging mechanisms of resistance to androgen receptor inhibitors in prostate cancer.** *Nat Rev Cancer* 2015;15(12):701-11.

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**.


**Emmanuel S Antonarakis, MD**


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

Carney B et al. **Target engagement imaging of PARP inhibitors in small-cell lung cancer.** *Nat Commun* 2018;9(1):176.

Clarke N et al. **Olaparib combined with abiraterone in patients with metastatic castration-resistant prostate cancer: A randomised, double-blind, placebo-controlled, phase 2 trial.** *Lancet Oncol* 2018;19(7):975-86.

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

Fraser M et al. **Genomic hallmarks of localized, non-indolent prostate cancer.** *Nature* 2017;541(7637):359-64.

Handy Marshall C et al. **Response to PARP inhibitor therapy in metastatic castrate-resistant prostate cancer (mCRPC) patients with *BRCA1/2* versus *ATM* mutations.** Genitourinary Cancers Symposium 2019;**Abstract 154**.

Isaacsson Velho P et al. **Intraductal/ductal histology and lymphovascular invasion are associated with germline DNA-repair gene mutations in prostate cancer.** *Prostate* 2018;78(5):401-7.

Mateo J et al. **DNA-Repair defects and olaparib in metastatic prostate cancer.** *N Engl J Med* 2015;373(18):1697-708.

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

Pritchard CC et al. **Inherited DNA-repair gene mutations in men with metastatic prostate cancer.** *N Engl J Med* 2016;375(5):443-53.

Robinson D et al. **Integrative clinical genomics of advanced prostate cancer.** *Cell* 2015;161(5):1215-28.

Schweizer MT et al. **Genomic characterization of ductal adenocarcinoma of the prostate.** *Proc ASCO* 2018;**Abstract 5030**.


**A Oliver Sartor, MD**


Hofman MS et al. **[$^{177}$Lu]-PSMA-617 radionuclide treatment in patients with metastatic castration-resistant prostate cancer (LuPSMA trial): A single-centre, single-arm, phase 2 study.** *Lancet Oncol* 2018;19(6):825-33.

Hofman MS et al. **Lutetium-177 PSMA (LuPSMA) theranostics phase II trial: Efficacy, safety and QoL in patients with castrate-resistant prostate cancer treated with LuPSMA.** *Proc ESMO* 2017;**Abstract 7850**.

O'Connor MJ. **Targeting the DNA damage response in cancer.** *Mol Cell* 2015;60(4):547-60.

Smith MR et al. **ERA 223: A phase III trial of radium-223 (Ra-223) in combination with abiraterone acetate and prednisone/prednisolone for the treatment of asymptomatic or mildly symptomatic chemotherapy-naïve patients (pts) with bone-predominant metastatic castration-resistant prostate cancer (mCRPC).** *Proc ESMO* 2018;**Abstract LBA30**.