Consensus or Controversy?

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

Audio Program

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 in the United States each year and account for more than one fourth of all new cancer diagnoses. Of this diverse array of distinct diseases, tumors of the prostate are among the most prevalent and thus the topic of extensive ongoing clinical research. Consequently, the clinical management of both early and more advanced presentations of prostate cancer is constantly evolving, necessitating rapid and consistent access to learning opportunities for clinicians who 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 prostate cancer experts to facilitate 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 the published research database supporting the recent FDA approvals of secondary hormonal agents in the management of nonmetastatic prostate cancer, and consider this information in the discussion of nonresearch treatment options for patients.
- Explore available data with cytotoxic and secondary hormonal therapy in the setting of hormone-sensitive metastatic prostate cancer to effectively design treatment plans for appropriate patients.
- Consider patient and disease characteristics in addition to available clinical trial data in the selection and sequencing of available local and systemic treatment modalities for patients with metastatic prostate cancer.
- Evaluate the rationale for testing for BRCA mutations in patients with metastatic prostate cancer, and advise individuals found to harbor these genetic abnormalities about participation in clinical trials investigating the role of PARP inhibitors.
- Recall the design of ongoing research studies evaluating other novel agents and strategies for prostate cancer, 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 1.25 *AMA PRA Category 1 Credits™*. 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 an audio component. To receive credit, the participant should review the CME information, listen to the MP3s, 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/CME**.

CONTENT VALIDATION AND DISCLOSURES

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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:

Emmanuel S Antonarakis, MD
Associate Professor of Oncology and Urology
Johns Hopkins Sidney Kimmel Comprehensive Cancer Center
Baltimore, Maryland

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.

A Oliver Sartor, MD
CE and Bernadine Laborde Professor for Cancer Research
Medical Director, Tulane Cancer Center
Assistant Dean for Oncology
Tulane Medical School
New Orleans, Louisiana

Advisory Committee: Bayer HealthCare Pharmaceuticals, EMD Serono Inc, Fusion Pharmaceuticals; **Consulting Agreements:** Advanced Accelerator Applications, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Blue Earth Diagnostics, Constellation Pharmaceuticals, Dendreon Pharmaceuticals Inc, EMD Serono Inc, Endocyte Inc, Hinova Pharmaceuticals Inc, Johnson & Johnson Pharmaceuticals, Myovant Sciences, Pfizer Inc, Progenics Pharmaceuticals Inc, Sanofi Genzyme; **Contracted Research:** AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Constellation Pharmaceuticals, Dendreon Pharmaceuticals Inc, Endocyte Inc, Innocrin Pharmaceuticals Inc, Invitae, Johnson & Johnson Pharmaceuticals, Merck, Progenics Pharmaceuticals Inc, Roche Laboratories Inc, Sanofi Genzyme, SOTIO LLC; **Data and Safety Monitoring Board/Committee:** AstraZeneca Pharmaceuticals LP, Johnson & Johnson Pharmaceuticals, Myovant Sciences, Pfizer Inc; **Ownership Interest:** Lilly.

Howard I Scher, MD
D Wayne Calloway Chair in Urologic Oncology
Co-Chair, Center for Mechanism Based Therapy
Head, Biomarker Development Initiative
Member and Attending Physician
Genitourinary Oncology Service
Department of Medicine
Memorial Sloan Kettering Cancer Center
Professor of Medicine
Weill Cornell Medical College
New York, New York

Board of Directors: Asterias Biotherapeutics; **Consulting Agreement:** WCG Oncology; **Contracted Research:** Epic Sciences, Illumina Inc, Innocrin Pharmaceuticals Inc, Janssen Biotech Inc, Menarini Silicon Biosystems, Thermo Fisher Scientific; **Uncompensated Consulting:** Amgen Inc, ESSA Pharma Inc, Janssen Biotech Inc, Menarini Silicon Biosystems.

Matthew R Smith, MD, PhD
Claire and John Bertucci Endowed Chair in Genitourinary Cancers
Professor of Medicine
Harvard Medical School
Director, Genitourinary Malignancies Program
Massachusetts General Hospital Cancer Center
Boston, Massachusetts

Advisory Committee and Consulting Agreements: AbbVie Inc, Amgen Inc, Astellas Pharma Global Development Inc, Bayer HealthCare Pharmaceuticals, Clovis Oncology, Gilead Sciences Inc, Hexal AG, Hinova Pharmaceuticals Inc, Janssen Biotech Inc, Lilly, Novartis, Orion Corporation, Pfizer Inc; **Contracted Research:** Amgen Inc, Bayer HealthCare Pharmaceuticals, Clovis Oncology, Janssen Biotech Inc, Lilly.

Cora N Sternberg, MD
Clinical Director, Englander Institute for Precision Medicine
Weill Cornell Medicine
Hematology/Oncology
New York, New York

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.

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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

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**.