Beyond the Guidelines

Investigator Perspectives on Current Clinical Issues and Ongoing Research in the Systemic Treatment 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 a quarter 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 management of this disease is constantly evolving, necessitating rapid and consistent access to learning opportunities for clinicians who provide care for these patients.

Several consensus- and evidence-based treatment guidelines are available and aim to assist clinicians with making PC management decisions in this dynamic clinical and research environment. However, in situations where multiple acceptable therapeutic options exist, such guidelines may not be particularly helpful at the time of decision-making. By exploring the perspectives of leading investigators regarding a number of clinical scenarios and reviewing key data sets, this activity will assist medical and radiation oncologists, urologists and other allied healthcare professionals in the development of evidence-based strategies for the treatment of PC.

LEARNING OBJECTIVES

- Appraise recent data on diagnostic and therapeutic advances in PC, and integrate this information, as appropriate, into current clinical care.
- Evaluate emerging clinical trial data with available and investigational immunotherapeutic, chemotherapeutic and secondary hormonal agents in the management of nonmetastatic PC, and consider this information in the discussion of protocol and nonresearch treatment options.
- Explore available data with cytotoxic and secondary hormonal therapy in the setting of hormone-sensitive metastatic PC, and consider this information when designing treatment plans for appropriate individuals.
- Effectively apply evidence-based research findings in the determination of best-practice sequencing of available immunotherapeutic, chemotherapeutic and secondary hormonal agents for patients with metastatic castration-resistant PC.
- Consider available research data and expert perspectives on the efficacy and safety of radium-223 chloride as monotherapy or in combination with other treatment modalities for advanced PC, and use this information to appropriately integrate this radiopharmaceutical agent into clinical practice.
- Assess emerging data on the prevalence and landscape of mutations in DNA repair genes (eg, BRCA1, BRCA2, ATM) in metastatic PC and their potential therapeutic relevance.

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.

CREDIT DESIGNATION STATEMENT

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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/GUCancers18/Prostate/CME**.

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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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Consulting Agreements: Advanced Accelerator Applications, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bellicum Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Constellation Pharmaceuticals, Dendreon Pharmaceuticals Inc, EMD Serono Inc, Endocyte Inc, Johnson & Johnson Pharmaceuticals, OncoGenex Pharmaceuticals Inc, Pfizer Inc, Sanofi Genzyme; **Contracted Research:** Bayer HealthCare Pharmaceuticals, Endocyte Inc, Innocrin Pharmaceuticals Inc, Johnson & Johnson Pharmaceuticals, 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

Daniel P Petrylak, MD

A multicenter, randomized, double-blind, placebo-controlled, phase III study of ARN-509 in men with non-metastatic (m0) castration-resistant prostate cancer. NCT01946204

Clegg N et al. **ARN-509: A novel antiandrogen for prostate cancer treatment.** *Cancer Res* 2012;72(6):1494-503.

Fizazi K et al. **Activity and safety of ODM-201 in patients with progressive metastatic castration-resistant prostate cancer (ARADES): An open-label phase 1 dose-escalation and randomised phase 2 dose expansion trial.** *Lancet Oncol* 2014;15(9):975-85.

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**.

Kirby M et al. **Characterising the castration-resistant prostate cancer population: A systematic review.** *Int J Clin Pract* 2011;65(11):1180-92.

Moilanen A et al. **Discovery of ODM-201, a new-generation androgen receptor inhibitor targeting resistance mechanisms to androgen signaling-directed prostate cancer therapies.** *Sci Rep* 2015;5:12007.

Penson DF et al. **Enzalutamide versus bicalutamide in castration-resistant prostate cancer: The STRIVE trial.** *J Clin Oncol* 2016;34(18):2098-106.

Prosper: A multinational, phase 3, randomized, double-blind, placebo-controlled, efficacy and safety study of enzalutamide in patients with nonmetastatic castration-resistant prostate cancer. NCT02003924

Rathkopf D et al. **ARN-509 in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) with and without prior abiraterone acetate (AA) treatment.** *Proc ASCO* 2014;**Abstract 5026**.

Small EJ et al. **SPARTAN, a phase 3 double-blind, randomized study of apalutamide (APA) versus placebo (PBO) in patients (pts) with nonmetastatic castration-resistant prostate cancer (nmCRPC).** Genitourinary Cancers Symposium 2018;**Abstract 161**.

Smith MR et al. **Phase 2 study of the safety and antitumor activity of apalutamide (ARN-509), a potent androgen receptor antagonist, in the high-risk nonmetastatic castration-resistant prostate cancer cohort.** *Eur Urol* 2016;70(6):963-70.

Smith MR et al. **Denosumab and bone-metastasis-free survival in men with castration-resistant prostate cancer: Results of a phase 3, randomised, placebo-controlled trial.** *Lancet* 2012;379(9801):39-46.

Smith MR et al. **Disease and host characteristics as predictors of time to first bone metastasis and death in men with progressive castration-resistant nonmetastatic prostate cancer.** *Cancer* 2011;117(10):2077-85.

Karim Fizazi, MD, PhD

A prospective randomised phase III study of androgen deprivation therapy with docetaxel with or without local radiotherapy with or without abiraterone acetate and prednisone in patients with metastatic hormone-naïve prostate cancer. NCT01957436

A randomized, double-blind, comparative study of abiraterone acetate plus low-dose prednisone plus androgen deprivation therapy (ADT) versus ADT alone in newly diagnosed subjects with high-risk, metastatic hormone-naive prostate cancer (mHNPC). NCT01715285

Chi K et al. **Benefits of abiraterone acetate plus prednisone (AA+P) when added to androgen deprivation therapy (ADT) in LATITUDE on patient (pt) reported outcomes (PRO).** *Proc ESMO* 2017;**Abstract 7830**.

Feyerabend S et al. **Indirect comparison of abiraterone acetate and docetaxel for treatment of metastatic "hormone-sensitive" prostate cancer.** *Proc ESMO* 2017;**Abstract 803P**.

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

Gravis G et al. **Androgen-deprivation therapy alone or with docetaxel in non-castrate metastatic prostate cancer (GETUG-AFU 15): A randomised, open-label, phase 3 trial.** *Lancet Oncol* 2013;14(2):149-58.

James ND et al; STAMPEDE Investigators. **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.

Rajpar S et al. **The benefit of combining docetaxel to androgen deprivation therapy in localized and metastatic castration-sensitive prostate cancer as predicted by ERG status: An analysis of two GETUG phase III trials.** *Proc ASCO* 2017;**Abstract 5012**.

Select Publications

Sweeney C et al. **Long term efficacy and QOL data of chemohormonal therapy (C-HT) in low and high volume hormone naïve metastatic prostate cancer (PrCa): E3805 CHAARTED trial.** *Proc ESMO* 2016;**Abstract 720PD**.

Sweeney C et al. **Chemohormonal therapy in metastatic hormone-sensitive prostate cancer.** *N Engl J Med* 2015;373(8):737-46.

Sydes MR et al. **Adding abiraterone acetate plus prednisolone (AAP) or docetaxel for patients (pts) with high-risk prostate cancer (PCa) starting long-term androgen deprivation therapy (ADT): Directly randomised data from STAMPEDE (NCT00268476).** *Proc ESMO* 2017;**Abstract LBA31_PR**.

Vale CL et al; STOpCaP Steering Group. **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.

Mary-Ellen Taplin, MD

Antonarakis ES et al. **Clinical significance of androgen receptor splice variant-7 mRNA detection in circulating tumor cells of men with metastatic castration-resistant prostate cancer treated with first- and second-line abiraterone and enzalutamide.** *J Clin Oncol* 2017;35(19):2149-56.

Goodall J et al. **Circulating cell-free DNA to guide prostate cancer treatment with PARP inhibition.** *Cancer Discov* 2017;7(9):1006-17.

Haber DA, Velculescu VE. **Blood-based analyses of cancer: Circulating tumor cells and circulating tumor DNA.** *Cancer Discov* 2014;4(6):650-61.

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

Sailer V et al. **Bone biopsy protocol for advanced prostate cancer in the era of precision medicine.** *Cancer* 2017;[Epub ahead of print].

Terada N et al. **Prognostic and predictive biomarkers in prostate cancer: Latest evidence and clinical implications.** *Ther Adv Med Oncol* 2017;9(8):565-73.

A Oliver Sartor, MD

Bruland OS et al. **High-linear energy transfer irradiation targeted to skeletal metastases by the alpha-emitter 223Ra: Adjuvant or alternative to conventional modalities?** *Clin Cancer Res* 2006;12(20 Pt 2):6250s-7s.

Chatolic KL et al. **Towards personalized treatment of prostate cancer: PSMA I&T, a promising prostate-specific membrane antigen-targeted theranostic agent.** *Theragnostics* 2016;6(6):849-61.

Parker C et al; ALSYMPCA Investigators. **Alpha emitter radium-223 and survival in metastatic prostate cancer.** *N Engl J Med* 2013;369(3):213-23.

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

Robert Dreicer, MD, MS

Abida W et al. **Prospective genomic profiling of prostate cancer across disease states reveals germline and somatic alterations that may affect clinical decision making.** *JCO Precis Oncol* 2017.

Cancer Genome Atlas Research Network. **The molecular taxonomy of primary prostate cancer.** *Cell* 2015;163(4):1011-25.

Cheng HH et al. **Biallelic inactivation of BRCA2 in platinum-sensitive metastatic castration-resistant prostate cancer.** *Eur Urol* 2016;69(6):992-5.

Goodman A et al. **Analysis of over 100,000 patients with cancer for *CD274* (PD-L1) amplification: Implications for treatment with immune checkpoint blockade.** *Proc ASCO* 2018;**Abstract 47**.

James ND et al. **Abiraterone in metastatic prostate cancer.** *N Engl J Med* 2017;377(17):1696-7.

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

Pomerantz MM et al. **The association between germline BRCA2 variants and sensitivity to platinum-based chemotherapy among men with metastatic prostate cancer.** *Cancer* 2017;123(18):3532-9.

Select Publications

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.

Wyatt AW et al. **Concordance of circulating tumor DNA and matched metastatic tissue biopsy in prostate cancer.** *J Natl Cancer Inst* 2017;109(12).