

Second Opinion

Case-Based Discussions

Focused on the Management of

Metastatic Prostate Cancer



A special audio supplement to a CME conference held during the 2014 Genitourinary Cancers Symposium featuring expert comments on the application of emerging research to patient care

Faculty Interviews

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UPDATE



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Second Opinion: *Case-Based Discussions Focused on the Management of Metastatic Prostate Cancer*

A Continuing Medical Education Activity

OVERVIEW OF ACTIVITY

Prostate cancer (PC) is the most frequently diagnosed cancer in men, with an estimated 233,000 new cases in 2014 in the United States. Although virtually all locally advanced or metastatic tumor sites are initially reliant on androgen stimulation for growth and respond to treatment with androgen deprivation therapy, inevitably resistance to hormone blockade develops, culminating in the recurrence of highly aggressive castration-resistant PC (CRPC). Recently published randomized, controlled studies focused specifically on this population have led to the emergence of novel therapeutic strategies for patients with CRPC and resulted in a paradigm shift to the multidisciplinary care of this disease. A number of pivotal data sets illustrating the benefits of several novel agents indicate that additional therapeutic options may soon be available that will warrant consideration for integration into PC care. The treatment landscape and available options for PC have thus broadened, making choices more challenging for many healthcare professionals and patients, and a once-stagnant systemic treatment algorithm, largely confined to medical or surgical castration, has evolved into delivery of cutting-edge antineoplastic therapy necessitating learning opportunities for urologists and medical oncologists. This CME program uses one-on-one interviews with 2 leading PC clinical investigators and faculty at a recent satellite symposium to discuss cases and questions submitted by attendees. This program will assist practicing clinicians in formulating up-to-date and appropriate clinical management strategies.

LEARNING OBJECTIVES

- Recall existing and emerging research information demonstrating the effects of secondary hormonal interventions on quality and quantity of life for patients with chemotherapy-naïve or pretreated CRPC, and use this information to guide treatment planning for these patients.
- Effectively apply evidence-based research findings in the determination of best-practice use of available immunotherapeutic, chemotherapeutic and secondary hormonal agents for patients with metastatic PC.
- Consider available Phase III clinical trial data documenting the efficacy of radium-223 dichloride in patients with PC and bone metastases, and formulate strategies to appropriately use this recently approved radiopharmaceutical agent.
- Explore the emerging data and active research evaluating novel agents in the setting of PSA-only recurrent or advanced PC, and discuss the biologic basis for their clinical activity.
- Counsel appropriately selected patients with biochemically recurrent, asymptomatic and symptomatic metastatic PC about availability of and participation in ongoing clinical trials.

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FACULTY — The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process: **Dr Beer** — Contracted Research: Astellas, Bristol-Myers Squibb Company, ImClone Systems, a wholly owned subsidiary of Eli Lilly and Company, Novartis Pharmaceuticals Corporation. **Dr Sartor** — Advisory Committee: Bayer HealthCare Pharmaceuticals, Sanofi; Consulting Agreements: Algeta ASA, Bavarian Nordic, Bayer HealthCare Pharmaceuticals, Biscayne Pharmaceuticals Inc, Medivation Inc, OncoGenex Pharmaceuticals Inc, Sanofi; Contracted Research: AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Millennium: The Takeda Oncology Company, Progenics Pharmaceuticals Inc, Sanofi.

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SELECT PUBLICATIONS

- Basch EM et al. **Effects of cabozantinib on pain and narcotic use in patients with castration-resistant prostate cancer: Results from a phase 2 nonrandomized expansion cohort.** *Eur Urol* 2014;[Epub ahead of print].
- Beer TM et al. **Enzalutamide in men with chemotherapy-naive metastatic prostate cancer (mCRPC): Results of phase III PREVAIL study.** Genitourinary Cancers Symposium 2014;**Abstract LBA1.**
- Beer TM et al. **Quality of life after sipuleucel-T therapy: Results from a randomized, double-blind study in patients with androgen-dependent prostate cancer.** *Urology* 2013;82(2):410-5.
- Dreicer R et al. **Results from a phase 3, randomized, double-blind, multicenter, placebo-controlled trial of orteronel (TAK-700) plus prednisone in patients with metastatic castration-resistant prostate cancer (mCRPC) that has progressed during or following docetaxel-based therapy (ELM-PC 5 trial).** Genitourinary Cancers Symposium 2014;**Abstract 7.**
- Fizazi K et al. **Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: Final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study.** *Lancet Oncol* 2012;13(10):983-92.
- Graff JN et al. **Complete biochemical (prostate-specific antigen) response to sipuleucel-T with enzalutamide in castration-resistant prostate cancer: A case report with implications for future research.** *Urology* 2013;81(2):381-3.
- Kantoff PW et al. **Sipuleucel-T immunotherapy for castration-resistant prostate cancer.** *N Engl J Med* 2010;363(5):411-22.
- Longo TA et al. **Consideration of height-based rather than weight-based dosing as a more appropriate method of treating with radium-223.** Genitourinary Cancers Symposium 2014;**Abstract 249.**
- Nilsson S et al. **1.5-year post-treatment follow-up of radium-223 dichloride (Ra-223) in patients with castration-resistant prostate cancer (CRPC) and bone metastases from the phase 3 ALSYMPCA study.** Genitourinary Cancers Symposium 2014;**Abstract 9.**
- Noonan KL et al. **Clinical activity of abiraterone acetate in patients with metastatic castration-resistant prostate cancer progressing after enzalutamide.** *Ann Oncol* 2013;24(7):1802-7.
- Parker C et al. **Alpha emitter radium-223 and survival in metastatic prostate cancer.** *N Engl J Med* 2013;369(3):213-23.
- Parker C et al. **Updated analysis of the Phase III, double-blind, randomized, multinational study of radium-223 chloride in castration-resistant prostate cancer (CRPC) patients with bone metastases (ALSYMPCA).** *Proc ASCO* 2012;**Abstract LBA4512.**
- Phase III trial of dose escalated radiation therapy and standard androgen deprivation therapy (ADT) with a GNRH agonist vs dose escalated radiation therapy and enhanced ADT with a GNRH agonist and TAK-700 for men with high risk prostate cancer.** **NCT01546987**
- Ryan CJ et al. **Abiraterone in metastatic prostate cancer without previous chemotherapy.** *N Engl J Med* 2013;368(2):138-48.
- Sartor OA et al. **Correlation between baseline variables and survival in the radium-223 dichloride (Ra-223) phase III ALSYMPCA trial with attention to total ALP changes.** *Proc ASCO* 2013;**Abstract 5080.**
- Scher HI et al. **Increased survival with enzalutamide in prostate cancer after chemotherapy.** *N Engl J Med* 2012;367(13):1187-97.
- 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(9810):39-46.

Second Opinion: Case-Based Discussions Focused on the Management of Metastatic Prostate Cancer**QUESTIONS (PLEASE CIRCLE ANSWER):**

1. Which of the following was observed in the Phase III PREVAIL study comparing enzalutamide to placebo in patients with chemotherapy-naïve metastatic CRPC (mCRPC)?
 - a. Risk of death was reduced by 29% with enzalutamide
 - b. Risk of radiographic disease progression was reduced by 81% with enzalutamide
 - c. Both a and b
2. A quality-of-life (QoL) analysis reported by Beer and colleagues of patients with asymptomatic androgen-dependent PC receiving sipuleucel-T demonstrated no clinically significant negative impact on QoL after sipuleucel-T treatment.
 - a. True
 - b. False
3. The Phase III ALSYMPCA study demonstrated which of the following with radium-223/best standard treatment compared to placebo/best standard treatment in men with symptomatic CRPC and bone metastases?
 - a. Improved survival but increased thrombocytopenia with radium-223
 - b. Improved survival but increased rate of second primary cancers with radium-223
4. In the ALSYMPCA study more than half of the patients had previously received docetaxel.
 - a. True
 - b. False
5. In the ELM-PC 5 trial evaluating orteronel/prednisone versus placebo/prednisone for patients with mCRPC that has progressed during or after docetaxel-based therapy, the primary endpoint of overall survival was met.
 - a. True
 - b. False
6. The ongoing Phase III RTOG-1115 trial is evaluating dose-escalated radiation therapy and androgen deprivation therapy with or without _____ for men with high-risk PC.
 - a. Abiraterone acetate
 - b. Cabazitaxel
 - c. Cabozantinib
 - d. Enzalutamide
 - e. Orteronel
7. Cabozantinib is a small molecule tyrosine kinase inhibitor that targets which of the following?
 - a. EGFR
 - b. VEGFR
 - c. MET
 - d. Both b and c
8. The Phase III CHARTED (ECOG-E3805) study is evaluating androgen ablation therapy with or without docetaxel in patients with hormone-sensitive metastatic PC.
 - a. True
 - b. False

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Second Opinion: *Case-Based Discussions Focused on the Management of Metastatic Prostate Cancer*

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

PART 1 — Please tell us about your experience with this educational activity

How would you characterize your level of knowledge on the following topics?

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

	BEFORE	AFTER
Results of the Phase III PREVAIL study of enzalutamide in patients with chemotherapy-naïve mCRPC	4 3 2 1	4 3 2 1
Efficacy of enzalutamide in patients with visceral metastases	4 3 2 1	4 3 2 1
ALSYMPCA safety update: Radium-223 and risk of myelosuppression and second primary cancers	4 3 2 1	4 3 2 1
Potential clinical implications of the Phase III CHARTED (ECOG-E3805) study evaluating androgen ablation therapy with or without docetaxel for hormone-sensitive metastatic PC	4 3 2 1	4 3 2 1
Effects of cabozantinib on bone pain in patients with CRPC	4 3 2 1	4 3 2 1

Was the activity evidence based, fair, balanced and free from commercial bias?

Yes No

If no, please explain:

Please identify how you will change your practice as a result of completing this activity (select all that apply).

- This activity validated my current practice
- Create/revise protocols, policies and/or procedures
- Change the management and/or treatment of my patients
- Other (please explain):

If you intend to implement any changes in your practice, please provide 1 or more examples:

.....

The content of this activity matched my current (or potential) scope of practice.

Yes No

If no, please explain:

Please respond to the following learning objectives (LOs) by circling the appropriate selection:

4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = LO not met N/A = Not applicable

As a result of this activity, I will be able to:

- Recall existing and emerging research information demonstrating the effects of secondary hormonal interventions on quality and quantity of life for patients with chemotherapy-naïve or pretreated CRPC, and use this information to guide treatment planning for these patients. 4 3 2 1 N/M N/A
- Effectively apply evidence-based research findings in the determination of best-practice use of available immunotherapeutic, chemotherapeutic and secondary hormonal agents for patients with metastatic PC. 4 3 2 1 N/M N/A
- Consider available Phase III clinical trial data documenting the efficacy of radium-223 dichloride in patients with PC and bone metastases, and formulate strategies to appropriately use this recently approved radiopharmaceutical agent. 4 3 2 1 N/M N/A
- Explore the emerging data and active research evaluating novel agents in the setting of PSA-only recurrent or advanced PC, and discuss the biologic basis for their clinical activity. 4 3 2 1 N/M N/A

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

- Counsel appropriately selected patients with biochemically recurrent, asymptomatic and symptomatic metastatic PC about availability of and participation in ongoing clinical trials..... 4 3 2 1 N/M N/A

Please describe any clinical situations that you find difficult to manage or resolve that you would like to see addressed in future educational activities:

Would you recommend this activity to a colleague?

Yes No

If no, please explain:

Additional comments about this activity:

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Yes, I am willing to participate in a follow-up survey.

No, I am not willing to participate in a follow-up survey.

PART 2 — Please tell us about the faculty and editor for this educational activity

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

Faculty	Knowledge of subject matter				Effectiveness as an educator			
Tomasz M Beer, MD	4	3	2	1	4	3	2	1
A Oliver Sartor, MD	4	3	2	1	4	3	2	1
Editor	Knowledge of subject matter				Effectiveness as an educator			
Neil Love, MD	4	3	2	1	4	3	2	1

Other comments about the faculty and editor for this activity:

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