Current Controversies, Recent Developments and Emerging Strategies in the Practical Management of Prostate Cancer

Proceedings from a Clinical Investigator Think Tank

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Neil Love, MD

Contents
2 Audio CDs
OVERVIEW OF ACTIVITY
Prostate cancer is the most frequently diagnosed cancer in men, with an estimated 241,740 new cases in 2012 in the United States. Although virtually all locally advanced or metastatic sites of tumor are initially reliant on androgen stimulation for growth and respond to treatment with androgen deprivation therapy, inevitable resistance to hormone blockade eventually develops, culminating in the recurrence of highly aggressive castration-resistant prostate cancer (CRPC). Recently published randomized controlled trials 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 in the management of prostate cancer. The treatment landscape and available options for prostate cancer 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 a roundtable discussion with leading prostate cancer clinical investigators to assist practicing clinicians in formulating up-to-date and appropriate clinical management strategies.

LEARNING OBJECTIVES
• Explore the emerging data and active research evaluating novel agents — including radiopharmaceuticals, androgen biosynthesis inhibitors, antiandrogens and custom antisense oligonucleotides — in the setting of advanced prostate cancer, and discuss the biologic basis for their clinical activity.
• Recall existing and emerging research demonstrating the effects of secondary hormonal interventions on quality and quantity of life for patients with chemotherapy-naïve and chemotherapy-pretreated CRPC, and use this information to guide treatment planning for these patients.
• Efficiently identify and educate patients with skeletal metastases about the efficacy and safety of emerging systemic bone-directed treatments.
• Employ case-based learning to effectively apply evidence-based research findings in the determination of best-practice sequencing of available systemic agents for patients with metastatic prostate cancer.
• Counsel appropriately selected patients with minimally symptomatic or asymptomatic advanced prostate cancer about sipuleucel-T as a treatment option, and define an approach to patient monitoring after treatment with this agent.

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Facebook.com/ResearchToPractice or Twitter @DrNeilLove
Track 1: Intermittent versus continuous androgen deprivation in patients with hormone-sensitive metastatic prostate cancer (PC) or rising prostate-specific antigen (PSA) after local therapy — Results and implications of the international Phase III SWOG-S9346 (INT-0162) and NCIC CTG PR.7 trials

Track 2: Case discussion: A 75-year-old man with a rising PSA and a doubling time of 8 months undergoes androgen deprivation therapy (ADT)

Track 3: Mechanism of action of androgen synthesis inhibitors — abiraterone acetate and orteronel

Track 4: Mechanism of action of the novel, oral, small-molecule androgen receptor signaling inhibitor enzalutamide (MDV3100)

Track 5: Interim analysis of the Phase III COU-AA-302 study: Abiraterone acetate in patients with chemotherapy-naïve metastatic castration-resistant PC (mCRPC)

Track 6: Perspectives on the clinical use of newly approved endocrine agents in PC

Track 7: AFFIRM study results: Overall survival advantage with enzalutamide in patients with mCRPC previously treated with docetaxel

Track 8: Perspectives on sequencing enzalutamide and abiraterone acetate

Track 9: Risk of seizures with enzalutamide

Track 10: Toxicity profile of abiraterone

Track 11: Case discussion: A 67-year-old man with progressive CRPC and bone metastases receives enzalutamide on a clinical trial

Track 12: Therapeutic options for patients with mCRPC whose disease progresses on enzalutamide

Track 13: Updated activity and tolerability results from a Phase II study of orteronel without prednisone for men with nonmetastatic CRPC and rising PSA levels

Track 14: Case discussion: A 68-year-old man with nonmetastatic CRPC treated with orteronel on a clinical trial

Track 15: Complications of long-term steroid administration

Track 16: Viewpoints on the inclusion and dosing of steroids with lyase inhibitor therapy

Track 17: ALSYMPCA: Updated analysis from a Phase III trial of radium-223 chloride for patients with CRPC and bone metastases

Track 18: Rationale for using radium-223

Track 19: Antitumor and bone-protective activity of radium-223

Track 20: Potential integration of radium-223 into the treatment algorithm for PC

Track 21: Case discussion: An 83-year-old man with symptomatic, metastatic PC and a T12 epidural spinal cord compression achieves improved pain control with radium-223

Track 22: Use of zoledronic acid or denosumab in combination with radiopharmaceutical therapy

Track 23: Perspectives on the future nonprotocol role of radium-223
Track 24 Correlation of immune parameters and overall survival among patients receiving sipuleucel-T

Track 25 Development of the immunotherapeutic agent sipuleucel-T in mCRPC

Track 26 Interdisciplinary critique of sipuleucel-T as immunotherapy for CRPC

Track 27 Case discussion: A 59-year-old man with asymptomatic CRPC, bone metastases and a rising PSA receives treatment with sipuleucel-T

Track 28 Viewpoints on the use of sipuleucel-T for asymptomatic CRPC

Track 29 Critical appraisal of the Phase III IMPACT trial results evaluating sipuleucel-T for mCRPC

Track 30 Expanding treatment options for mCRPC

Track 31 Monitoring patient response after completion of sipuleucel-T therapy

Track 32 Case discussion: A 70-year-old man with mCRPC refractory to docetaxel and endocrine therapies experiences a rapid PSA decline with cabazitaxel treatment on the Phase III PROSELICA trial

Track 33 Approach to the use of preemptive growth factors with cabazitaxel

Track 34 Use of cabazitaxel for patients with docetaxel-refractory mCRPC

Track 35 Analysis of the TROPIC trial (cabazitaxel/prednisone versus mitoxantrone/prednisone): PSA decline as a surrogate for overall survival in patients with mCRPC that progressed on first-line chemotherapy

Track 36 Key ongoing Phase III trials of cabazitaxel in mCRPC: FIRSTANA — first-line docetaxel versus cabazitaxel — and PROSELICA — evaluation of 2 different doses of cabazitaxel in patients who previously received docetaxel

Track 37 Treatment options for patients with asymptomatic mCRPC progressing on docetaxel

Track 38 Treatment algorithms for patients with asymptomatic and symptomatic mCRPC

Track 39 Potential incorporation of next-generation endocrine agents — abiraterone and enzalutamide — into earlier lines of treatment

Track 40 Benefits and risks of long-term endocrine therapy in PC

Track 41 Mechanism of action of the novel antisense agent custirsen (OGX-011)

Track 42 Results from the Phase II CUOG trial P-06c: Custirsen in combination with docetaxel or mitoxantrone as second-line therapy for patients with mCRPC progressing after first-line docetaxel

Track 43 Ongoing Phase III trials evaluating custirsen in combination with taxane-based chemotherapy versus taxane-based therapy alone as first- or second-line therapy for patients with mCRPC

**Video Highlights of the Clinical Investigator Think Tank**

Check out highlight clips from this fascinating Think Tank featuring our esteemed clinical investigator panel discussing and debating some of the key clinical management issues in the field of prostate cancer. Visit [www.ResearchToPractice.com/PCUTT112/Video](http://www.ResearchToPractice.com/PCUTT112/Video) for more information.
SELECT PUBLICATIONS

AFFINITY: A randomized phase 3 study comparing cabazitaxel/prednisone in combination with custirsen to cabazitaxel/prednisone for second-line chemotherapy in men with metastatic castrate resistant prostate cancer. NCT01578655
Crook JM et al. A phase III randomized trial of intermittent versus continuous androgen suppression for PSA progression after radical therapy (NCIC CTG PR.7/SWOG JPR.7/CTSU JPR.7/UK Intercontinental Trial CRUKE/01/013). Proc ASCO 2011; Abstract 4514.
Hussain M et al. Intermittent (IAD) versus continuous androgen deprivation (CAD) in hormone sensitive metastatic prostate cancer (HSM1PC) patients (pts): Results of S9346 (INT-0162), an international phase III trial. Proc ASCO 2012; Abstract 4.
Scher HI et al. Effect of MDV3100, an androgen receptor signaling inhibitor (ARSI), on overall survival in patients with prostate cancer postdocetaxel: Results from the phase III AFFIRM study. Genitourinary Cancers Symposium 2012; Abstract LBA1.
SYNERGY: A randomized phase 3 study comparing standard first-line docetaxel/prednisone to docetaxel/prednisone in combination with custirsen in men with metastatic castrate resistant prostate cancer. NCT01188187
6. Sipuleucel-T is a(n) ______________________.
   a. Third-generation taxane
   b. Immunotherapeutic agent
   c. Antiandrogen with a high affinity for the androgen receptor

7. The ongoing Phase III PROSELICA trial is evaluating ________________ as second-line therapy for patients with mCRPC previously treated with docetaxel.
   a. Cabazitaxel at 20 mg/m²
   b. Cabazitaxel at 25 mg/m²
   c. Docetaxel re-treatment
   d. Both a and b
   e. Both a and c

8. Phase III trial data have reported a low incidence of treatment-associated seizures with which of the following agents?
   a. Cabazitaxel
   b. Enzalutamide
   c. Sipuleucel-T
   d. Radium-223

9. On the Phase II CUOG trial P-06c, which evaluated the novel antisense agent custirsen (OGX-011) in combination with docetaxel or mitoxantrone as second-line therapy for patients with mCRPC progressing after first-line docetaxel, patients who received the custirsen/docetaxel combination experienced a significant improvement in pain relief versus those who received custirsen/mitoxantrone.
   a. True
   b. False

10. The ongoing Phase III FIRSTANA trial is evaluating docetaxel versus __________ as first-line therapy for patients with mCRPC.
    a. Cabazitaxel
    b. Radium-223
    c. Sipuleucel-T
    d. All of the above
**EDUCATIONAL ASSESSMENT AND CREDIT FORM**

**Current Controversies, Recent Developments and Emerging Strategies in the Practical Management of 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**

<table>
<thead>
<tr>
<th>How would you characterize your level of knowledge on the following topics?</th>
<th>4 = Excellent</th>
<th>3 = Good</th>
<th>2 = Adequate</th>
<th>1 = Suboptimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Results with intermittent versus continuous androgen deprivation in patients with hormone-sensitive metastatic PC — SWOG-S9346 (INT-0162) trial — or rising PSA after radical therapy — NCIC CTG PR.7 trial</td>
<td>BEFORE</td>
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<td>Mechanism of action and available research evidence with enzalutamide in CRPC</td>
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<td>Updated results from a Phase II study of orteronel without prednisone for men with nonmetastatic CRPC and rising PSA levels</td>
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<td>Phase II trial results and ongoing Phase III trials evaluating the novel antisense agent custirsen in mCRPC</td>
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<td>Ongoing trials of cabazitaxel in mCRPC: FIRSTANA — first-line docetaxel versus cabazitaxel — and PROSELICA — 2 doses of cabazitaxel in patients who previously received docetaxel</td>
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<td>Updated analysis of the Phase III ALSYMPCA study evaluating radium-223 chloride in patients with CRPC with bone metastases</td>
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**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. |
|---|---|---|---|---|---|
| 4 = Yes | 3 = Will consider | 2 = No | 1 = Already doing | N/M = LO not met | N/A = Not applicable |

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

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

- Explore the emerging data and active research evaluating novel agents — including radiopharmaceuticals, androgen biosynthesis inhibitors, antiandrogens and clustatin antisense oligonucleotides — in the setting of advanced prostate cancer, and discuss the biologic basis for their clinical activity. ................................. 4 3 2 1 N/M N/A
- Recall existing and emerging research demonstrating the effects of secondary hormonal interventions on quality and quantity of life for patients with chemotherapy-naïve and chemotherapy-pretreated CRPC, and use this information to guide treatment planning for these patients. ......................................................... 4 3 2 1 N/M N/A
- Efficiently identify and educate patients with skeletal metastases about the efficacy and safety of emerging systemic bone-directed treatments. ............................................. 4 3 2 1 N/M N/A
- Employ case-based learning to effectively apply evidence-based research findings in the determination of best-practice sequencing of available systemic agents for patients with metastatic prostate cancer. ............................................................. 4 3 2 1 N/M N/A
- Counsel appropriately selected patients with minimally symptomatic or asymptomatic advanced prostate cancer about sipuleucel-T as a treatment option, and define an approach to patient monitoring after treatment with this agent. ................................................. 4 3 2 1 N/M N/A
EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

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Would you recommend this activity to a colleague?
☐ Yes  ☐ No
If no, please explain:

Additional comments about this activity:

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

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

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

<table>
<thead>
<tr>
<th>Faculty</th>
<th>Knowledge of subject matter</th>
<th>Effectiveness as an educator</th>
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<tr>
<td>Tomasz M Beer, MD</td>
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<td>Matthew R Smith, MD, PhD</td>
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<tr>
<td>Moderator</td>
<td>Knowledge of subject matter</td>
<td>Effectiveness as an educator</td>
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<tr>
<td>Neil Love, MD</td>
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</tbody>
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Please recommend additional faculty for future activities:

Other comments about the faculty and moderator for this activity:

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