Highlights from the 2015 St. Gallen Advanced Prostate Cancer Consensus Conference

EXPERT EDITORIAL

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In advanced prostate cancer, rapid and successful drug development has resulted in several new treatment options. Clinicians encounter the increasingly difficult task of counseling patients regarding the selection of multiple potentially effective treatments with different indications that vary in toxicity and cost. Newer imaging technologies are also in use or in development, but there are not enough data to show how to implement these in an optimal fashion to guide treatment decisions and improve patient outcomes.

Multiple national and international guidelines provide treatment recommendations based on the available evidence from clinical trials. However, in daily clinical practice, many uncertainties remain in the treatment of men with advanced prostate cancer because there are several topics for which there are no data, conflicting data, or only sparse, low-level data from the literature.

Since 1978, the international Breast Cancer Consensus Conference has been conducted in St. Gallen, Switzerland. This conference focuses on early-stage breast cancer treatment and results in highly valued St. Gallen recommendations on early-stage breast cancer management. Analogous to this well-known conference, the inaugural St. Gallen Advanced Prostate Cancer Consensus Conference (APCCC) was held in March 2015 to address some of the clinically relevant questions in advanced prostate cancer management. APCCC was created to provide a forum for discussion and debate on the current care for men with advanced prostate cancer.

Key Areas of Controversy

Prior to the conference, 10 key areas of controversy in the treatment of men with advanced prostate cancer were identified (Table 1). An international expert consensus panel consisting of 41 prostate cancer specialists (mostly from Europe and the United States) from different disciplines (urologists, radiotherapists, oncologists, radiologists, pathologists, basic and translational researchers, a nuclear medicine specialist, a geneticist, and a statistician) was established and prepared the actual consensus conference. The first 2 days of the meeting were devoted to presentations and debates on the 10 topics. The conference concluded with an expert panel discussion and a vote on almost 100 predefined and agreed-upon consensus questions. The anonymous voting was done exclusively by the panelists but was open for viewing by the audience. If a panelist did not make clinical decisions regularly on the topic of the question, they had to choose the option "unqualified to answer" (Fig. 1).

Table 1. Areas of Controversy in Advanced Prostate Cancer Management

Treatment of men with castration-naive metastatic prostate cancer
Treatment of men with oligometastatic prostate cancer
Definition of castration resistance
Treatment of men with nonmetastatic (M0) castration-resistant prostate cancer (CRPC)
Value of endocrine manipulations without proven survival benefit in men with metastatic CRPC
Treatment choice and sequencing for men with metastatic CRPC
Staging and monitoring of treatment
Use of osteoclast-targeted agents for reducing risk of skeletal-related events and symptomatic skeletal events in men with CRPC
Value and use of predictive markers
Multidisciplinary care of men with prostate cancer

The questions focused on the treatment of men with advanced prostate cancer treated outside of clinical trials and had been prepared using a modified Delphi method by the panelists over several months before the conference (Fig. 2). Based on the voting results, expert recommendations have been formulated and summarized in a manuscript, which was recently published.[1] If 75% or more of the panelists chose the same answer option, this was defined as consensus. There was strong consensus among the panelists for some questions; nonetheless, for other questions there was an almost equal distribution on each of the different answers, and no consensus was reached. These areas of disparate opinion are obviously topics for which further research should be conducted to better inform upon these unresolved issues in the management of advanced prostate cancer.

Identifying these areas and hopefully stimulating collaborative efforts for trials addressing these open challenges was an additional achievement of the conference, beyond the recommendations. As an example, some of these areas included the dose, scheduling, and duration of osteoclast-targeted therapies for men with castration-resistant prostate cancer (CRPC), especially in the setting of new effective treatments that can also reduce the risk of skeletal-related events.

Another evolving area for which there is lack of evidence-based medicine and, thus, significant uncertainty regarding best management choices is oligometastatic disease. Identified questions include:

- What defines oligometastatic disease?
- What is the optimal imaging to define oligometastatic disease?
- For men with oligometastatic disease, should local treatment of all the known disease be considered, and if so, should additive systemic treatment be administered?
- If systemic treatment should be considered, which treatment and for what treatment duration?

Other open questions were identified concerning imaging and the inclusion of novel imaging techniques (PET-CT with different tracers, multiparametric MRI) as opposed to conventional imaging with CT and bone scintigraphy in clinical settings, such as M0 prostate cancer, as well as for staging of men with clinically localized disease and disease monitoring in men with metastatic disease. It has been shown that some newer imaging modalities are more accurate; however, there is a lack of robust data to guide treatment decisions or to provide prognostic information in our patients. Trials including imaging questions have to be encouraged and supported.

Important points for which consensus was reached are summarized under the "APCCC Recommendations" section of this editorial. For details of the consensus questions, voting results, and interpretation by the expert panel we refer to the APCCC publication.[1] Figure 1 provides an example of the pie charts resulting from the voting (available online as supplemental material).

APCCC Recommendations

Do:

- Total testosterone should be measured before classifying disease as castration resistant. Rising PSA on androgen deprivation therapy (ADT) with a documented suppressed testosterone level was recommended for the definition of CRPC.

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Fig. 1. Example of a Consensus Question and Voting Result*

Do you **recommend** denosumab (120 mg every 4 weeks) in patients with castration-naive M1 prostate cancer with bone metastases?

1: Yes, in the majority of patients
2: In a minority of selected patients
3: No
4: Abstain
5: Unqualified to answer

Percent Voting Results, Excluding Unqualified to Answer

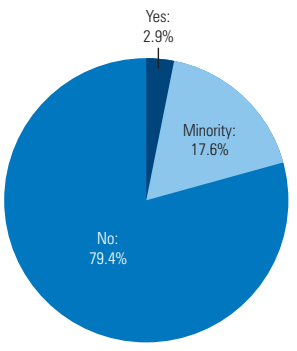

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Fig. 2. How the Consensus Process Worked*

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- Baseline staging examinations, including laboratory parameters and imaging, should be performed in every man with CRPC before starting a new treatment. Without baseline staging information, subsequent interpretation of antitumor outcome is extremely challenging.
- Disease activity should be monitored (including imaging) for men on agents that have been shown to prolong survival. Monitoring by PSA alone is insufficient.
- Patients should be informed of the availability of and the possibility to participate in a clinical trial to offer them novel therapies. Further advances in the treatment of men with CRPC can only be achieved through clinical trials.

Do Not:

- A man with metastatic castration-naive prostate cancer should not be treated with bisphosphonates or denosumab in the dose established for reduction of risk of skeletal-related events or symptomatic skeletal events in patients with CRPC. However, adequate calcium and vitamin D supplementation, lifestyle changes, and bisphosphonates or denosumab at a lower dose or schedule for the prevention of osteoporosis or osteoporotic fractures should be considered.
- A man with CRPC and M0 disease should not be treated with one of the agents that have been shown to prolong overall survival in the metastatic CRPC setting (abiraterone, cabazitaxel, docetaxel, enzalutamide, radium-223, or sipuleucel-T) outside of a clinical trial. Large phase III clinical trials with different androgen receptor–pathway inhibitors in this indication are ongoing, and patients should be included in these trials.
- Bicalutamide should not be routinely added for the treatment of metastatic disease progressing on ADT if abiraterone or enzalutamide are available. For the definition of CRPC, the addition of bicalutamide to ADT and confirmed PSA rise on combined ADT is no longer required.
- Because it is unknown whether abiraterone or enzalutamide is better in terms of antitumor activity, the main question that should be evaluated is when to use a novel endocrine agent and when to use chemotherapy, radium-223, or sipuleucel-T in a man with metastatic CRPC.
- Do not stop treatment with an agent that has been shown to prolong survival (abiraterone, cabazitaxel, docetaxel, enzalutamide, radium-223, or sipuleucel-T) in a man with CRPC based on PSA rise only in the absence of clinical or radiological progression. A combination of at least two out of the three progression criteria (PSA and/or symptoms and/or radiographic evidence) is recommended for stopping or switching treatment.

Following the first conference publication, the APCCC recommendations should now be discussed, disseminated, and hopefully endorsed to improve care of men with advanced prostate cancer in daily clinical practice.

Based on the very successful completion of the first consensus conference, a large number of questions that remain open, and ongoing studies that will possibly change the landscape again, the organizers will hold another consensus conference in 2017. The scientific committee has been formed, and the 10 areas of controversy covered in the next conference will be identified soon. Please visit apccc.org for details. ●

The inaugural St. Gallen Advanced Prostate Cancer Consensus Conference (APCCC) addressed some of the clinically relevant questions in advanced prostate cancer management.

Reference:

1. Gillessen S, Omlin A, Attard G, et al. Management of patients with advanced prostate cancer: recommendations of the St. Gallen Advanced Prostate Cancer Consensus Conference (APCCC) 2015. *Ann Oncol*. 2015; 26:1589-1604.

ARTICLE HIGHLIGHTS

- Many uncertainties remain in daily clinical treatment of men with advanced prostate cancer because there are several topics for which there are no data, conflicting data, or only sparse, low-level data from the literature.
- The inaugural St. Gallen Advanced Prostate Cancer Consensus Conference (APCCC) was held in March 2015 to address some of the clinically relevant questions in advanced prostate cancer management.
- Expert recommendations from the APCCC were formulated and summarized in a recently published article.

MY MEETING EXPERIENCE A UROLOGIST'S PERSPECTIVE

Hyung L. Kim, MD, of Cedars-Sinai Medical Center in Los Angeles, has previously attended four Genitourinary (GU) Cancers Symposia. In the following interview, Dr. Kim discusses his plans for this year's Symposium and provides advice to first-time attendees.

Daily News: **What brings you back to the GU Cancers Symposium?**
Dr. Kim: The surgeon works closely with other disciplines to treat patients. As such, the multidisciplinary format of GU Cancers Symposium makes this meeting particularly valuable for me. I look forward to hearing about the latest research in medical and radiation oncology that is important to the modern practice of urologic oncology.

Daily News: **How does research presented at the GU Cancers Symposium affect how you practice?**
Dr. Kim: The GU Cancers Symposium is a venue where practice-changing clinical trial results are presented. Over the last couple years, the Symposium has included abstracts and lectures on biomarker research for patients with prostate cancer.

For example, during last year's Symposium, Emmanuel S. Antonarakis, MD, and Philip W. Kantoff, MD, gave presentations on two genetic markers that may someday be used to steer treatment selection for individual patients with prostate cancer: AR-V7 and single nucleotide polymorphisms within the anionic transporter SLCO2B1.

As a result of attending the GU Cancers Symposium, I now use biomarkers to help me manage challenging cases in my own practice.

Daily News: **What sessions are you planning to attend during this year's Symposium?**
Dr. Kim: I am looking forward to attending today's General Session on "Potential Targets for Advanced Prostate Cancer" (10:00 AM–11:30 AM). Although we have made great progress in the treatment of metastatic prostate cancer, patients continue to die of the disease. Therefore, I am particularly interested in new and innovative approaches that can lead to novel strategies for treating prostate cancer.

I am also looking forward to Saturday's General Session on "Clear and Non–Clear Cell Renal Cancer" (2:45 PM–4:15 PM). There are multiple approved agents for the treatment of clear and non–clear cell renal cancers, and best ways to combine or sequence these drugs continue to be debated. Additionally, immunotherapy is expected to make a resurgence. I expect this session to provide the latest thinking on how existing and near-future therapies will be integrated into the treatment of all histologic subtypes of renal cancers.

Daily News: **What advice do you have for first-time attendees to get the most out of their meeting experience?**
Dr. Kim: The field of oncology is rapidly changing. I would encourage urologists attending the GU Cancers Symposium for the first time to pay particular attention to the talks on radiation and medical oncology. Those presentations are highly likely to impart new information that attendees can take back to their urologic oncology practice. ●

Dr. Kim is the director of the Academic Urology Program and co-medical director of the Urologic Oncology Center at Cedars-Sinai Medical Center in Los Angeles. Dr. Kim specializes in the surgical treatment of kidney, testis, prostate, and bladder cancers.