Results from a Canadian consensus forum of key controversial areas in the management of advanced prostate cancer: Recommendations for Canadian healthcare providers

Fred Saad[1]; Sebastien J. Hotte[2]; Antonio Finelli[3]; Shawn Malone[4]; Tamim Niazi[5]; Krista Noonan[6]; Bobby Shayegan[7]; Alan I. So[8]; Brita Danielson[9]; Naveen S. Basappa[9]; Ilias Cagiannos[4]; Christina Canil[4]; Guila Delouya[1]; Ricardo Fernandes[10]; Cristiano Ferrario[5]; Geoffrey T. Gotto[11]; Robert J. Hamilton[3]. Jason P. Izard[12]; Anil Kapoor[7]; Daniel Khalaf[13]; Michael Kolinsky[9]; Aly-Khan Lalani[2]; Luke T. Lavallée[4]; Christopher Morash[4]; Scott C. Morgan[4]; Michael Ong[4]; Frédéric Pouliot[14]; Ricardo A. Rendon[15]; Steven Yip[16]; Anousheh Zardan[17]; Laura Park-Wyllie[17]; Kim Chi[13]

[1]Centre Hospitalier de l'Université de Montréal, University of Montreal, Montreal, QC, Canada; [2]Juravinski Cancer Centre, McMaster University, Hamilton, ON, Canada; [3]Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada; [4]The Ottawa Hospital, University of Ottawa, Ottawa, ON, Canada; [5]Jewish General Hospital, McGill University, Montreal, QC, Canada; [6]BC Cancer Agency, University of British Columbia, Surrey, BC, Canada; [7]St. Joseph's Healthcare, McMaster University, Hamilton, ON, Canada; [8]Prostate Centre at Vancouver General Hospital, University of British Columbia, Vancouver, BC, Canada; [9]Cross Cancer Institute, University of Alberta, Edmonton, AB, Canada; [10]London Health Sciences Centre, Western University, London, ON, Canada; [11]Southern Alberta Institute of Urology, University of Calgary, Calgary, AB, Canada; [12]Kingston Health Sciences Centre, Queen's University, Kingston, ON; [13]BC Cancer Agency, University of British Columbia, Vancouver, BC, Canada; [14]Quebec City University Hospital Center & Centre de Recherche of Quebec City University Hospital Center, University of Laval, QC, Canada; [15]Queen Elizabeth II Health Sciences Centre, Dalhousie University, Halifax, NS, Canada; [16]Tom Baker Cancer Centre, University of Calgary, Calgary, AB, Canada; [17]Medical Affairs, Janssen Inc, Toronto, ON, Canada

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Corresponding author: Dr. Sebastien Hotte, 2uravinski Cancer Centre, McMaster University, Hamilton, ON, Canada; hotte@HHSC.CA

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Abstract

Introduction: Rapid progress in diagnostics and therapeutics for the management of prostate cancer (PCa) have created areas where high-level evidence to guide practice is lacking. The Genitourinary Research Consortium (GURC) conducted its second Canadian consensus forum to address areas of controversy in the management of PCa and provide recommendations to guide treatment.

Methods: A panel of PCa specialists discussed topics related to the management of PCa. The core scientific committee finalized the design, questions and the analysis of the consensus results. Attendees then voted to indicate their management choice regarding each statement/topic. Questions for voting were adapted from the 2019 Advanced Prostate Cancer Consensus Conference. The thresholds for agreement were set at ≥ 75% for 'consensus agreement', > 50% for "near-consensus", and ≤ 50% for "no consensus".

Results: The panel was comprised of 29 PCa experts including urologists (n=12), medical oncologists (n= 12), and radiation oncologists (n= 5). Voting took place for 65 pre-determined questions and three ad hoc questions. Consensus was reached for 34 questions, spanning a variety of areas including biochemical recurrence, treatment of metastatic castration-sensitive PCa, management of non-metastatic and metastatic castration-resistant PCa, bone health, and molecular profiling.

Conclusion: The consensus forum identified areas of consensus or near-consensus in more than half of the questions discussed. Areas of consensus typically aligned with available evidence, and areas of variability may indicate a lack of high-quality evidence and point to future opportunities for further research and education.

Introduction

Prostate cancer (PCa) is the most common type of cancer among Canadian men, accounting for 20% of all new cancer cases.[1] Five-year survival rates range from nearly 100% for localized to 30% for metastatic PCa,[2] and treatment and management strategies evolve considerably over the disease course.[3] Careful decision-making is required to choose between treatments that can be effective but carry adverse effects. Regular adaptation of clinical guidelines that incorporate recent evidence is important for supporting decision-making. Rapid development of therapeutics and diagnostics have introduced more options for treatment and management but have created areas lacking high-level evidence to guide decision-making.

In 2018, the Genitourinary Research Consortium (GURC) conducted a consensus initiative to synthesize evidence and expert opinion to address areas of controversy in the management of PCa, and identified areas where additional research is needed.[4] Building off the success of the first consensus forum, the GURC recently conducted its 2nd Canadian Consensus

Forum (CCF). The aim of this initiative was to address controversial areas in the management of PCa patients, particularly in areas of limited evidence to guide treatment practices.

Methods

This was a consensus forum to ascertain the extent of agreement for various aspects of the management and treatment of PCa in an expert panel of PCa specialists from Canadian academic institutions. The panel was a select group of multidisciplinary physicians who are members of the GURC.

A core scientific committee of eight physicians identified topics for discussion and developed questions adapted and updated from the Advanced Prostate Cancer Consensus Conference (APCCC) 2019[5] that were then voted on by the expert panel. Janssen authors did not participate in the consensus voting. Questions were administered in two formats: an online component (responses collected via the online platform, Qualtrics[6]), and a subsequent live virtual forum. Through a voting procedure, 65 questions were chosen for live voting and discussion, and 51 were subject to online voting prior to the forum by the expert panel. The forum took place on November 27th, 2020. The predetermined thresholds were set at ≥ 75% for 'consensus agreement', > 50% for "near-consensus", and ≤ 50% for "no consensus", and were applied for both the live forum and online questions. All voting was analyzed descriptively as counts and percentages of total panel size. No hypothesis testing was performed.

Results

The expert panel included 29 PCa specialists, comprised of urologists (n= 12, 41%), medical oncologists (n= 12, 41%), and radiation oncologists (n= 5, 17%), with geographic representation from Ontario (n= 15, 52%), British Columbia and Alberta (n= 8, 28%), and Quebec and Atlantic provinces (n= 6, 21%). Areas of consensus and near-consensus from live voting are herein described. Further results from the forum and online questions are described in Supplementary material.

Questions from the live forum covered six topic areas, one of which was further split into sub-topics:

1. Biochemical (i.e. PSA) recurrence after local therapy
2. Treatment of newly diagnosed metastatic castration-sensitive PCa (mCSPC)
    a. Imaging modality to guide treatment
    b. Oligometastatic PCa (no prior systemic therapy for metastatic disease)
3. Management of non-metastatic CRPC (nmCRPC)
4. Management of metastatic CRPC (mCRPC)
5. Bone and bone metastases
6. Molecular characterization and genomic profiling: Tissue and blood

Voting took place for 65 predetermined questions and three ad hoc questions. Consensus was reached for 34 questions, with unanimous agreement on four questions (Table 1).

Reporting areas of consensus, simple majority, and variability

1. Biochemical recurrence after local therapy

Consensus was reached on which imaging modality participants most often use for patients with rising prostate-specific antigen (PSA) after radical prostatectomy (RP), with 82% of physicians ordering conventional computed tomography (CT) and bone scintigraphy [± pelvic magnetic resonance imagining (MRI)]. There was near-consensus (71%) that positive PSMA PET findings should change the treatment and monitoring plan.

2. Treatment of newly diagnosed mCSPC

Patient stratification to guide initial systemic therapy

90% of physicians agreed high/low-volume disease prognostic stratification is still needed to select patients for docetaxel use. There was 100% consensus that androgen receptor axis targeted agents (ARATs), apalutamide or enzalutamide can be used in all-comer populations (i.e., not stratified by prognosis).

Preferred treatment for patients with low-volume disease

A number of recent clinical trials have investigated the addition of chemotherapy or ARATs to ADT for patients with mCSPC[7–11]. For de-novo low-volume disease without symptoms from the primary, 97% recommended an ARAT plus treatment of the prostate. Following relapse after local treatment, 100% recommended an ARAT. An ad hoc question asked whether metastasis directed therapy (MDT) should be considered for patients with low-volume disease if they are experiencing bothersome side effects from their ARAT or systemic therapies, and 79% indicated they would consider MDT for a low-volume patient while acknowledging limited data and a need for further research.

For patients with de-novo high-volume mCSPC without symptoms from the primary tumour, near-consensus (59%) indicated an ARAT is preferred, while 41% indicated either an ARAT or docetaxel is acceptable. An ad hoc question indicated 93% considered docetaxel an option for these patients, albeit not necessarily the preferred choice. Similar results were observed for patients with high-volume disease relapsing after local treatment of the prostate.

Limited role of docetaxel as up-front treatment prior to ARAT therapy

76% recommended against the use of docetaxel prior to ARAT in mCSPC and 20.7% felt ARAT use should sequentially follow docetaxel (as per the TITAN[8] and ARCHES[12] trials) as opposed to combined therapy (as per the ENZAMET study).

Preferred treatment for high-volume/high-risk disease in patients with PSA <20 ng/mL

In mCSPC patients with de-novo high-volume and/or high-risk disease based on criteria from CHAARTED or LATITUDE, with a PSA value <20 ng/mL but no histopathological evidence of small cell carcinoma, docetaxel was the preferred treatment (86% agreement).

2a. Imaging modality to guide treatment

Nearly all participants (97%) ordered CT/bone scan to guide treatment for newly diagnosed low-volume mCSPC. Most (83%) agreed with the need for additional imaging beyond just baseline and disease progression, such as at 6-12 months or the expected timing of a nadir response.

2b. Oligometastatic PCa (no prior systemic therapy for metastatic disease)

Definition of oligometastatic PCa to guide MDT

A number of different definitions of oligometastatic PCa exist in the literature.[13] The panel reached consensus that the most useful definition to guide MDT was "*limited bone and/or lymph node metastases, excluding visceral metastases",* with 79% agreement. Some clinicians felt that PCa oligometastases also included patients with lung, but not liver, metastases.

Importance of distinguishing lymph node-only disease

For treatment decisions in untreated de-novo oligometastatic PCa, 76% of the panel said it was important to distinguish lymph node-only disease from disease that includes metastatic lesions at other sites. However, 69% said it was not necessary to distinguish de-novo oligometastatic PCa (synchronous) from a recurrent oligometastatic PCa patient (metachronous).

Treatment with ARAT together with treatment of the primary and use of MDT for all lesions

ARAT plus treatment of the primary was preferred among 86% of physicians. The panel was also in consensus (86%) that they would not use (or only rarely consider) MDT **instead** of systemic therapy (ADT +/- ARAT) in patients with oligometastatic prostate cancer. On further discussion, the panel felt that the more appropriate use of MDT was to **add** it to systemic therapy (ADT ± ARAT) in a minority of patients (59% of votes) or the majority of patients (14% of votes) of patients. Although most physicians did not recommend MDT as a primary therapy for mCSPC, 83% expressed that the treatment goal when adding MDT to systemic therapy is to prolong PFS and 86% felt there is 'some' evidence that MDT confers benefit to ADT-free survival or PFS. These results generated much discussion and the closing comments focused on clarifying that the existing evidence for MDT resides in a different setting, the oligorecurrent setting, and further research is needed, especially with regards to the benefit of MDT for de novo oligometastatic disease.

Use of advanced imaging for patients without metastases on conventional imaging

86% of panelists felt a positive PSMA PET result showing low-volume metastatic disease in a patient without metastases on conventional imaging would lead them to change their management strategy and treat the patient as having metastatic disease. However, consensus was not reached on whether management strategy should change if PSMA PET showed high-volume disease in patients who appeared to have low-volume disease on conventional imaging.

3. Management of non-metastatic CRPC (nmCRPC)

Imaging modality to use to distinguish nmCRPC from mCRPC
All participants agreed that CT and/or bone scintigraphy are sufficient to determine if patient is nmCRPC and to guide treatment decisions.

Timing of imaging in nmCRPC
Among asymptomatic nmCRPC patients on ADT with a PSADT ≤10 months, 83% of physicians recommended imaging at a total PSA level > 2ng/mL. 72% agreed there may be a rationale to lower the PSA threshold to less than 2 ng/mL but further study is needed at these lower levels.
Treatment preference when PSADT ≤ 10 months
90% of the panel indicated they would recommend any of apalutamide, darolutamide, or enzalutamide, in addition to ADT, and aligns with the positive results seen in the SPARTAN[14], PROSPER[15], and ARAMIS[16] trials.

Sequencing ARAT to ARAT in nmCRPC to mCRPC
93% of participants would not recommend back-to-back ARAT sequencing for the majority of patients who progress from nmCRPC to mCRPC but most (86%) would recommend its use in a minority (i.e., ineligible or refuse other options). For this minority of patients for whom back-to-back sequencing could be recommended, most (72%) respondents said they would recommend changing AR pathway treatment at occurrence of metastases alone.

4. Management of mCRPC

Waiting for progression beyond PSA progression alone to switch treatments
In the absence of other signs of progression, 79% of physicians did not recommend switching treatments at PSA progression alone.

Sequencing ARAT to ARAT in mCSPC to mCRPC
There was consensus agreement (79%) that back-to-back ARAT sequencing could be considered in a minority of patients (i.e., ineligible or refuse other options). Although not recommended for the majority of patients, when ARAT sequencing is used, the preference was abiraterone acetate + prednisone followed by enzalutamide.

Sequencing ARAT to ARAT in a minority of cases within the mCRPC setting
93% of panelists said there is a role for back-to-back ARAT sequencing within the mCRPC setting in a select minority of patients (ineligible for or refuse other options), for which 62% preferred abiraterone acetate + prednisone followed by enzalutamide.

Definition of oligoprogressive PCa
Most (76%) physicians agreed the most useful definition for oligoprogressive PCa was *"a limited number of progressing pre-existing or new lesion(s) in a patient with metastatic disease that is otherwise stable/treatment-responsive."* When treating disease-progression for oligoprogressive chemotherapy-naïve mCRPC on a combination of ADT and ARAT, 65% said they would consider switching from the current ARAT to another systemic therapy but acknowledged the lack of evidence to support this.

5. Bone and bone metastases
Consensus was reached (86% agreement) on using denosumab or a bisphosphonate at the dose and schedule used for osteoporosis for patients with mCSPC starting on long-term ADT plus ARATs, and only for nmCRPC patients with an increased risk of fracture starting ADT plus ARATs, in order to prevent cancer treatment-induced bone loss (CTIBL) and fractures.

6. Molecular profiling

Testing for BRCA1/2 and other DNA repair gene alterations
83% of participants recommended that the majority of PCa patients with metastatic disease get germline and somatic testing for BRCA1/2 and other relevant gene alterations. When asked which specialty should order genetic/genomic testing and lead treatment and management (including hereditary cancer referrals) for those with a positive result, 86% said all specialists with experience in genetic/genomic screening and treating PCa should be able to order and plan optimum treatment for patients with a positive result.

Relevance of BRCA1/2 aberrations in treating low-risk localized PCa
In the presence of a BRCA1/2 germline aberration, 83% of physicians recommended radical therapy (either surgery or radiation) over surveillance in patients with low-risk localized PCa.
PARP inhibitors (PARPis) for patients with BRCA1/2 (and other homologous recombination repair (HRR) gene) mutated cancers: 97% of participants recommended that men with cancers with a pathogenic BRCA1/2 mutation (or other HRR gene mutation) and metastatic disease receive a PARPi during the course of their disease.

Preferred treatment for metastatic PCa with a pathogenic BRCA1/2 (or other HRR gene) aberration
86% of physicians recommended a PARPi or platinum therapy during disease course, when available, in patients with metastatic PCa with a pathogenic BRCA1/2 aberration (somatic and/or germline).

Discussion

To support clinical decision-making in the management of men with PCa, this consensus forum aimed to address areas of controversy by collecting and synthesizing expert opinion and develop recommendations.

In men with mCSPC, consensus aligned with evidence from the ARCHES[12], ENZAMET[17] and TITAN[8] trials showing the benefit of enzalutamide and apalutamide regardless of metastatic volume. Participants were unanimous in recommending that both agents could be used in an all-comer population, and were the preferred treatment choices following metastastic relapse in those that originally present with local disease only. Docetaxel and abiraterone acetate plus prednisone continued to be recommended for high-risk/high-volume patients (defined by the LATITUDE[10] and CHAARTED[7] trials), as supported by evidence from STAMPEDE[9] and CHAARTED[7.]. Recommendations for patients with BRCA 1/2 mutated cancers reflected the promising results for PARPis such as olaparib seen in the PROfound trial.[18] Lastly, recommendations across several clinical states indicated that current evidence does not inform fully on the value of PSMA PET when compared with the evidence base conventional standard imaging modalities.[11]

Voting results also indicated new trends in management, and areas of consensus opinion despite a lack of level 1 evidence. For mCSPC patients, there was consensus or near-consensus that PCa treaters are moving away from chemotherapy in favour of ARAT for high-volume disease, though chemotherapy was still considered an option. This was echoed for low-volume disease, where there was almost unanimous agreement that an ARAT plus ADT and treatment of the primary was the recommended approach patients with oligometastatic mCSPC with an untreated primary. This is a compelling message on an otherwise controversial issue, as there is no level 1 evidence that has directly assessed the addition of radiation therapy to the prostate primary with standard ARAT + ADT . Similarly, despite ongoing debate regarding an oligometastatic PCa definition to guide MDT, there was consensus agreement that “limited bone and/or lymph node metastases, excluding visceral metastases” was a useful definition; however, there was debate on whether patients with limited lung metastases could also be included in oligometastatic group.

With some exceptions, questions for which voting did not reach consensus were often reflective of unclear evidence, though near-consensus was still achieved in some of these areas. There was near-consensus that de-novo synchronous oligometastatic patients need not be distinguished from metachronous oligometastatic patients in treatment decisions. Majority said they would recommend MDT in addition to systemic therapy in at least a minority of oligometastatic patients with no prior systemic treatment, but also highlighted that there is need for better clinical trial data to support that adding MDT extends PFS. Voting also showed increased interest and advocacy for biomarker and genomic testing. The majority recommended tumour genomic testing, though there was some disagreement on when it should first be offered,

The majority agreed that larger panel testing, for example of homologous recombination deficiencies, mismatch repair evaluations, and tumour mutation burden were all relevant to metastatic prostate cancer. There was also agreement on an unmet need for biomarker testing for selecting potential responders to a second ARAT, at least in a minority of cases. That said, discussion highlighted that most do not have access to genomic testing outside of clinical trials, and further education and improved availability could produce stronger recommendations. Compared to the results of the 2018 consensus forum, there were several noticeable shifts in expert opinion[4]. In nmCRPC patients, there was a shift to lowered thresholds for changing treatment, with near consensus agreement that treatment should be changed at occurrence of metastases alone, rather than waiting for multiple signs of progression. Similarly, for mCSPC, there was a trend towards more regular monitoring/imaging, rather than simply in response to PSA or clinical progression. The consensus on a definition of oligometastatic PCa for guiding MDT, mentioned previously, represents increased recommendation for treating oligometastatic patients relative to the 2018 forum. Lastly, there was increased confidence on recommendations for patients with BRCA1/2 and other HRR gene mutated cancers, with physicians now routinely recommending PARPis for mCRPC patients and shifting away from the option of active surveillance in patients with localized disease.

This methodology has some limitations. First, the ability to make strong recommendations is dependent on available evidence, which can evolve rapidly. The recommendations derived from this initiative are based on the synthesis of expert opinion and the current state of evidence at the time of the forum; therefore, these recommendations may conflict with newer, incoming evidence, particularly in areas where recommendations were founded on lower level evidence. Second, although a multidisciplinary panel is useful for capturing expert opinion across clinical areas, certain questions may have had variable relevance across the panel. Similarly, opinions may have varied depending on the therapies and technologies to which each physician has access, and different interpretations of each question. However, a strength of the live forum was the opportunity for further clarification and discussion, and follow-up questions or re-voting.

Conclusions

The consensus recommendations provided from this forum represent an important initiative to identify and address controversial topics in the management of PCa patients in Canada. Consensus was reached for almost half of questions voted on at the live forum, and near-consensus was reached for an additional 25 questions. Areas of consensus mostly aligned with the available evidence, though consensus was still reached on topics where a need for further research was acknowledged. Areas of variability may highlight where high-quality evidence is lacking and point to future topics for further research.

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Figures and Tables

Table 1. Areas of consensus (≥ 75%) at live forum	
1. Biochemical recurrence after local therapy	
For patients with rising PSA after radical prostatectomy, CT and bone scintigraphy (± pelvic MRI) are the recommended imaging modalities	82.1%
2. Treatment of newly diagnosed mCSPC/mCNPC	
Among mCSPC/mCNPC patients, disease stratification into high/low-volume disease is recommended to select patients for docetaxel*	89.7%
Among mCSPC/mCNPC patients, Apalutamide in addition to ADT is a recommended treatment in an all-comer population	100.0%
Among mCSPC/mCNPC patients, Enzalutamide in addition to ADT is a recommended treatment in an all-comer population	100.0%
Docetaxel in addition to ADT is a treatment option for patients with de-novo high-volume mCSPC/mCNPC without symptoms from the primary tumour	93.1%
For patients with de-novo low-volume mCSPC/mCNPC without symptoms from the primary tumour, treatment of the primary plus an ARAT (in addition to ADT) is recommended	96.6%
For patients with mCSPC/mCNPC, upfront docetaxel followed by ARAT is not recommended	75.9%
For patients with low-volume mCSPC/CNPC relapsing after local treatment of the primary tumour, an ARAT (in addition to ADT) is recommended	100.0%
Outside of clinical trials, MDT should be considered in low-volume patients, particularly for those having many symptoms from ARATs or systemic therapies	79.3%
For patients with de-novo high-volume and/or high-risk mCSPC/mCNPC, with a Gleason score of 9, multiple liver metastases and/or lytic bone metastases, and a PSA value <20 ng/mL but no histopathological evidence of small cell carcinoma, docetaxel (in addition to ADT) is the preferred treatment**	86.2%
2a. Imaging modality to guide treatment	
For the majority of patients with newly diagnosed low-volume mCSPC/mCNPC, CT and bone scintigraphy are sufficient to guide the decision to treat the primary tumour	96.6%
2b. Oligometastatic PCa (no prior systemic therapy for metastatic disease)	

The following definition of oligometastatic prostate cancer is recommended to guide metastasis-directed ablative therapy: *Limited bone and/or lymph node metastases, excluding visceral metastases*	79.3%
ARAT plus treatment of the primary is the recommended treatment approach in addition to ADT in the majority of patients with oligometastatic CNPC/CSPC with an untreated primary	86.2%
It is important to distinguish lymph node-only disease from disease that includes metastatic lesions at other sites when making treatment decisions in untreated de-novo oligometastatic PCa	75.9%
Some evidence can be extrapolated to the oligometastatic setting that local treatment of metastatic lesions (MDT) confers ADT-free survival or progression-free survival in treatment-naïve oligometastatic PCa, but further study is needed	86.2%
Metastasis-directed ablative treatment of all lesions is is not recommended for the majority or minority of patients over systemic therapy (ADT ± ARAT) in oligometastatic PCa (no prior systemic treatment)	86.2%
Prolongation of progression-free survival is the treatment goal if adding metastasis-directed ablative treatment of all lesions to systemic treatment (ADT ± ARAT) in oligometastatic PCa	82.8%
Management strategy should be changed if a PSMA PET positive result is found for low-volume metastatic disease in a patient who is negative for metastases on conventional imaging (CT/Bone scan) result	86.2%
3. Management of nmCRPC	
CT and/or bone scintigraphy is the recommended imaging modality to guide treatment decisions for the majority of patients with recent onset of CRPC and rising PSA in order to determine if patient is nmCRPC or mCRPC	100.0%
For asymptomatic nmCRPC (M0 CRPC) patients (no metastatic diseases documented on past imaging) on ADT who have rising PSA and PSADT ≤10 months, imaging is recommended once the confirmed total PSA level is >2 ng/mL	82.8%
In addition to ADT, AR antagonist treatment (e.g., apalutamide, darolutamide, or enzalutamide) is recommended for the majority of nmCRPC (M0 CRPC) patients who have PSA >2 ng/mL and PSADT ≤10 months	89.7%
In a minority of patients (i.e., who are ineligible or refuse other options), there is a role for ARAT to ARAT (back-to-back) sequencing, from nmCRPC to mCRPC	86.2%
ARAT to ARAT sequencing is not a preferred sequencing strategy for the majority of patients who progress from nmCRPC to mCRPC	93.1%
In a minority of patients (i.e., who are ineligible or refuse other options), there is a role for ARAT to ARAT (back-to-back) sequencing from mCNPC/mCSPC to mCRPC	79.3%

Oligoprogressive PCa is defined as: *A limited number of progressing pre-existing or new lesion(s) in a patient with metastatic disease that is otherwise stable/treatment-responsive*	75.9%
4. Management of mCRPC	
In the absence of other signs of progression, switching treatments at PSA progression alone in patients with mCRPC is not recommended	79.3%
In a minority of patients (i.e., who are ineligible or refuse other options), there is a role for ARAT to ARAT (back-to-back) sequencing within the mCRPC setting	93.1%
5. Bone and bone metastases	
For mCSPC patients starting on long-term ADT plus abiraterone acetate + prednisone who have NO documented osteoporosis, denosumab or a bisphosphonate at the dose and schedule used for osteoporosis in order to prevent cancer treatment-induced bone loss (CTIBL)/ fractures is recommended only in patients with an increased risk of fracture (e.g., 10-year FRAX risk of 3% for hip fractures and/or 20% for all major fractures)	86.2%
For nmCRPC patients starting on long-term ADT plus ARATs who have NO documented osteoporosis, denosumab or a bisphosphonate at the dose and schedule used for osteoporosis in order to prevent cancer treatment-induced bone loss (CTIBL)/ fractures is recommended only in patients with an increased risk of fracture (e.g., 10-year FRAX risk of 3% for hip fractures and/or 20% for all major fractures)	86.2%
6. Molecular characterization: Tissue and blood	
Radical therapy (either surgery or radiation) is recommended over surveillance for patients presenting with a tumour BRCA1/2 germline aberration in patients with low-risk localized PCa	82.8%
It is recommended that the majority of metastatic PCa patients have their tumours tested for BRCA1/2 aberrations	82.8%
It is recommended that the majority of metastatic PCa patients with a deleterious germline BRCA1/2 mutation receive a PARP inhibitor during their disease course outside of a clinical trial if none is available	96.6%
All specialists with experience in screening and treating should be able to order BRCA 1/2 genetic testing and lead the treatment planning for patients with a positive result	86.2%
PARP inhibitor or platinum therapy during disease course (when available) is recommended for metastatic PCa with a pathogenic BRCA 1/2 aberration (somatic and/or germline)	86.2%

* Physicians could select multiple options for question. This was the only option that reached consensus-level agreement.
** This question was originally framed as "choose all that apply". It was re-voted to extract the true preferred treatment option.

Table 2. Areas of near-consensus (> 50-74%) at live forum	
1. Biochemical recurrence after local therapy	
For asymptomatic patients with rising PSA after radical RT, imaging is recommended at PSA ≥2 ng/mL above nadir (Phoenix criteria)	62.1%
For a patient with positive findings on PSMA PET after reaching biochemical recurrence, a change in treatment and monitoring plan is recommended	70.8%
2. Treatment of newly diagnosed mCSPC/mCNPC	
Either a high-volume or high-risk definition can be used to guide treatment selection of abiraterone acetate + prednisone in mCSPC/mCNPC, as long as the patient is classified as at least one	58.6%
An ARAT (abiraterone acetate + prednisone, apalutamide, or enzalutamide) in addition to ADT is recommended for patents with de-novo high-volume mCSPC/mCNPC without symptoms from the primary tumour	58.6%
For patients with high-volume mCSPC/mCNPC relapsing after local treatment of the primary tumour, treatment with an ARAT(abiraterone acetate + prednisone, apalutamide, or enzalutamide) is recommended	69.0%
2a. Imaging modality to guide treatment	
For patients receiving treatment for newly diagnosed mCSPC/mCNPC, the following monitoring schedule is recommended: Baseline imaging, imaging at best response (i.e., 6-12 months), PSA monitoring for progression, further imaging at progression	65.5%
2b. Oligometastatic PCa (no prior systemic therapy for metastatic disease)	
For treatment decisions, it is not necessary to distinguish de-novo treatment-naïve (synchronous) oligometastatic PCa from oligometastatic PCa recurring after local therapy (metachronous)	69.0%
MDT of all lesions, in addition to systemic therapy (ADT ± ARAT), is recommended in a minority of oligometastatic PCa patients	58.6%
Changing management strategy is warranted for a patient showing high-volume metastatic disease on PSMA PET that showed low-volume metastatic disease on conventional imaging	51.7%
For patients with low-volume disease on conventional imaging that show results consistent with high-volume disease on advanced imaging, it is recommended to treat the patient as low-volume disease	51.7%

In addition to ADT, ARAT + treatment of the primary is the recommended treatment approach for the majority of patients with an untreated primary who are non-metastatic based on conventional imaging, but have de novo oligometastatic PCa on advanced imaging	55.2%
2c. Imaging modalities in management of de-novo oligometastatic PCa (no prior metastatic disease or prior treatment for PCa)	
For patients with oligometastatic disease on CT/bone scintigraphy, PSMA PET-CT/MRI is recommended for guiding planning for MDT	65.5%
2d. Newly diagnosed oligorecurrent oligometastatic disease after local treatment with curative intent	
ARAT + ADT is recommended for the majority of patients with oligorecurrent (metachronous) oligometastatic PCa	51.7%
3. Management of nmCRPC	
There is rationale for lowering the PSA threshold of 2 ng/mL or greater for defining CRPC, but further study is needed	72.4%
For a patient being treated with an ARAT(apalutamide, darolutamide, or enzalutamide) for nmCRPC, it is recommended that treatment be changed (apart from ADT) at occurrence of metastases alone (apart from changes related to toxicity)	72.4%
Back-to-back ARAT to ARAT sequencing is not recommended for patients who progress from mCSPC/mCNPC to mCRPC	58.6%
Among patients with oligoprogressive chemotherapy-naïve mCRPC with disease progression (no visceral metastases) on a combination of ADT + ARAT, switching from current ARAT to another systemic therapy is recommended	65.5%
4. Management of mCRPC	
Switching treatment in patients with mCRPC based on unequivocal progression on next-generation imaging (wb-MRI, PET/CT with different tracers) alone (without PSA or clinical progression)	62.1%
Abiraterone acetate + prednisone to enzalutamide is the recommended ARAT to ARAT sequencing in the mCRPC setting	62.1%
5. Molecular characterization: Tissue and blood	
Tumour genomic testing should be recommended at first diagnosis of metastatic disease	58.6%
When recommending tumour genomic testing, PCa-specific, larger panel testing is recommended (including testing for homologous recombination deficiency, mismatch repair evaluation, and tumour mutation burden)	72.4%
PCa patients with mCSPC/mCNPC should be tested for somatic BRCA 1/2 mutation	58.6%
Any PCa patients with a strong family history of BRCA-associated concerns and undocumented somatic and germline aberration should be tested for germline BRCA1/2 mutation	72.4%

Platinum therapy is recommended during the disease course (including outside of a clinical trial if no trials are available) in selected patients with a deleterious germline BRCA 1/2 mutation	55.2%
Genetic counselling and/or germline DNA testing is recommended in the majority of newly diagnosed mCSPC/mCNPC patients	65.5%

Table 3. Areas of no consensus (≤ 50%) at live forum		
1. Biochemical recurrence after local therapy		
	Do you recommend repeat imaging (negative pre-operative imaging) for an asymptomatic pN0 patient with PSA persistence (≥0.1 ng/mL) four to six weeks after RP?	
	No	45.0%
	Yes, to establish a new baseline following RP	35.0%
	Yes, but only in the presence of other adverse factors (e.g., Gleason score, intraductal, etc.)	20.0%
	Should mCSPC/CNPC patients still be stratified as high/low volume and high/low risk to inform treatment decision making or can we consider this as an all comer population? Choose all correct responses.*	
	Apalutamide and enzalutamide can be used in an all-comer population	36.5%
	All approved systemic treatments for mCSPC/mCNPC can be used in an all-comer population regardless of disease volume or disease risk	11.1%
	High/low-risk disease stratification still needed to select patients for abiraterone acetate + prednisone *use*	20.0%
2. Treatment of newly diagnosed mCSPC/mCNPC		
2b. Oligometastatic PCa (no prior systemic therapy for metastatic disease)		
	What is your treatment goal when recommending MDT of all lesions instead of systemic therapy (ADT+/-ARAT) in oligometastatic PCa (no prior systemic therapy)?	
	Delay start of ADT	44.8%
	I do not recommend, or only rarely recommend, MDT of all lesions instead of systemic therapy in oligometastatic PCa	31.0%
	Prolongation of PFS	24.1%

	What is your cut-off for the number of metastases when considering PCa to be oligometastatic to guide treatment decisions regarding MDT of all lesions? Choose all correct responses.*	
	<3 metastases	48.3%
	<5 metastases	41.2%
	<2 organs	8.8%
	I don't recommend, or only rarely recommend MDT of all lesions	8.8%
	Is imaging by CT and bone scintigraphy sufficient to define the oligometastatic state for treatment planning?	
	Yes	50.0%
	No	50.0%
2c. Imaging modalities in management of de-novo oligometastatic PCa (no prior metastatic disease or prior treatment for PCa)		
	Does PET change your decision to treat the primary tumour in a patient originally classified as low-volume on conventional imaging now appears to be high volume?	
	Yes, in a minority of patients	38.0%
	Yes, in the majority of patients	31.0%
	No, or very rarely	31.0%
2d. Newly diagnosed oligorecurrent oligometastatic disease after local treatment (EBRT or RP ± EBRT) with curative intent (± salvage RT)		
	What is your recommended treatment approach for the majority of patients with oligorecurrent oligometastatic disease, who is non-metastatic based on conventional imaging, but has low-volume oligorecurrent oligometastatic PCa on advanced imaging (PET or MRI)?	
	MDT + ADT	41.4%
	ARAT + ADT	37.9%
	ADT alone	13.8%
	ARAT+ MDT + ADT	6.9%
4. Management of mCRPC		
	Is there a need for biomarker testing as an approach to select candidates who may potentially respond to a second AR pathway inhibitor at some point later in the treatment continuum?	

	Yes, in the majority of cases	48.3%
	Yes, in select cases	38.3%
	No	3.4%
5. Molecular characterization: Tissue and blood		
	Does the presence of a tumour BRCA1/2 germline aberration in patients with intermediate or high-risk localized prostate cancer influence your treatment decision?	
	No, I make the standard treatment recommendation but more intense monitoring	48.0%
	Yes, I recommend RP over RT	44.0%
	No, I make the standard treatment recommendation	8.0%
	What do you believe is the best way to test for BRCA 1/2 mutations in prostate cancer patients?	
	I don't know enough about this topic to answer the question	41.4%
	ctDNA	37.9%
	Tissue biopsy	13.8%
	Fresh biopsy	3.4%
	Saliva testing	3.4%
* These questions allowed panelists to select multiple responses, and thus each possible recommendation does not preclude the other options. Therefore, level of agreement should be interpreted separately for each possible response.		

Table 4. Areas of consensus (≥ 75%) in online component	
Locally advanced PCa	
For the majority of patients with newly diagnosed cN1 (pelvic lymph nodes), non-metastatic PCa, radical loco-regional treatment with systemic therapy is recommended	82.1%
For cN1, non-metastatic PCa, radiation therapy is recommended for primary loco-regional treatment`	75.0%
Biochemical recurrence after local therapy	
Among patients with rising PSA after radical radiation therapy, CT and bone scintigraphy (± pelvic MRI) are the recommended imaging modalities	85.7%
An LHRH agonist or antagonist are recommended for use in combination with salvage radiation therapy	89.3%
Among men with non-metastatic disease on conventional imagining and confirmed rising PSA following or ineligible for salvage radiation therapy, long-term ADT (continuous or intermittent) is recommended for patients with PSA >10 ng/mL post radiation therapy (RT), PSA >5 ng/mL post radical prostatectomy (RP), or PSADT ≤ 10 months	75.0%
Management of the primary tumour in the metastatic setting	
Local treatment of the primary tumour has an overall survival benefit only in low-volume/burden newly diagnosed mCSPC/mCNPC	92.9%
For patients with newly diagnosed low-volume/burden mCSPC/mCNPC, the recommended local treatment of the prostate is radiation therapy to the prostate	92.9%
Treatment of newly diagnosed mCSPC/mCNPC	
Castration-resistant PCa (CRPC) is the recommended terminology for describing patients with metastatic PCa who are progressing (testosterone level <50ng/mL)	92.9%
In patients with high suspicion of metastatic PCa (based on PSA and imaging), histopathological confirmation of PCa (either before or after initiation of ADT) is recommended in most patients	85.7%
In the majority of patients with newly diagnosed mCSPC/mCNPC, a short course of a first-generation non-steroidal AR antagonist (NSAA) is recommended as flare protection when initiating GnRH antagonist therapy and AR targeted therapy	78.6%
Imaging modality to guide treatment	

For the majority of patients with newly diagnosed mCSPC/mCNPC based on conventional imaging, no further imaging beyond CT and bone scintigraphy should be required to guide selection of systemic treatment	96.4%
Management of mCRPC	
In patients with asymptomatic mCRPC treated with abiraterone acetate plus prednisone, it is recommended to switch the steroid from prednisone to dexamethasone at the time of PSA progression	85.7%
In patients with mCPRC, bicalutamide is not recommended as sole additional therapy to ADT	89.3%
Bone and bone metastases	
In the majority of patients with PCa starting on long-term ADT, measurement of bone mineral density is recommended	85.7%
In the majority of patients with CRPC and bone metastasis, or mCRPC patients treated with radium-223, osteoclast-targeted therapy (zoledronic acid or denosumab) is recommended at the higher dose and more frequent schedule for reducing the risk of skeletal-related events (SRE)	82.1%
Genetic counselling and germline testing in daily clinical practice	
Collecting a detailed family history of cancer is recommended for all patients with newly diagnosed mCSPC/mCNPC	89.3%
Heterogeneity of patients with PCa (ethnicity, elderly)	
mCRPC clinical trial data regarding efficacy can be extrapolated to the treatment of patients who are older than the majority of patients enrolled in these trials	85.7%
mCRPC clinical trial data regarding efficacy can be extrapolated to the treatment of patients of other ethnicities than the majority of patients enrolled in these trials	78.6%
mCRPC clinical trial data regarding toxicity can be extrapolated to the treatment of patients of other ethnicities than the majority of patients enrolled in these trials	82.1%
Side effects of hormonal treatments and their management	
Apart from therapy dose reduction, resistance and aerobic exercise are recommended for first management to reduce fatigue in patients receiving systemic therapy for PCa	96.4%