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CONFLICTS OF INTEREST

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Expert Perspectives on Controversies in Castration-Sensitive Prostate Cancer Management: Narrative Review and Report of the First US Prostate Cancer Conference Part 1

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Abstract

Purpose: Castration-sensitive prostate cancer (CSPC) is a complex and heterogeneous condition encompassing a range of clinical presentations. As new approaches have expanded management options, clinicians are left with myriad questions and controversies regarding the optimal individualized management of CSPC.

Materials and Methods: The US Prostate Cancer Conference (USPCC) multidisciplinary panel was assembled to address the challenges of prostate cancer management. The first annual USPCC meeting included experts in urology, medical oncology, radiation oncology, and nuclear medicine. USPCC co-chairs and session moderators identified key areas of controversy and uncertainty in prostate cancer management and organized the sessions with multidisciplinary presentations and discussion. Throughout the meeting, experts responded to questions prepared by chairs and moderators to identify areas of agreement and controversy.

Results: The USPCC panel discussion and question responses for CSPC-related topics are presented. Key advances in CSPC management endorsed by USPCC experts included the development and clinical utilization of gene expression classifiers and artificial intelligence (AI) models for risk stratification and treatment selection in specific patient populations, the use of advanced imaging modalities in patients with clinically localized unfavorable intermediate or high-risk disease and those with biochemical recurrence, recommendations of doublet or triplet therapy for metastatic CSPC (mCSPC), and consideration of prostate and/or metastasis-directed radiation therapy in select patients with mCSPC.

Conclusions: CSPC is a diverse disease with many therapeutic options and the potential for adverse outcomes associated with either undertreatment or overtreatment. Future studies

are needed to validate and clinically integrate novel technologies, including genomics, AI, and advanced imaging, to optimize outcomes among patients with CSPC.

Keywords

prostatic neoplasms; ndrogen antagonists; radiotherapy; biomarkers; precision medicine

Over the past decade, the science of prostate cancer (PCa) management has progressed rapidly across treatment settings, from localized to end-stage disease. New tools such as gene expression classifiers (GECs), molecular targeted imaging (MTI), and artificial intelligence (AI)-based histopathology have underscored the clinical heterogeneity of the disease, and treatment paradigms have shifted to focus on individualized management. Nevertheless, uncertainties remain regarding optimal PCa management, with every advance engendering new questions.

To address these issues, a multidisciplinary panel of PCa experts convened in 2023 for the first US Prostate Cancer Conference (USPCC) meeting. With the goal of identifying areas of expert agreement, uncertainty, and controversy in the management of PCa, the meeting was structured around current challenges in clinical decision making. In this article, which is part 1 of a 2-part series, we report the USPCC discussions relevant to the management of castration-sensitive PCa (CSPC) (also known as hormone-sensitive PCa).

METHODS

The USPCC meeting was held on February 18 to 19, 2023, and was attended by 38 PCa experts, including 3 co-chairs and 8 session moderators. The panel included 20 medical oncologists, 11 urologists, 3 radiation oncologists, 3 nuclear medicine physicians, and a patient advocacy expert from the Prostate Conditions Education Council.

The co-chairs determined the topics for panel discussions in advance. Part 1 topics included use of androgen deprivation therapy (ADT), high-risk localized disease, biochemical recurrence (BCR), metastatic CSPC (mCSPC), and metastasis-directed therapy (MDT). Part 2 topics (presented separately) included aggressive variant/neuroendocrine PCa, metastatic castration-resistant PCa, poly (ADP-ribose) polymerase (PARP) inhibitors, and theranostics.

Before the meeting, experts in each topic area developed short presentations to guide discussions and discrete-choice questions to inform this summary. Meeting sessions were structured as follows: expert presentation(s) on topic areas, full-panel discussions moderated by session leads and co-chairs, and anonymous electronic voting on prepared questions. Panel members, including co-chairs and moderators, were encouraged to respond to all questions, but responses were not required for every question. Questions and responses for the sessions reviewed in this article are presented in Supplementary Appendix 1 (http://links.lww.com/JU9/A63). After the meeting, panel discussions and question results were used to develop this narrative summary.

RESULTS AND DISCUSSION

Localized PCa

Although progress has been made in the early diagnosis and treatment of PCa, optimal stratification and management remains a challenge. Recently, advances in diagnostic imaging and biopsy techniques have reduced the detection of indolent, low-risk PCa,[1,2] but risk stratification remains complex, potentially leading to undertreatment or overtreatment. Given the adverse effects of localized PCa treatments on patient health and quality of life (QoL), there is a need for improved risk stratification and treatment selection.

Risk Stratification

Commonly used PCa risk-stratification strategies include the National Comprehensive Cancer Network (NCCN) and the AUA risk groups, both of which are based on the clinicopathologic features defined by D'Amico et al in 1998.[3–5] Although differences exist among these risk-stratification approaches, key criteria include PSA levels, Grade Group, T stage, and, more recently, extent of biopsy core involvement. Studies have shown these clinicopathologic risk-stratification systems may not adequately predict prognosis across groups.[6–8] For example, a patient with a PSA level of 11 ng/mL, cT1 stage, Grade Group 2, and 2 of 12 positive cores would be in the same unfavorable intermediate-risk group as a patient with a PSA of 19 ng/mL, cT2c stage, Grade Group 3, and 8 of 12 positive cores.[3]

Among the USPCC panel members, there was strong endorsement of newer risk-stratification systems, such as CAPRA and STAR-CAP, with only 8% of panelists preferring the original D'Amico-based stratification.[9–13] In contrast to older systems, which have a small number of discrete risk groups, newer tools incorporate mathematical models to predict risk along a spectrum, making them more informative at the individual patient level. In head-to-head comparisons with standard clinicopathologic classification systems, newer nomograms and algorithms more accurately predicted risk of PCa recurrence and/or death.[8,14]

Although newer clinical risk scores were preferred by the panel, the USPCC still voiced several concerns regarding the inherent limitations of the clinicopathologic features used in newer assessments: Gleason scoring and clinical T stage are subject to interobserver and intraobserver variability, PSA levels have suboptimal sensitivity and specificity, and the number of involved biopsy cores is neither reproducible nor reliable.[15]

GECs in Localized PCa

More recently, predictive models have improved with the development of GECs, which are multigene biomarker panels that predict oncologic outcomes such as disease progression, metastasis, and death. Of these, the Decipher Prostate Biopsy 22-gene GEC (Veracyte Labs SD, San Diego, CA) is the most widely studied. This test fulfills several important objectives for PCa biomarker assays, including assessment and validation in diverse populations, high probability of affecting management decisions, and independent prognostic value.[16] Across risk groups, prospective studies indicate that GEC scores can identify patients who may benefit from treatment intensification or deintensification.[17] These results

await confirmation from randomized controlled trials (RCTs), such as the ongoing NRG-GU010 (NCT05050084) and NRG-GU009 (NCT04513717) trials comparing GEC-guided (de)intensification and the G-MAJOR study (NCT04396808) comparing the management effects of clinicopathologic risk scores alone or with GEC scores. Given the widespread third-party coverage and broad validation of the Decipher tool, the USPCC panel recommended consideration of its use in patients for whom the results might affect treatment decisions.

MTI in Localized PCa

MTI is a tool that can affect localized PCa risk stratification because of high sensitivity, specificity, and accuracy as supported by a multitude of prospective studies and several years of clinical use. The clinical role for MTI in localized disease, however, has yet to be clearly defined. In the proPSMA trial, patients with high-risk PCa were randomized to receive first-line conventional imaging or prostate-specific membrane antigen (PSMA) positron emission tomography (PET), followed by crossover to the alternative arm. Compared with conventional imaging, PSMA PET was superior for determining whether disease was truly localized or had spread to lymph nodes or distant sites.[18] Other trials supporting the accuracy of PSMA PET in intermediate and high-risk patients with PCa include OSPREY for ^{18}F-DCFPyL and the UCLA/UCSF coled trials for ^{68}Ga-PSMA-11.[19,20] As such, PSMA PET is an appropriate imaging modality for patients deemed to be at substantial risk of metastasis.[3,21,22]

Although USPCC faculty largely agreed that PSMA PET is likely to substantially change the future of PCa management, uncertainty remained regarding current MTI applications. A total of 63% of USPCC members considered PSMA PET testing appropriate at diagnosis for men with unfavorable intermediate and high-risk disease, 24% disagreed, and 13% were not sure. Furthermore, the panel did not agree regarding the use of PSMA PET to guide pelvic nodal disease management: 42% indicated pretreatment PSMA PET should be used to determine the need for lymphadenectomy or pelvic radiation while 37% indicated clinical characteristics alone should be considered. Concerns regarding the use of PSMA PET for risk stratification included the impact of stage migration (ie, identification of extraprostatic lesions before detection by traditional methods) and imperfect operating characteristics (ie, false positives and negatives). The panel emphasized the need for additional prospective studies to define the benefits and limitations of MTI across different disease states.
Panel members agreed that systematic prostate biopsy remains the standard of care (SoC) for diagnosis, and MTI alone should not replace biopsies. Furthermore, USPCC faculty emphasized the need for caution in altering SoC treatment based on MTI in situations where conventional imaging was used to establish the SoC in the original clinical trials.
To better understand the utility of MTI for treatment decision making, the panel stressed the importance of prospective trials, such as PATRON (NCT04557501), which is comparing treatment based on conventional imaging with PSMA PET–guided intensification.

AI in Localized PCa

Another emerging approach to PCa risk stratification is the use of AI, such as AI-based digital histopathology to detect cancer and assign cancer grade.[23] Combining digital

histopathology with clinical data, such as in the multimodal AI (MMAI) models developed by Artera (Los Altos, CA), expands the potential of AI to also estimate prognosis (ie, prognostic biomarkers) or clinical outcomes with a specific treatment (ie, predictive biomarkers).[24,25] For risk stratification, the Artera multimodal artificial intelligence (MMAI) model was superior to standard clinicopathologic systems for predicting distant metastasis and PCa-specific survival.[24]

USPCC faculty recognized the ability of MMAI models to generate validated biomarkers from large data sets at unprecedented speed. Many predicted that MMAI models and other AI-based tools will challenge the current pace of clinical validation and adoption of biomarkers. While early data for AI-based approaches are exciting, the panel emphasized the barriers to entry for new tests are low. To address concerns about lack of generalizability and bias from low-quality training and validation methods, robust validation is needed as new models emerge.

Androgen Deprivation Therapy

ADT is the backbone of systemic therapy for PCa and is administered with the goal of maintaining testosterone at castrate levels, historically defined as < 50 ng/dL.[26] However, newer testosterone assays have higher sensitivity, and some guidelines cite 20 ng/dL as a more appropriate cutoff.[27] Nonetheless, AUA and NCCN continue to use the cutoff of 50 ng/dL.[3,28] The level of testosterone needed to achieve optimal outcomes with ADT remains a source of debate. Although most of the USPCC faculty (68%) endorsed 20 ng/dL as the cutoff for castrate levels, 26% of respondents considered testosterone levels of < 50 ng/dL to be adequate. Regardless of the target testosterone level, most of the panel members (74%) were in support of regular testosterone monitoring in patients receiving ADT to ensure castration and avoid misdiagnosis of CRPC.

One of the major challenges of localized PCa management is identifying the patients who will benefit most from adding ADT to localized therapy. ADT is associated with substantial side effects that adversely affect overall health and QoL, highlighting the need for careful initial patient selection.[29] For those who are deemed ADT candidates, another important consideration is duration of treatment. A short-term course of ADT (4–6 months) has been shown to improve survival in patients with intermediate-risk disease. However, evidence shows longer term ADT (18–36 months) is more effective than short-term ADT for high-risk disease (relative risk reduction for overall survival [OS], 12%).[30–32] In general, USPCC faculty agreed with NCCN recommendations for ADT in localized PCa when using standard clinicopathologic risk stratification: short-term ADT for unfavorable intermediate-risk disease treated with radiation therapy (RT), long-term ADT for high or very high–risk disease treated with RT, and shared decision making for patients with adverse features after radical prostatectomy (RP).[3]

ADT decision making is increasingly benefitting from novel technologies. Decipher scores correlate with risk for disease progression following definitive RT with or without ADT for men with intermediate and high-risk disease. Nonetheless, GECs cannot yet be considered truly predictive biomarkers. As such, the panel endorsed consideration of GEC scores together with clinicopathologic features during shared decision-making discussions about

ADT risks and benefits. GEC scores were also cited as potential tools for identifying patients who may benefit from combination ADT and abiraterone, as in the STAMPEDE trials.[33] The Artera MMAI model may also be used for ADT decision making and has been shown to accurately predict which patients will benefit from adding ADT to RT. In patients who were MMAI biomarker-positive, the addition of short-term ADT to RT reduced the risk of distant metastasis by 36%.[25]

Other ongoing studies that may better inform the use of systemic therapy for early PCa are the biomarker-driven GUNS trial (NCT04812366), which is evaluating the utility of genomic testing to guide neoadjuvant treatment before RP; the PROTEUS trial (NCT03767244), which is comparing neoadjuvant and adjuvant ADT with or without apalutamide in patients with high-risk or locally advanced PCa undergoing RP and pelvic lymphadenectomy; DASL-HiCaP (NCT04136353), which is assessing the addition of darolutamide to post-RT ADT; and the NRG-GU010 (NCT05050084) and NRG-GU009 (PREDICT-RT; NCT04513717) trials, which are using Decipher scores to (de)intensify treatment in patients with unfavorable intermediate and high-risk disease, respectively.

Post-RP Adjuvant RT

Adjuvant RT is not routinely recommended for patients treated with RP. Because early salvage RT (SRT) has proven superior in 3 RCTs,[34–36] adjuvant RT may lead to overtreatment and unnecessary side effects. Nonetheless, there remains an evidence gap regarding whether adjuvant RT offers benefit in select cases, including patients with nodal disease, multiple adverse pathologic features, and/or high-risk GEC scores.[37,38] The panel acknowledged the challenges of demonstrating superiority for adjuvant RT over early SRT, even for men with aggressive prognostic features. Thus, well-validated predictive biomarkers are needed to identify individuals who are good candidates for adjuvant RT.

BCR

BCR after definitive treatment is common in men with high-risk PCa, particularly those with Grade Group 4 to 5, stage ≥ T3b, high pretreatment PSA levels, or PSA persistence.[39–41] Several BCR management options are available, including monitoring or early SRT with or without ADT. When selecting among these options, clinicians must consider the optimal timing, duration, and intensity of interventions and the utility of MTI and other technologies for treatment decision making.

MTI Indications for BCR

The optimal use of MTI for patients with BCR remains uncertain, both in the literature and among the USPCC panel. PSMA PET has high positive predictive values (PPVs) for the identification of the site of recurrence and may facilitate decision making for certain patients.[22,42,43] For example, the EMPIRE-1 RCT showed that the exclusion of patients with positive findings on fluciclovine-PET led to improved event-free survival with salvage RT.[44] While this finding validates that negative selection by PET successfully defines a lower risk population for salvage RT, it does not necessarily support negative selection as an appropriate management strategy.

However, MTI has limitations that concern some members of the USPCC panel. Particularly relevant for BCR is the reduced sensitivity and specificity of PSMA PET at very low PSA levels. The sensitivity and positive predictive value (PPV) of PSMA PET for detecting pelvic nodal metastases are approximately 40% and 75%, respectively.[20] Thus, USPCC members felt that clinicians should be aware of the potential for false negatives in patients with low PSA levels (<0.5 ng/mL) who may have metastases smaller than the detection limit. However, these tracers were approved on the basis of their high PPVs across a spectrum of PSA values. For example, in the CONDOR trial of PSMA PET, the correct localization rate (defined as PPV with disease localization) was 73% in patients with BCR and PSA < 0.5 ng/mL and 96% in patients with PSA levels of ≥ 5 ng/mL or higher.[42] For patients with BCR and rising PSA levels, however, most of the USPCC faculty (89%) considered PSMA PET to be the optimal imaging test—particularly for patients with PSA levels higher than 5 ng/mL.

Systemic Therapy: ADT and ADT Intensification

The benefits of ADT in patients with BCR—a largely asymptomatic disease—have not been conclusively defined.[45] As such, clinicians must carefully consider the timing, duration, and intensity of ADT for BCR based on individualized risk factors. One of the most significant predictors of metastasis and PCa-related death among patients with BCR is PSA doubling time (PSA-DT), with the strongest association for patients with PSA-DT of ≤ 3 months.[46–48] GEC scores and other clinicopathologic features (eg, interval to BCR < 18 months) may also be used to identify patients with high-risk BCR.[49–51]

USPCC faculty generally discussed ADT intensification strategies in the context of high-risk BCR, preferring active surveillance and deferred ADT for patients with low-risk BCR.[52,53] Only 21% of faculty indicated that they always recommend ADT with SRT; the remainder indicated that they only offer ADT for patients at high risk by multivariable clinical tools (50%) or by GEC scores (16%).

Germline Testing

Hereditary cancer genetic testing (ie, germline testing) is recommended by NCCN for men with high-risk and very high–risk localized PCa as well as those with nodal or distant metastases. Patients may also be candidates for germline testing if they have certain risk factors in their family or personal histories.[3,54] Among patients with CSPC, germline testing can have implications for prognosis, family counseling and cascade screening, and future treatment planning. However, guidelines do not currently explicitly recommend testing for patients with BCR. Among USPCC faculty, 53% recommend germline testing for BCR based on its intermediate status between localized and metastatic disease. The remainder indicated that they would only recommend germline testing for patients with strong family history or high-risk ancestry (37%) or for those with metastases (11%).

Metastatic Castration-Sensitive PCa

In the United States, the incidence of mCSPC is rising—a phenomenon that has been linked to the declining use of screening in the 2010s and improved imaging sensitivity, along with other epidemiologic factors.[55,56] For most men with mCSPC, prolonged systemic therapy is

recommended to improve survival and delay symptomatic progression. The armamentarium of systemic therapies from which to choose has rapidly expanded, and the role of prostate RT and MDT continues to evolve, introducing several critical decision points for patients and clinicians.

Systemic Therapy

Although ADT is the foundation of mCSPC systemic therapy, strong evidence now supports the benefits of treatment intensification with the addition of an ARPi (with or without docetaxel). With 9 positive clinical trials of treatment intensification,[57–72] substantial controversy exists around regimen selection. As of 2023, 4 doublet regimens and 2 triplet regimens have shown benefit in phase 3 clinical trials, and 2 additional trials have included subsets treated with triplet therapy. The panel discussed the merits of the various regimens and considerations for individualized selection.

Compared with ADT alone, doublet regimens have been shown to delay time to CRPC and significantly extend OS.[57,60,62,64,68,70,71] The magnitude of benefit for docetaxel doublets has been shown to vary according to clinical factors,[64,73] whereas ARPis have been shown to confer survival benefit in patients with mCSPC regardless of disease volume (ie, low vs high, with high typically defined as any visceral metastases or ≥ 4 bone metastases with ≥ 1 outside of the pelvis and spine) or metastatic timing (ie, synchronous vs or metachronous).[60,62] Given the better tolerability of ARPis and the widespread survival benefits regardless of disease subtype, the USPCC panel generally preferred the use of doublet therapy with an ARPi over doublet therapy with docetaxel, but acknowledged the potential financial toxicity that may limit access for some patients. Furthermore, data show that 10% to 20% of men with mCSPC survive for 10 years on ADT alone, indicating a subset of patients who may not need doublet therapy[74]; unfortunately, biomarkers are still needed to prospectively identify this population.

Triplet therapy with ADT, docetaxel, and an ARPi is a new option for mCSPC. In the ARASENS trial, triplet therapy with ADT, darolutamide, and docetaxel was compared with ADT plus docetaxel. The addition of darolutamide significantly improved OS in the overall mCSPC population (86% of whom had synchronous metastases).[72] When the results were stratified by disease volume, however, a clear survival benefit was reported only for high-volume disease.[75] ARASENS, however, did not use RT to the primary. In contrast, PEACE-1 included the option of prostate RT and showed that triplet therapy with ADT, abiraterone, and docetaxel with or without prostate RT improved OS over ADT and docetaxel in patients with synchronous mCSPC. When evaluated by metastatic burden, OS benefit in PEACE-1 was pronounced in patients with high-volume disease and had not yet reached maturity for low-volume disease.[58]

Metastatic timing is also an important consideration for triplet therapy because of its prognostic implications. Data from ENZAMET suggest that the addition of enzalutamide to ADT and docetaxel may confer a survival benefit only in patients with synchronous mCSPC, regardless of disease volume.[71] In a recent meta-analysis, ARPi doublets were superior for low-volume metachronous disease, whereas triplet therapy was superior for high-volume synchronous disease. The populations of low-volume synchronous and high-

volume metachronous disease comprised an intermediate-risk population with no clear differentiation in outcomes between doublets and triplets.[76]

The panel acknowledged that current clinical decision making for the application of triplet therapy is limited by the lack of ARPi doublet comparator arms and inconsistent use of RT across trials. RCT data suggest the benefits of triplet therapy should be considered within the context of disease volume and metastatic timing. Most of the USPCC faculty (95%) would not recommend triplet therapy for all patients with mCSPC. However, panel members were divided on the best way to identify patients most likely to benefit from triplet therapy, with some using trial inclusion criteria and others considering disease volume and metastatic timing. Most panel members agreed that predictive biomarkers for triplet therapy are urgently needed, particularly for patients with newly diagnosed low-volume disease that could represent early, aggressive disease.

Treatment of the Primary Tumor

Prostate RT is a guideline-recommended option for patients with low-burden synchronous mCSPC, with supporting evidence from the STAMPEDE and HORRAD trials.[3,28,77] In STAMPEDE, which included patients with synchronous disease, prostate RT extended time to treatment failure, but did not improve OS. In a subgroup of patients with low-burden disease, however, prostate RT significantly improved OS, with no QoL effects.[78,79] In the PEACE-1 trial, prostate RT in low-volume mCSPC delayed progression-free survival (PFS) and serious genitourinary complications.[80] In total, 86% of USPCC faculty “usually” recommended prostate RT for patients with low-burden mCSPC. USPCC faculty also acknowledged that several questions remained, including optimal patient selection, timing, RT dosing and schedules, and the role of ARPis with RT.

When considering prostate RT for mCSPC, the definition of low versus high-burden disease remains uncertain. CHAARTED and STAMPEDE defined high volume as the presence of any visceral metastases or ≥ 4 bone metastases, with ≥ 1 outside of the pelvis and spine.[79] However, STAMPEDE data showed that osseous burden and metastasis location can influence prostate RT effectiveness, with the greatest benefit reported for patients with < 4 bone metastases.[81] These data indicate some patients with CHAARTED-defined low-volume disease (eg, 5 bone metastases confined within the pelvis) may not benefit from prostate RT. Nonetheless, 68% of USPCC faculty preferred the CHAARTED definition of volume when considering prostate RT while only 8% considered number of bone metastases. When asked about the threshold number of bone metastases when offering prostate RT, 57% selected 5 bone metastases. Importantly, prostate RT studies to date have used conventional imaging to determine metastatic volume. As such, US guidelines and USPCC panelists consider conventional imaging SoC for selection of patients for prostate RT.

The ongoing SWOG S1802 trial (NCT03678025) will provide more information regarding optimal primary tumor treatment of mCSPC, including definitive surgery. In this phase 3 trial, standard systemic therapy is being compared with surgery or RT in patients with mCSPC.

Metastasis-Directed RT

Short courses of RT for palliation of isolated bone metastases can be considered in patients with oligometastatic disease (usually defined as < 5 lesions). RCTs have primarily evaluated MDT in the context of oligorecurrent PCa. The ORIOLE and STOMP trials showed that MDT improved ADT-free survival and PFS when compared with observation.[82,83] Furthermore, in the EXTEND phase 2 RCT, MDT combined with intermittent ADT was shown to improve PFS and extend time spent off of ADT.[84] Although OS benefits have not been conclusively shown, 76% of USPCC faculty felt ADT-free survival and longer ADT-free intervals were meaningful end points. In the SABR-COMET phase 2 RCT, which evaluated MDT added to standard systemic therapy in patients with PCa and other types of cancer, MDT was associated with a durable OS benefit.[85] However, the number of patients with PCa were imbalanced between the SABR-COMET study groups, and MDT-related toxicity led to 3 deaths. Most of the USPCC faculty usually or sometimes recommend MDT with or without ADT for patients with oligorecurrent disease by conventional imaging (92%) or by MTI (97%).

CONCLUSIONS

We have summarized some of the advances and challenges of managing the broad spectrum of CSPC discussed at the USPCC meeting. A potential limitation of this review is the lack of a standardized consensus process for developing questions and assessing results. At future USPCC meetings, a Delphi process will be beneficial for standardizing reports of consensus and controversy. Nonetheless, the USPCC meeting led to robust discussion of the novel technologies and treatments that have altered the definition of CSPC and its management. Key advances that most of the USPCC faculty endorsed for consideration included GECs and AI-based tools for patients in whom the results may affect treatment, PSMA PET for patients with unfavorable intermediate or high-risk disease and for BCR, triplet therapy for high-volume mCSPC, prostate RT in patients with low-volume mCSPC, and MDT for oligometastases.

With the wide array of treatment options now available, USPCC panel members endorsed the need for clinical trials focused on refining treatment approaches with currently approved agents. Biomarkers are needed to optimize treatment combinations, dosing, timing, and duration to improve outcomes for patients with CSPC, both in terms of oncologic outcomes and patient-reported outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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