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ORIGINAL ARTICLE

Clinical recommendations in the management of advanced prostate cancer: International Gastrointestinal, Liver and Uro-oncology (IGILUC 2019) experts

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Abstract

Purpose Advancements in the diagnosis and treatment of prostate cancer (PC) have rapidly progressed through the past years. Various factors should be taken into account while treating individual patients to ensure optimal and careful decision making. The purpose of this consensus review is to summarize the current practice patterns when managing patients with advanced prostate cancer (APC) as there is still a lack of or very limited evidence on its clinical management in some areas.

Methods Pre-defined questions were shared with experts prior to the consensus session that took place in Cairo, Egypt in April 2019 during the 8th International gastrointestinal, liver and uro-oncology conference (IGILUC). Voting was based mainly on the expert opinions of the panel after a thorough discussion and review of available evidence from guidelines or best evidence available concerning the topic at hand.

Results A strong consensus or unanimity was reached on 47% of the proposed questions. Notably, the panelists reached consensus on several topics based on high-level expert opinion. These findings contribute in several ways to our understanding of the management of PC and provide a basis for future recommendations. There was also a lack of consensus on other several topics, which suggests the need for further supporting data addressing these knowledge gaps.

Conclusion This review offers a thorough understanding of APC practice and offers insight on the various opinions shared amongst experts in the field that can serve as guidance regionally and deepens our understanding of disease management globally.

Keywords Prostate cancer · Consensus · Advanced prostate cancer · Metastatic prostate cancer

Introduction

Prostate cancer (PC) is the second most common cancer in men worldwide. In 2018, it was estimated to affect more than 1.3 million new cases globally. More than 359 thousand deaths were reported from PC in the same year [1]. In Egypt, the incidence of PC was ranked the 9th most common cancer [2]. The 8th International gastrointestinal, liver and uro-oncology conference (IGILUC) was held in April 2019 in Cairo, Egypt. A consensus session was held during this meeting and was devoted to discussing the debatable issues in the management of APC.

Methods

The session represented the evidence-based opinions and clinical experience of a group of experts in the management of prostate cancer. The aim of the final consensus statement was to help enhance knowledge and practice to provide a better service to patients. The panel included 19 regional and international various specialty experts from the Middle East, Africa, Europe and the United States of America (Table 1). Panel members addressed current controversial concepts in management of APC.

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Table 1 Panel members with their corresponding countries and specialties (in alphabetical order)

Name	Country	Specialty
Prof. Khaled AbdelKarim	Egypt	Clinical Oncology
Prof. Mohamed Abou Elfotouh	Egypt	Clinical Oncology
Prof. Claude Abouu	France	Urology
Prof. Mohamed Saad Alashry	Egypt	Clinical Oncology
Prof. Akram Assem	Egypt	Urology
Prof. Shouki Bazarbashi	KSA	Medical Oncology
Prof. Hesham Elwakil	Egypt	Clinical Oncology
Prof. Amr Emara	UK	Urology
Prof. Lobna Ezz El-Arab	Egypt	Clinical Oncology
Prof. Jorge Garcia	USA	Medical Oncology
Prof. Ola Khorshid	Egypt	Medical Oncology
Prof. Axel Merseburger	Germany	Urology
Prof. Nicolas Mottet	France	Urology
Prof. Abbass Omar	Egypt	Clinical Oncology
Prof. Stephane Oudard	France	Clinical Oncology
Prof. Mack Roach	USA	Radiation Oncology
Prof. Ahmed Selim	Egypt	Clinical Oncology
Prof. Samir Shehata	Egypt	Clinical Oncology
Prof. Hesham Tawfik	Egypt	Clinical Oncology

Prior to the meeting, questions were formulated and sent to the participating experts, where their recommendations and amendments were considered. In the meeting, the questions were presented as multiple choice answers. The panel experts chose their preferred management options via an electronic voting system. This assured the confidentiality of the votes of the participating panelists. In case the participating expert chose not to answer the presented question, the 'abstain' choice was the available option. A consensus was considered when there was a majority vote of more than 75% of the panelists' votes, after excluding the 'abstain' votes. All questions were answered with several assumptions, including the absence of any contraindications to the management options, the absence of any the cost or access restrictions, and the availability of the therapeutic options presented.

Discussion

Localized prostate cancer

Adjuvant radiation therapy after RP

Previous literature suggested the benefit of immediate radiotherapy (RT) for pT3 prostate cancer patients, with postoperatively undetectable PSA, in reducing the risk of biochemical progression [3–5]. Adjuvant RT is not routinely recommended in the absence of high-risk pathological features including positive surgical margins or seminal vesicle involvement. In pN0 patients with undetectable postoperative PSA, 88.5% of the panel advised that the administration of adjuvant RT in case of seminal vesicle involvement, while 80% of the panel recommended the adjuvant RT in case of positive surgical margins involvement. In case of high Gleason score ≥ 8 or ISUP grade group ≥ 4 as the only high-risk feature, 80% of the panel advised against the administration of adjuvant radiotherapy in these patients. This is quite different from the APCCC vote in 2017 (Table 2), where no consensus was reached regarding these indications [6]. However, the recent unveiling of the RADICALS-RT trial [7] and the ARTISTIC meta-analysis [7] have shed light on this long-standing grey area. Both studies found that sparing patients adjuvant RT was acceptable in favor of observation and early salvage RT. The outcome of freedom-from-distant metastases at 10 years from the RADICALS-RT trial still requires longer follow-up. However, this makes us wonder if this question will continue to be posed to experts in future consensus queries.

Adjuvant radiation therapy after RP for pN1 prostate cancer

There is no current agreement regarding the optimum management of patients with pN1, especially after extended lymph node dissection. Touijer et al. found that a considerable number of PC patients with lymph node metastasis remained free of disease 10 years after RP and eLND alone, especially patients with Gleason score < 8 and low nodal metastatic burden [8]. Thus the EAU guidelines stated three options for patients with pN + disease after eLND, based on nodal involvement characteristics ranging from observation if after eLND < 2 nodes with microscopic involvement are found having no extranodal extension coupled by a PSA < 0.1 ng/mL, adjuvant ADT alone and thirdly adjuvant ADT with added radiotherapy [9]. When our panel was asked about the possible role of adjuvant RT, in post-prostatectomy patients with pN1 and no local adverse features (T3b or R1) and with undetectable PSA (ultrasensitive < 0.02 ng/ml), 83% of the panel advised against giving adjuvant RT in these patients. In the 2017 APCCC, no consensus on adjuvant RT in pN1 disease was reached with 43% of the panel not endorsing for RT in this setting [6].

ADT and abiraterone for castration-sensitive N1M0 PC

The STAMPEDE trial, overall survival (OS) and failure-free survival were significantly increased with the addition of abiraterone to ADT in both metastatic and non-metastatic patients [10] thus it was incorporated in the NCCN guidelines [11]. This question was not included in the APCCC as it was not yet released at the time [6]. Even though the

Table 2 Statements that received panel consensus (> 75% agreement) compared to their equivalent in the 2017 APCCC consensus

Statement	Agreement (%)	2017 APCCC (%)
Extended lymph node dissection is recommended in patients with cN0 cM0 high-risk prostate cancer patients undergoing prostatectomy	100	84
In pN0 patients with undetectable postoperative PSA, adjuvant RT is recommended in case of seminal vesicle involvement	88	38%
In pN0 patients with undetectable postoperative PSA, adjuvant RT is recommended in case of positive surgical margins involvement	80	48% (any R1) 27% (multifocal or extensive R1)
In pN0 patients with undetectable postoperative PSA, adjuvant RT is *not recommended* in patients with high Gleason score (≥ 8) or grade group (≥ 4) as the only high-risk feature	80	55
Adjuvant RT is *not recommended* in patients with pN1 and no local adverse features (T3b or R1), undetectable PSA (ultrasensitive < 0.02 ng/ml) and underwent prostatectomy	83	43
LHRH antagonists are the preferred regimen for medical castration in patients with impending spinal cord compression	91	NS
PSMA is the recommended tracer in mCNPC undergoing PET/CT. [2017 APCCC] PSMA is the recommended tracer in case of a PET/CT in men with apparent oligometastatic castration-naïve disease:	93	76
In case of non-metastatic CRPC patients with negative conventional imaging & a PSADT ≤ 10 months, either apalutamide or enzalutamide are valid additional treatment options along with ADT	100	NS
Radiotherapy is the preferred local therapy choice in newly diagnosed oligometastatic PC patients	82	45
AR-V7 testing is not recommended to be done to further tailor treatment decision in patients with metastatic PC [2017 APCCC] For liquid biomarkers, AR-V7 testing is not recommended in routine clinical practice in CRPC	78	96
Either abiraterone or enzalutamide are recommended as the first-line treatment option for asymptomatic or minimally symptomatic metastatic CRPC patients who did not receive docetaxel in the castration-sensitive setting	100	86
Either abiraterone or enzalutamide is the first-line treatment option in patients with asymptomatic or minimally symptomatic metastatic CRPC who previously received docetaxel in the castration-sensitive stage	90	90
Taxanes are the recommended second-line option in patients with symptomatic metastatic CRPC and developed an upfront resistance on first-line abiraterone or enzalutamide	93	96
Taxanes are the recommended second-line option in patients with symptomatic metastatic CRPC and progressed after the initial response (acquired resistance) to first-line abiraterone or enzalutamide	92	90
Either abiraterone or enzalutamide is recommended as the second-line treatment of choice for asymptomatic or minimally symptomatic patients with metastatic CRPC who progressed on first-line docetaxel	93	92
Either abiraterone or enzalutamide is recommended as the second-line treatment of choice for symptomatic patients with metastatic CRPC who progressed on first-line docetaxel	92	76
In diabetic patients with metastatic CRPC receiving novel anti-androgens, enzalutamide is recommended therapeutic option	85	84

STAMPEDE trial results were in favor of this regimen, 67% of the panel advised against adding abiraterone with ADT in castration-sensitive N1M0 prostate cancer. Only 17% of the panelists agreed on this regimen and another 17% favored this regimen considering the patients' age is less than 70 years.

Imaging techniques

PSMA PET/CT, including ^{68}Ga-PSMA-11, is considered valuable in diagnosing advanced prostate cancer especially in patients with low PSA levels (mean PSA < 2 ng/mL) and skeletal lesions [12, 13]. Choline-based PET/CT, using ^{11}C and ^{18}F-choline tracers, are also used in detecting various stages of prostate cancer and was found superior to conventional imaging methods in detecting metastatic lesions with biochemical recurrence [12, 14]. Fluciclovine, 18F-FACBC is also used to trace prostate cancer in detecting metastatic lesions [12, 15, 16]. Around 55% of the panel recommended PET/CT scan, including PSMA, choline, and fluciclovine radiotracers, as the imaging modality of choice in the staging of advanced PC. While the rest of the panel (45%) agreed that conventional imaging, including CT scan, MRI and bone scan was the modality of choice in advanced PC staging. Interestingly, whole-body MRI was not recommended by any of the panelists. Choosing from the previous three tracers, 93% of the panel advised using PSMA as the recommended tracer in mCNPC undergoing PET/CT, while only 7% chose choline as the preferred tracer and none of the panelists chose fluciclovine in these patients.

Metastatic castration-naïve disease

Medical castration

Management of PC has a solid base of ADT usage [17]. Regarding the preferred method for medical castration, the majority of the panel (54%) advised that either LHRH agonists or antagonists can be given as a medical castration regimen. Only 15% of the panel preferred using an LHRH agonist, while 23% preferred using an LHRH antagonist. However, only 8% of the panelists believe that a combination of LHRH agonist plus antiandrogen is the preferred regimen.

The use of LHRH agonists or combination therapy with LHRH agonists was linked to a higher risk of cardiovascular (CV) events [18]. Several studies compared CV morbidity after the administration of GnRH agonists and antagonists in patients with preexisting cardiovascular diseases. Pooled data from 6 randomized studies proved that after 1 year of administration, GnRH antagonists had 56% fewer cardiac events when compared to GnRH agonists (HR, 0.44; 95% confidence interval, 0.26–0.74; $p = 0.002$) [19]. Regarding medical castration in patients with previous cardiovascular disease, more than half of the panelists (55%) preferred using an LHRH antagonist in this patient group. Still, 18% advised that either LHRH agonists or antagonists can be successfully used in this group. Another 18% of the panel preferred using LHRH agonists, while only 9% believed that a combination of LHRH agonist plus antiandrogen is the preferred option.

As for the preferred regimen for medical castration in patients with impending spinal cord compression, 91% of the panel recommended LHRH antagonists as the preferred regimen in these patients, while only 9% advised that LHRH agonist plus antiandrogen can be given in these patients. This consensus was related to the testosterone surge associated with LHRH agonists in advanced prostate cancer-causing spinal cord compression, bone pain, urinary retention, ureteral obstruction, and even death [20]. Since 2017, the EAU guidelines recommended LHRH antagonists in patients with metastatic prostate cancer with impending spinal cord compression [21]. Degarelix, a third-generation GnRH antagonist, was suggested to be the preferred treatment option in this patient subgroup [22]. It also spares the administration of concurrent anti-androgens, with its potential toxic safety profile, which is usually required with LHRH agonists to prevent the serious flare effects including spinal cord compression [23].

Management of metastatic CNPC

High-volume/risk disease In patients with metastatic high-volume CNPC, ADT is considered the cornerstone of management. ADT can be administered along with second-generation antiandrogen agents, including abiraterone or enzalutamide, or with docetaxel [11]. The chemo-hormonal recommendation was supported by the results of the ECOG 3805 CHAARTED and the STAMPEDE trials [24, 25]. These results differed from the GETUG-AFU 15 trial, where only a PFS benefit was reached from adding docetaxel to ADT [25]. Adding abiraterone acetate to ADT in patients with high-risk, metastatic, castration-naïve PC is supported by the results from the LATITUDE and the STAMPEDE trials which showed better OS results than ADT alone in both trials [26, 27].

In addressing high-volume/risk disease criteria from CHAARTED and LATITUDE were put into consideration. Since the meeting, approvals have extended to enzalutamide and apalutamide [26, 28]. Regarding the optimal therapy choice for men with high-volume metastatic castration-sensitive PC, the majority of the panel (57%) believed that continuous ADT with abiraterone acetate is the preferred option for these patients. Twenty-nine percent of the panel recommended continuous ADT with docetaxel, while only 14% of the panelists choose continuous ADT alone. None of the panel members believed that continuous combined ADT had a role in these patients.

The APCCC showed a 96% strong consensus favoring docetaxel in de novo mCNPC high-volume diseases, as defined by CHAARTED, provided that no contraindications for its implementation existed. Abiraterone acetate was not posed as a choice in mCNPC in the 2017 consensus [6]. Furthermore, the relevance of the disease burden dilemma has sharply declined after recent updates and analysis dispelled the notion that chemotherapy was the most suitable choice for high-volume de novo mCNPC and provided evidence of its benefit irrespective of metastatic burden [27, 29].

Radiation therapy to the primary tumor was not recommended in men with high-volume metastatic disease according to the HORRAD and STAMPEDE trials which showed no improvement in OS after the administration of EBRT to the primary tumor as a combination regimen with the standard systemic therapy. Worthy of note, that the STAMPEDE did find a benefit for local irradiation in low-volume CNPC [30, 31].

The majority of the panel (60%) advised against local therapy to the primary tumor as an adjunct to the systemic treatment in newly diagnosed patients with high-volume castration-sensitive PC, while 40% of the panelists believed there could be a role for local RT in these patients.

Similarly, 52% of the 2017 APCCC panel did not endorse primary tumor therapy as an adjunct to systemic therapy in men with de novo high-volume mCNPC who were not symptomatic from their primary [6].

Low volume/risk disease As for patients with low-volume castration-sensitive metastatic PC, 44% of the panel recom-

mended the administration of continuous ADT alone, while 33% recommended continuous ADT along with abiraterone acetate as the preferred treatment regimen. Only 11% preferred continuous ADT and docetaxel for these patients; however, another 11% of the panelists preferred continuous combined ADT (with a first generation AR antagonist). The panels' choice of continuous ADT alone was supported by the results of the CHAARTED study. The subgroup analysis of patients with low-volume disease receiving docetaxel and continuous ADT showed no additional benefit compared to ADT alone (HR, 1.04; 95% CI 0.70–1.55; $p < 0.86$) clarifying the choice for this low-volume group [24]. Intriguingly, rapidly advancing data presented from an extended follow-up provided benefit for chemotherapy inclusion earlier even for low-volume men. This dispels the previous futility notion in this subset with a "hit them early and hit them hard" attitude for maximum gain [27]. Additionally, a post hoc STAMPEDE analysis found that abiraterone improved OS in low-risk patients with a 3-year OS benefit of 4.4% (HR 0.66, $p = 0.041$) compared with ADT alone. Although it is less beneficial for high volume patients (3-year OS benefit 19.7%), yet still it is an improvement [29].

As therapeutic options have increased, the "best" choice for individual patients remains to be defined and a consensus including two appropriate therapies (guideline approved at the time) would depend on the panelist's preference and in real life availability and patient's choice.

The 2017 APCCC recommended the addition of docetaxel for men with low-volume de novo metastatic CNPC as per CHAARTED criteria in the majority of cases by 29% and in a minority by 65% [6]. This very question was further analyzed [32] according to the association of panelists` specialization and geographical allocation to the consensus results. A proven difference in the preference for docetaxel (in a majority) in low-volume men was found. By region, preference was 53% in Europe, 13% in North America, and 22% in other regions. Docetaxel preference was demonstrated with possible differences in other matters such as specialty (urology: 27%, medical oncology: 23%, radiation oncology: 45%). This finding reflects the diverse patterns adopted by not only experts, but by physicians from various areas in the world. So, as some pointed out during the meeting that ADT alone would be regarded as under-treatment, others found it sufficient in what they regarded as a more or less "indolent" disease.

Metastatic castration-resistant prostate cancer

First-line therapy

First-line therapy in asymptomatic CRPC with no prior chemotherapy There was a unanimous agreement (100%) between the panel members that either abiraterone or enzalutamide are recommended as the first-line treatment option for asymptomatic or minimally symptomatic metastatic castration-resistant PC those who did not receive docetaxel in the castration-sensitive setting. The panel's decision was supported by the results of the COU-AA-302 and PREVAIL trials [33, 34]. The 2017 APCCC [6] issued a consensus that asymptomatic men with mCRPC should receive first-line abiraterone or enzalutamide if prior castration-naïve treatment given was with only ADT (86%).

First-line therapy in symptomatic CRPC with no prior chemotherapy In the TAX 327 and the SWOG9916 trials placed docetaxel as the frontline therapy in CRPC [35, 36]. The majority of the panel (71%) agreed that docetaxel should be used as the first-line treatment option in patients with symptomatic metastatic CRPC and did not previously receive docetaxel. However, 14% of the panel chose either abiraterone or enzalutamide as the first option in these patients and 14% stated that there is no specific option preferred in these patients. The APCCC 2017 referred to this issue practically by acknowledging the fact that most men received docetaxel in the first-line setting and that further management remains undefined by prospective data. However, in this particular instance, a 46% vote was set for docetaxel in symptomatic men who did not receive it in the castration-naive setting [6].

First-line therapy in asymptomatic mCRPC with prior chemotherapy in the mCNPC Recently several agents have been incorporated into the CNPC scene [10, 26, 28, 37] making further treatment decisions difficult due to lack of prospective data [10, 37], or relatively small numbers of patients that received prior docetaxel [26, 28] and the relatively short follow-up period required to draw firm conclusions. [6].

The 2017 APCCC panel recommended at a 90% vote that asymptomatic men with mCRPC should receive first-line abiraterone or enzalutamide if previous docetaxel in the castration-naïve treatment phase was given [6]. This was consistent with the decision of the current panel members. There was a consensus (90%) that patients with asymptomatic or minimally symptomatic metastatic CRPC who previously received docetaxel in the castration-sensitive stage, should receive abiraterone or enzalutamide as the first-line treatment option in this patient profile. Only 10% recommended cabazitaxel as the first-line treatment option. The choice for cabazitaxel after docetaxel in mCRPC is supported by the TROPIC trial [36] but its position after mCNPC docetaxel remains unclear.

First-line therapy in symptomatic mCRPC with prior chemotherapy in the mCNPC In case the patient with metastatic CRPC is symptomatic, and previously received docetaxel in the castration-sensitive stage, 42% of the panel preferred

either abiraterone or enzalutamide as first-line treatment, while 25% preferred cabazitaxel. Yet, 33% believed that no preferred option specifically for this group of patients. Cabazitaxel, being a member of the taxane family, is considered a derivative of docetaxel.

Gillessen et al. reported in the 2017 APCCC recommendations that in symptomatic men who received upfront chemo-hormonal therapy in the castrate naïve stage, the majority of the votes at 73% favored abiraterone or enzalutamide, 19% cabazitaxel, 6% docetaxel, and 2% only chose Radium-223. However, given the same circumstances, if progression was within 6 months of docetaxel completion, a slight decrease in the abiraterone/enzalutamide choice occurred (57%) with a mild increase for cabazitaxel usage (27%) and of course rechallenge was zero. The early relapse scenario was not posed in the current report of this consensus [6].

Second-line therapy in mCRPC

Second-line therapy in asymptomatic CRPC with prior novel anti-androgens The latest guidelines recommended various treatment options in patients with metastatic CRPC who progress on abiraterone or enzalutamide. Therapy options include docetaxel, radium-223, sipuleucel-T -and enzalutamide or abiraterone (depending on the primarily used drug) [9, 11]. However, there is a debate around the choice of second-line treatment. Another factor that alters treatment decision is whether resistance to abiraterone or enzalutamide occurred upfront or there was an initial response and acquired resistance developed. After upfront resistance and progression on first-line abiraterone or enzalutamide in patients with asymptomatic metastatic CRPC, 60% of the panel recommended a taxane (docetaxel) as the preferred second-line option, while 20% advised sipuleucel-T in these patients. Twenty percent of the panel recommended switching between abiraterone and enzalutamide as second-line option depending on the previously used drug. In case of asymptomatic metastatic CRPC patients who progressed after an initial response on first-line abiraterone or enzalutamide (acquired resistance), more than half of the panel (55%) recommended taxane as the preferred second-line option, while 9% preferred abiraterone or enzalutamide depending on the used drug. The rest of the panel (36%) believed that there is no specifically preferred option for these patients.

Second-line therapy in symptomatic CRPC with prior novel anti-androgens The decision of the panel differed completely when the patient with metastatic CRPC developed symptoms such as visceral metastasis. Whether the resistance to abiraterone or enzalutamide was upfront or acquired of the initial response, there was a consensus around taxane, preferably docetaxel, being the recommended second-line treatment option for both of the patient profiles. Regarding patients with symptomatic metastatic CRPC and developed an upfront resistance on first-line abiraterone or enzalutamide, 93% believed that taxane is the preferred second-line option, while the rest believed that there is no specifically preferred second-line option for these patients. Similarly, 92% of the panel recommended taxane as the preferred second-line option and only 8% believed that there is no preferred option for the same patients but with acquired resistance to abiraterone or enzalutamide after an initial response.

Second-line therapy in CRPC with prior chemotherapy Abiraterone and enzalutamide are considered the standard of care in patients with metastatic CRPC who received and progressed on docetaxel. Both drugs showed benefits in patients according to the COU-AA-301 trial and the AFFIRM trial [38, 39]. There was a consensus between panel members regarding asymptomatic or minimally symptomatic patients with metastatic CRPC who progressed on first-line docetaxel, where 93% of the panel recommended either abiraterone or enzalutamide as the second-line treatment of choice for these patients. Only 7% of the panelists preferred cabazitaxel after docetaxel. The panel members had a similar consensus regarding symptomatic metastatic CRPC patients who progressed on first-line docetaxel, where 92% of the panel recommended either abiraterone or enzalutamide as the preferred second-line option. Also, 8% of the panelists advised the administration of a taxane in these patients.

Third-line therapy

Regarding progression after second-line management of metastatic CRPC, the guidelines recommended either of the previously mentioned regimens depending on their previous administration [9, 11]. When our panel members were addressed with the recommended third-line therapeutic option in patients who progressed on second-line therapy, the majority of the panel (73%) mentioned that cabazitaxel as a preferred option. While 9% of the panel recommended abiraterone or enzalutamide provided that they were not administered before. Another 9% of the panelists believed platinum-based chemotherapy is the preferred regimen and the rest of the panel members believed there is no specific option preferred as the third-line option.

Special considerations in novel anti-androgens

Low-dose vs. standard-dose abiraterone acetate A recent study conducted on 72 patients with CRPC receiving abiraterone acetate were randomly assigned to low-dose abiraterone acetate (250 mg with a low-fat meal) and the standard

dose (1000 mg in a fasting state). Low-dose abiraterone was found to be non-inferior to the standard dose in relation to the PFS and the PSA response [40]. Only 33% of the panel members considered administering abiraterone at a reduced dose (250 mg/day) with a low-fat meal versus the standard dosage in a fasting state, while 67% did not recommend the reduced dose of abiraterone for patients with metastatic CRPC.

Conclusion

The main aim of this meeting was to have a joint effort between international and regional experts to reflect the similarities or differences that may exist in the perceived management of certain debatable areas of interest. This consensus was carried out on a much smaller scale than the APCCC in the number of queries posed and time allotted, nevertheless, it was thought to represent briefly the major areas encountered in the clinical setting. Although some agreed-upon statements were contradicting the common literature, however, this forum of expert opinions gave a fresh perspective at key issues in the management of PC. These recommendations help promote the current guidelines based on best practices from experts in this field.

A universal agreement in specific areas or even one item occasionally seems difficult, guidelines set the pathway but sometimes several options exist and choosing the ideal therapy becomes cumbersome. Many times advice is sought in the areas lacking sufficient evidence. The panel reached a consensus on several topics included in Table 2.

However, the panel did not reach a common consensus on other several topics which may help in the understanding of the difference of expert clinician practices and opinions. The panel did not reach a consensus across various topics of special situations including the role of adjuvant RT and novel anti-androgens after RT in locally advanced stages, indications of salvage prostatectomy, the administration of adjuvant ADT after RT, preferred medical castration method, imaging modality in advanced PC staging; definition of oligometastatic PC, therapeutic options in low- and high-volume metastatic castration-sensitive PC, certain considerations in symptomatic metastatic CRPC, special conditions indicating novel anti-androgens and their preference, third-line options for metastatic CRPC, and finally administration differences of abiraterone.

The lack of consensus in these previous vital topics suggests the need for further supporting data addressing these knowledge gaps. The panel recommended that these areas of disagreement should serve as a potential for further investigation. The generalizability of these results is subject to certain limitations as they are based on high-level expert opinion; however, these findings contribute in several ways to our understanding of the management of PC and provide a basis for future recommendations.

Though not all regions are represented, the current report represents an expert international opinion combined with a local outlook on the issues at hand in the prostate consensus reflecting variations in management of this disease. So as we shift toward more personalized treatment in oncology and tailor therapy according to clinical and molecular signatures, we should also take into consideration geographic trends in the management of cancer patients.

Future directions to promote these consensus meetings around the world regularly and with the presence of international experts serves as a forum, where the many faces of prostate cancer as a whole can be appreciated and the rapid advancements in the field recapped.

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Author contributions HE: Project development and manuscript editing. NM: Manuscript editing. AM: Manuscript editing. TO: Project development. MEED: Project development and manuscript editing.

Compliance with ethical standards

Involvement of human participants and/or animals This article does not contain any studies with human participants or animals performed by any of the authors.

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