Management of metastatic hormone-sensitive prostate cancer in Hong Kong: Aligning local practice with recommendations of the Advanced Prostate Cancer Consensus Conference

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A survey and meeting of experts in Hong Kong identified differences between local clinical practice for metastatic hormone-sensitive prostate cancer (mHSPC) and the global standards set by the Advanced Prostate Cancer Consensus Conference (APCCC). In this newsletter, we highlight the differences found and discuss steps to close these gaps.

Introduction

Prostate cancer is the third most common cancer among men in Hong Kong and the fourth most common cause of cancer death.[1] The latest guidance on management is summarised in consensus statements from the APCCC 2022, an international meeting that defined consensus across areas of clinical controversy.[2,3] In Hong Kong, local clinical guidelines were last updated in 2019[4], and experience among oncologists suggests there are discrepancies between local clinical practice for mHSPC and international standards. To understand these discrepancies and discuss strategies to better align local practice with international standards, the Hong Kong Society of Uro-Oncology (HKSUO) and the Hong Kong Urological Association (HKUA) coordinated an online survey of local experts and a follow-up committee meeting to evaluate and discuss the gaps between local practice and APCCC guidance. The results are summarised herein.

Meeting description/methods

In February 2023, local experts in the management of prostate cancer participated in an online survey comprising 38 questions and multiple choice responses from the APCCC consensus for the management of mHSPC and metastatic castration-resistant prostate cancer (mCRPC). Consensus was defined as an answer option that achieved ≥75% agreement and strong consensus as an option with ≥90% agreement. Following the online survey, an expert committee meeting was held in February 2023 to identify and discuss discrepancies between the Hong Kong and global opinions.

Discussion of identified discrepancies in practice for mHSPC

Survey responses were received from 28 (64%) oncologists and 16 (36%) urologists. Notable discrepancies were identified in 7/14 (50%) of questions relating to the management of mHSPC (Table). The questions below are numbered as per the original APCCC publication.[3]

Question	Options	Response (%)	
		APCCC (n=105)	HK (n=44)
Q74. What is your general treatment recommendation for the majority of patients with synchronous low-volume (on conventional imaging or unequivocal on NGI) mHSPC?	**1.** Combination therapy (ADT plus additional systemic therapy and/or local radiotherapy)	98.1	72.7
	2. ADT alone	1.0	27.3
	3. Abstain/unqualified to answer	1.0	0.0
Q77. In which patients with metachronous mHSPC that are chemotherapy fit, do you recommend the triplet therapy ADT plus docetaxel plus ARPI?	**1.** In the majority of patients independent of disease volume	4.8	56.8
	2. Only in high-volume patients	55.2	38.6
	3. I usually do not recommend this combination	35.2	2.3
	4. Abstain/unqualified to answer	4.8	2.3
Q78. In the majority of patients with synchronous high-volume (on conventional imaging or unequivocal on NGI with corresponding sclerotic lesions on CT if PSMA PET) mHSPC, what is your preferred systemic treatment in addition to ADT?	**1.** ARPI as sole additional therapy	31.4	65.9
	2. Docetaxel as sole additional therapy	5.7	0.0
	3. Docetaxel plus an ARPI	58.1	20.5
	4. ADT alone	0.0	2.3
	5. Abstain/unqualified to answer	4.8	11.4
Q79. What is your recommended treatment strategy for the majority of patients with mHSPC that have low-volume disease on conventional imaging but high-volume on next-generation imaging?	**1.** Treat as per high-volume	45.7	90.9
	2. Treat as per low-volume	51.4	9.1
	3. Abstain/unqualified to answer	2.9	0.0
Q81. In the majority of patients with synchronous low-volume mHSPC, where you have decided for triplet systemic therapy (ADT plus docetaxel plus ARPI) do you recommend radiation therapy of the primary tumour in addition?	**1.** Yes	42.9	47.7
	2. No	10.5	43.2
	3. Abstain/unqualified to answer (including I do not use triplet systemic therapy)	46.7	9.1

Q83. If you recommend triplet therapy (ADT plus docetaxel plus an ARPI) in patients with mHSPC, what is your preferred strategy?	**1.** Sequential administration (docetaxel completed first, as for TITAN, ARCHES)	**13.3**	**45.5**
	2. Concurrent administration (as for ARASENS, PEACE-1, ENZAMET)	**59.0**	**50.0**
	3. Abstain/unqualified to answer (including I do not use triplet systemic therapy)	**27.6**	**4.5**
Q85. In patients with high-volume mHSPC, do you recommend the addition of docetaxel alone to ADT (assuming that ARPIs are available)?	**1.** Yes, in the majority of patients	**10.5**	**59.1**
	2. Yes, but only in a minority of selected patients	**39.0**	**36.4**
	3. No	**47.6**	**4.5**
	4. Abstain/unqualified to answer	**2.9**	**0.0**

Table. Results of APCCC and Hong Kong consensus surveys on the management of mHSPC

The APCCC voting results are reproduced from Gillessen, et al. 2023.[3] ADT, androgen deprivation therapy; APCCC, Advanced Prostate Cancer Consensus Conference; ARPI, androgen receptor pathway inhibitor; CT, computed tomography; HK, Hong Kong; mHSPC, metastatic hormone-sensitive prostate cancer; NGI, next-generation imaging; PET, positron emission tomography; PSMA, prostate-specific membrane antigen.

Q74. What is your general treatment recommendation for the majority of patients with synchronous low-volume (on conventional imaging or unequivocal on next-generation imaging [NGI]) mHSPC?

Androgen deprivation therapy (ADT) plus systemic therapy and/or local radiotherapy was supported by a strong consensus among APCCC respondents (96.2%), and although this option was the most common among local experts (72.3%), it did not reach the consensus threshold, with 27.3% of panellists selecting ADT monotherapy. This difference may be due to the positioning of ADT plus radiotherapy to the primary cancer as the standard treatment option for most low-volume mHSPC patients in Hong Kong. Adding systemic therapy to ADT is supported by TITAN and other studies, which showed a significant overall survival benefit of combination therapy versus ADT alone.[5,6] Although the local oncology community is familiar with these studies, the lower support for combination therapy may be due to the lack of reimbursement for novel hormonal agents in the public healthcare system. Other barriers may be logistics or the adverse event profile of combination therapy, even though local clinical experience suggests radiotherapy is well tolerated. Additionally, older patients in Hong Kong are often satisfied with reductions in prostate-specific antigen following ADT and are reluctant to add radiotherapy due to fears of adverse events. Better patient education on the balance of efficacy and safety of adding radiotherapy may address this hesitancy.

Q77. In which patients with metachronous mHSPC who are chemotherapy fit, do you recommend the triplet therapy ADT + docetaxel + androgen receptor pathway inhibitor (ARPI)?

Compared with APCCC respondents, Hong Kong experts had a stronger preference for triplet therapy in most patients (4.8% vs 56.8%). Patients with metachronous mHSPC have failed local treatments, their systemic recurrence is usually low-volume and less aggressive. Experts who selected Option 3 *(I usually do not recommend this combination)* expressed a preference for ADT plus either chemotherapy or a novel hormonal agent instead of triplet therapy. Evidence supporting triplet therapy in mHSPC is available from studies such as PEACE-1, ARASENS, and others[7-9], but these studies enrolled patients with exclusively or predominantly synchronous disease, not metachronous. This result suggests local experts may benefit from education on the data for triplet therapy and the differences between metachronous and synchronous disease.

Q78. In the majority of patients with synchronous high-volume (on conventional imaging or unequivocal on NGI with corresponding sclerotic lesions on computed tomography [CT] if prostate-specific membrane antigen [PSMA] positron emission tomography [PET]) mHSPC, what is your preferred systemic treatment in addition to ADT?

Among Hong Kong experts, adding ARPI only to ADT for patients with synchronous high-volume mHSPC was considerably more popular than among global experts (65.9% vs 31.4%). Adding docetaxel + ARPI (i.e. triplet therapy) was less popular with Hong Kong experts compared with APCCC respondents (20.5% vs 58.1%). Patients with this profile are common in Hong Kong, and data, such as the ARASENS study of darolutamide or placebo to ADT + docetaxel, demonstrate a survival advantage of triplet therapy over ADT plus chemotherapy.[8] However, there are no data to show an advantage of triplet therapy over ADT + ARPI. The preference for adding ARPI alone over adding ARPI + chemotherapy to ADT may be due to the better tolerability profile of the former. Furthermore, many local patients fitting this profile are elderly and less fit for chemotherapy; therefore ADT + ARPI would be preferred to triplet therapy. In an analysis of patients with visceral metastases from six phase III trials, adding an ARPI after chemotherapy showed minimal therapeutic benefit.[10] These patients may have low hormone sensitivity and may be more suited to chemotherapy, thus explaining the low preference for triplet therapy in Hong Kong. Approximately 30% of Hong Kong urologists abstained from voting — this may reflect a tendency to rely on oncologists for such decisions, or incomplete knowledge of recent studies. Fostering closer collaborations between oncologists and urologists, including multidisciplinary team meetings, may improve this situation.

Q79. What is your recommended treatment strategy for the majority of patients with mHSPC that have low-volume disease on conventional imaging but high-volume on NGI?

Unlike the APCCC, the Hong Kong experts reached a strong consensus (90.9%) in favour of treatment as per high-volume. This scenario is unlikely in Hong Kong because most patients would have received a bone scan and would not need a subsequent PET scan (or vice versa). Interpretation of PSMA PET scans is highly variable, operator-dependent, and may be confounded by comorbidities.[11,12] If the result of PSMA PET scan is equivocal, additional parameters such as the maximum standardised uptake volume (SUV_{max}), site of metastasis, Gleason score, and additional conventional imaging should inform the decision. When patients have equivocal PSMA PET findings, a potential therapeutic approach would be doublet therapy with ADT and an ARPI, which has proven efficacy in both low- and high-volume mHSPC. Another approach could be the initiation of ADT followed by a repeat PSMA PET scan to evaluate their response.

Q81. In the majority of patients with synchronous low-volume mHSPC, where you have decided for triplet systemic therapy (ADT + docetaxel + ARPI), do you recommend radiotherapy of the primary tumour in addition?

Hong Kong experts expressed a stronger opinion against radiotherapy compared with the APCCC (43.2% vs 10.5%). Clinical experience in Hong Kong suggested triplet therapy would be unsuitable for most patients; such patients would need to be carefully selected based on their higher general well-being, younger age, and pattern of low-volume disease. The initial response to triplet therapy would be an important factor when choosing which patients should receive add-on radiotherapy for local control. However, the evidence base supporting prostate primary radiotherapy in mHSPC patients receiving triplet therapy is limited, which may explain the absence of a strong preference for this approach.

Q83. If you recommend triplet therapy (ADT + docetaxel + an ARPI) in patients with mHSPC, what is the preferred strategy?

In Hong Kong, there was a higher preference for sequential rather than concurrent administration compared with the APCCC (45.5% vs 13.3%). The APCCC result is likely due to the positive results of the concurrent approach in the ARASENS, ENZAMET and PEACE-1 studies.[7,8,13] The lower preference for concurrent administration in Hong Kong may be the expectation of a worse tolerability profile than with sequential administration.

Q85. In patients with high-volume mHSPC, do you recommend the addition of docetaxel alone to ADT (assuming that ARPIs are available)?

The Hong Kong expert group expressed a stronger preference for the addition of docetaxel alone to ADT in the majority of patients compared with the APCCC consensus (59.1% vs 10.5%), with notable differences between HK urologists and oncologists (81.3% vs 46.4%, respectively). A potential explanation is that oncologists may be more familiar with triplet therapy than urologists. Therefore, they may prefer this option, or ADT + ARPI, to ADT + docetaxcel.

Conclusions

Although this study may be limited by the sample size, it included 28 of 174 (16%) registered clinical oncologists and 16 of 150 (11%) registered urologists in Hong Kong and is likely to be broadly representative of clinical practice. Participants were instructed not to consider resource limitations and reimbursement in their answers, but these factors may still indirectly influence respondents by reducing their familiarity with some options. Resource limitations would lead to a preference in favour of lower-cost agents such as chemotherapy and against newer, more expensive agents such as ARPI or poly (ADP-ribose) polymerase inhibitors. Therefore, expanded reimbursement support from the region's government and expanded access programs from industry have the potential to better align local practice with global standards. Furthermore, there may be a need to enhance the training of local experts on the differences between metachronous and synchronous disease. Discrepancies in answers from local urologists and oncologists suggest there is a need to foster closer collaborations between the two specialties by implementing a multidisciplinary team approach for the treatment of prostate cancer.

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EM-164254

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