# Management of patients with advanced prostate cancer in the Asia Pacific region: 'real-world' consideration of results from the Advanced Prostate Cancer Consensus Conference APCCC 2017

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Cost and access to treatment



**Abstract**

***Objective***

The Asia Pacific Advanced Prostate Cancer Consensus Conference (APAC APCCC 2018) brought together 20 experts from 15 APAC countries to discuss the real-world application of consensus statements from the 2nd Advanced Prostate Cancer Consensus Conference held in St Gallen in 2017 (APCCC 2017).

***Findings***

Differences in genetics, environment, lifestyle, diet and culture are all likely to influence the management of advanced prostate cancer in the APAC region when compared with the rest of the world. When considering the strong APCCC 2017 recommendation for the use of upfront docetaxel in metastatic castration-naive prostate cancer, the panel noted possible increased toxicity in Asian men receiving docetaxel which would affect this recommendation in the APAC region. Although androgen-receptor targeting agents appear to be well tolerated in Asian men with metastatic castration-resistant prostate cancer, access to these drugs is very limited for financial reasons across the region. The meeting highlighted that cost and access to contemporary treatments and technologies are key factors influencing therapeutic decision making in the APAC region. While lower cost / older treatments and technologies may be an option, issues of culture, and patient or physician preference mean these may not always be acceptable. Although generic products can reduce cost in some countries, costs may still be prohibitive for lower income patients or communities. Panellists noted the opportunity for a coordinated approach across the APAC region to address issues of access and cost. Developments in technologies and treatments are presenting new opportunities for the diagnosis and treatment of advanced prostate cancer. Differences in genetics and epidemiology affect the side-effect profiles of some drugs and influence prescribing.

***Conclusions***

As the field continues to evolve, collaboration across the APAC region will be important to facilitate relevant research and collection and appraisal of data relevant to APAC populations. In

the meantime, the APAC APCCC 2018 meeting highlighted the critical importance of a multidisciplinary team-based approach to treatment planning and care, delivery of best-practice care by clinicians with appropriate expertise, and the importance of patient information and support for informed patient choice.



**Introduction**

The 2018 Asia Pacific Advanced Prostate Cancer Consensus Conference (APAC APCCC 2018) was convened to reflect on consensus statements from the 2017 Advanced Prostate Cancer Consensus Conference (APCCC 2017) held in St Gallen [1]. The 61 St Gallen panellists were highly regarded key opinion leaders in the field of advanced prostate cancer. Although St Gallen included global representation from 21 countries, only four panellists were from the APAC region. Voting at APCCC 2017 was based on idealised assumptions that all diagnostic procedures and treatments were available, and participants were instructed not to consider cost, reimbursement and access in their deliberations. Meetings in Taiwan, the Philippines and Lebanon have considered the local relevance of APCCC outcomes. Discussions are ongoing in the APAC region about the regional appropriateness of some St Gallen recommendations, especially as much of the data informing the recommendations is based, at best, on studies involving small numbers of patients from the region. With the endorsement of the St Gallen leadership, the APAC APCCC 2018 Satellite Meeting was convened to consider the real-world application of APCCC 2017 recommendations across the APAC region.

**The panel**

The panel for the one-day APAC APCCC 2018 meeting included 20 experts from 15 APAC countries (Table 1). Panellists were selected based on their expertise in advanced prostate cancer and are leaders in the region. The panel met in Melbourne, Australia, in February 2018, hosted by the Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP).

Prior to the meeting the panel considered the ten topic areas discussed during APCCC 2017 and agreed on the five most contentious areas to discuss at APAC APCCC 2018, based on their relevance for the APAC region:

1. Management of castration sensitive/naïve prostate cancer (CNPC)
2. Management of castration resistant prostate cancer (CRPC)

3. Management of high-risk localised and locally advanced prostate cancer
4. Management of oligometastatic prostate cancer
5. Global access to prostate cancer drugs and treatment in countries with limited resources.

Self-nominated groups were established before the meeting to discuss the APCCC 2017 statements and review evidence relevant to the APAC region. At the meeting, nominated leads presented a summary of evidence and APAC considerations. Panellists then discussed areas of variation within and across the APAC region and agreed key themes for each of the five topics. A separate systematic review was not conducted as our goal was to consider the existing APCCC 2017 recommendations from an APAC perspective, and to use the opinions of a multidisciplinary panel of APAC prostate cancer experts to provide a regional interpretation of these recommendations. Consensus was reached by discussion among the 20 strong panel.

**Management of advanced prostate cancer in the Asia Pacific region**

Prostate cancer is the most common cancer in men globally [2]. Incidence varies according to sociodemographic index (SDI). Age-standardised incidence rates (ASIR) and age-standardised death rates (ASDR) for prostate cancer are among the lowest globally in South Asia and East Asia, but are higher in South East Asia, and highest in Australasia. ASIR is increasing across all SDI quintiles globally [2].

The PREVAIL study highlights several differences in baseline characteristics in East Asian men with prostate cancer compared with the overall study population. This includes a higher percentage of patients with a Gleason score ≥ 8 and a higher percentage with bone disease (likely a result of less frequent prostate-specific antigen (PSA) testing). However, PREVAIL also found lower median PSA levels and fewer patients with soft tissue disease and bone pain in the East Asian population [3].

Differences in genetics, environment, lifestyle, diet and culture are all likely to influence the management of advanced prostate cancer in the APAC region. Some of these differences are highlighted in recent post-hoc analyses of data from the PREVAIL trial in different population groups [3–5]. While numbers are small, differences in the East Asian patients compared with the overall study population included more common upper respiratory tract infection, urinary frequency, falls, and decreased appetite. Fatigue and back pain were rare in East Asian patients.

Management of advanced prostate cancer may also be influenced by which disciplines are involved in treatment planning and delivery, with variation in specialties who prescribe chemotherapy in the APAC region. Table 1 provides a snapshot of chemotherapy-prescribing practices by discipline in each of the countries represented at APAC APCCC 2018.

Another factor influencing advanced prostate cancer management is the status of registration and reimbursement for diagnostic technologies and treatments. Table 2 provides a summary of the status of prostate cancer drugs (Table 2a) and imaging technologies (Table 2b) as reported for the countries represented at APAC APCCC 2018 in early 2018.

**APAC APCCC 2018 outcomes**

**1. Management of metastatic castration naïve prostate cancer (mCNPC)**

***1.1 Addition of docetaxel to ADT in mCNPC***

APCCC 2017 reported strong consensus (96%) for the addition of docetaxel (3-weekly at 75mg/m$^2$) to androgen deprivation therapy (ADT) in men with de novo mCNPC and high-volume disease, as defined in CHAARTED (visceral [lung or liver] and/or ≥ 4 bone metastases, at least one beyond pelvis and vertebral column) [6]. While not reaching the cut-off for consensus, there was a high degree of agreement (74%) for the addition of docetaxel to ADT in men relapsing after prior treatment for localised prostate cancer, non-castrate serum testosterone, and high-volume metastatic disease (as defined in CHAARTED). There was no consensus (29%) for the addition of docetaxel to ADT in men with de novo mCNPC and low-volume disease (as defined in CHAARTED).

APAC APCCC 2018 panellists reflected on recently published 53-month follow-up data from CHAARTED showing overall survival (OS) benefit for the addition of docetaxel (3-weekly at 75mg/m$^2$) in patients with high-volume disease (HR 0.63) but no OS benefit for low-volume disease (HR 1.04) [7]. There was unanimous agreement for the addition of docetaxel to ADT in high-volume mCNPC if cost / access was not an issue. Only one panellist indicated that addition of docetaxel to ADT would be considered in low-volume mCNPC. This contrasts with practice in the US, UK and other regions.

Factors identified by panellists that may influence whether docetaxel is offered in addition to ADT to men with mCNPC in the APAC region included:

- increased toxicity of docetaxel in Asian men, specifically a higher incidence of febrile neutropenia
- patient concerns about chemotherapy toxicity and a perception that chemotherapy may not be required if they are already seeing a benefit on ADT
- differences in docetaxel registration / reimbursement for use in mCNPC (see Table 2a).

The issue of increased toxicity of docetaxel in Asian men was notable during discussions about mCNPC and mCRPC. Studies in CRPC have shown an incidence of grade 3 or 4 neutropenia in Asian men almost double that of Caucasian cohorts (57.7% vs 32%) [8,9]. A requirement for dose reduction has been demonstrated in some studies due to toxicity [8,10,11]. The question of whether to use granulocyte colony stimulating factor (G-CSF) in men receiving docetaxel also generated significant discussion at APAC APCCC 2018. US and European guidelines state that G-CSF prophylaxis should be considered in men with risk factors [12,13,14]. No consensus was reached at APCCC 2017 for the use of white blood cell growth factors from start of therapy (6% voted for use in a majority of patients and 50% for use in a minority of patients). Most APAC APCCC 2018 panellists indicated that G-CSF is used routinely in men receiving docetaxel for the management of mCNPC in the APAC region. However, in some areas, including Australia, G-CSF is not used at all in the palliative setting.

The toxicity in Asian men of docetaxel at a dose of 75mg/$m^2$ has been reported in men with castration resistant prostate cancer [15]. Panellists reported that toxicity concerns also result in dose reductions in the management of mCNPC, with four panellists indicating that docetaxel is routinely started at a dose of 60mg/$m^2$. A similar finding was reported from the Taiwan consensus meeting held after APCCC 2017: only 50% of participating doctors indicated that they use a starting dose of docetaxel of 75mg/$m^2$ [Personal correspondence. Dr Yeong-Shiau Pu, Department of Urology, National Taiwan University Hospital, Taipei, Taiwan]. In addition to toxicity concerns, the cost of treatment (including the cost of G-CSF) was also identified as a factor influencing the starting dose.

***1.2 Addition of abiraterone to ADT in mCNPC***

Panellists at APCCC 2017 did not vote on the addition of abiraterone to ADT in mCNPC as data from the LATITUDE [16] and STAMPEDE [17] trials were not yet available. European Association of Urology guidelines were updated in late 2017 [18] to reflect these updated data.

No differences in side effect profile for abiraterone have been reported in Asian men compared with the global population [19]. At APAC APCCC 2018, 83% of panellists indicated that they would consider addition of abiraterone to ADT in patients with mCNPC if cost / access was not an issue. However, in reality, prescribing is influenced by the registration and reimbursement status of abiraterone across the region (see Table 2a).

***1.3 Imaging to determine therapeutic strategies***

APCCC 2017 focused on the use of increasingly sensitive imaging techniques, such as $^{68}$Ga-PSMA-PET, as a diagnostic modality, means of response assessment, and guide to decisions about therapy [20].

The availability of new or more conventional imaging technologies varies across the APAC region and may have implications for the implementation of clinical trial outcomes (see Table 2b). For example, limited availability of bone scanners and radioisotopes can be an obstacle to the detection of high-volume disease according to CHAARTED criteria. There was significant interest among panellists in the potential to use other imaging techniques, such as magnetic resonance imaging (MRI), as a means of determining stage of disease [21,22].

***1.4 Other issues related to management of mCNPC***

Other issues discussed in relation to mCNPC included:

- agreement that local treatment of the primary in mCNPC should best be undertaken in the context of a clinical trial
- an interest in identifying biomarkers specific to the Asian population that may improve understanding of mechanisms of resistance to ADT and help to inform the therapeutic strategy for men with mCNPC (noting that, in the absence of biomarkers, phenotypic and clinical characteristics can provide some indication of risk level)
- when to start ADT in men with rising PSA (on an LHRH agonist) and non-castrate testosterone levels.

## 2. Management of metastatic castration-resistant prostate cancer (mCRPC)

APCCC 2017 reflected on the remarkable progress in prostate cancer drug development over the past 10 years and since the first APCCC meeting in 2015. Questions focused on sequencing and treatment combinations in the mCRPC management for which evidence limited and clinical trials underway.

### *2.1 Sequencing of treatment for mCRPC*

Table 3 summarises the areas of consensus at APCCC 2017 related to sequencing of treatment for mCRPC.

APAC APCCC 2018 panellists reflected on the large number of trials that have demonstrated an OS advantage for survival-prolonging agents in mCRPC when used pre- and post-chemotherapy [9,23–29]. Benefits are particularly apparent in the pre-chemotherapy setting where stratification informs the choice of treatment.

Studies in Asian populations (China, Malaysia, Thailand) suggest no difference in safety data for abiraterone [19] or enzalutamide [3] compared with data from global studies. APAC APCCC 2018 panellists agreed with APCCC 2017 conclusions that clinical factors, such as performance status, symptoms, co-morbidities, disease site and extent of disease, are important in influencing choice and sequence of treatment.

Specific issues relevant to the APAC region noted by panellists included:

- a preference in the APAC region for enzalutamide over abiraterone for patients with diabetes mellitus (especially when poorly controlled) because of the potential for symptom exacerbation and complications through concomitant steroid use
- use of lower starting doses for docetaxel due to concerns about toxicity [11].

A recurring theme at APAC APCCC 2018 was the impact of cost and access on prescribing habits (see Table 2a). As with docetaxel, dose adjustment of abiraterone occurs in some countries as a way of reducing treatment costs. [30] A small prospective phase 2 study has shown low-dose abiraterone with a low-fat meal may have benefits comparable to the standard dosing schedule in the fasting state [31]. Data were presented showing the cost of generic abiraterone in India, which is 5% of the cost of branded abiraterone in the USA. If generic abiraterone were to become more

widely available in the region, this would likely lead to significant changes in patterns of care for mCRPC.

It was also noted that older treatments targeting androgen synthesis or activity, such as ketoconazole and bicalutamide, are still widely used in some countries instead of newer androgen-receptor pathway targeted therapies. Surgical castration was also discussed as a lower cost option; noting that cultural and other patient factors play a role in influencing its use.

### *2.2 Combination treatment*

APCCC 2017 noted that no combination treatment strategies using survival-prolonging agents have shown an OS benefit compared with monotherapy. Results from ongoing combination trials are ongoing (NCT02194842M, NCT02043678, NCT01949337) are awaited.

Although trials using radium-223 dichloride were acknowledged at APAC APCCC 2018, this treatment is not yet reimbursed in any of the countries represented at the meeting. Panellists agreed that clinical trial outcomes for radium-223 combinations in mCRPC will be required before progress will be seen in radium-223 use in the region.

### *2.3 Other issues related to the management of mCRPC*

Other issues discussed in relation to mCRPC included:

- whether the clinical benefits of starting treatment for mCRPC earlier (e.g. while patients are asymptomatic or have a lower Gleason score or PSA level) [32] are sufficient to justify the additional cost
- a comparison of approaches used across the region to manage skeletal-related events in men with mCRPC receiving ADT.

Variation was noted in the use of bisphosphonates / RANK ligand inhibitor for the management of bone density loss. Panellists noted inconsistency in clinical uptake of information about benefits of exercise programs offering advice on resistance training or access to an exercise physiologist, to mitigate loss of bone density associated with androgen deprivation therapy.

## 3. High-risk localised and locally advanced prostate cancer

APCCC 2017 highlighted discipline-specific variation in the definition of 'high risk' as it relates to prostate cancer. The European Association of Urology, European Society for Radiation Therapy and Oncology, International Society of Geriatric Oncology (EAU-ESTRO-SIOG) definition was used at the APCCC 2017 meeting (localised disease: PSA > 20ng/mL, or Gleason score > 7 or cT2c; locally advanced disease: any PSA, any Gleason score, cT3–4 or cN+) [33]. In the APAC region, the National Comprehensive Cancer Network (NCCN) definition of high-risk is more commonly used (T3a or Gleason score 8 / Gleason grade group 4 or Gleason score 9–10 / Gleason grade group 5 and PSA >20 ng/mL) [12].

### *3.1 Treatment preferences for high-risk and locally advanced prostate cancer*

APCCC 2017 did not discuss the choice of primary treatment for high-risk and locally advanced prostate cancer.

Panellists at APAC APCCC 2018 discussed primary treatment for high-risk and locally advanced disease. It was noted that use of radical prostatectomy (RP) with or without radiation therapy (RT) and ADT depends on a range of factors, including patient age and fitness, co-morbidities, and likelihood of local complications based on symptoms and performance status. Access to appropriate expertise and contemporary RT technology was recognised as important with treatment choice influenced by which discipline the patient sees first.

A key agreement from APAC APCCC 2018 was the importance of a multidisciplinary team approach to developing treatment recommendations for advanced prostate cancer. While geography and access to specialist cancer centres can be a significant barrier to multidisciplinary team working, the benefits of virtual participation in multidisciplinary team discussions were noted. For example, in China, a virtual network of 100 centres provides the option of a second opinion to inform treatment planning [34].

### *3.2 Pelvic lymph node dissection (PLND) for high-risk and locally advanced prostate cancer*

At APCCC 2017 there was consensus for the use of PLND in the majority of men with cN0 cM0 high-risk prostate cancer undergoing RP (84%), and for removal of more than 10 lymph nodes (76%). European [33] and NCCN guidelines [12] recommend RP with an extended PLND for men with high-risk and locally advanced prostate cancer.

APAC APCCC 2018 panellists discussed a range of questions about PLND, including what constitutes an 'adequate' lymph node dissection, the importance of appropriate pathology review of removed nodes, and the appropriateness of extended PLND in the absence of OS benefit and given the potential for poorer intraoperative and perioperative outcomes [35].

Panellists noted differing preferences regarding standard or extended PLND. Concerns were noted about possible complications following extended PLND and their potential to limit opportunities for further treatment such as radiation therapy. Panellists concluded that PLND is helpful for staging but should be undertaken by health professionals with appropriate expertise who undertake a sufficient volume of the procedures to minimise the risk of complications. The importance of appropriate pathology expertise and processes was also noted.

### *3.3 Use of adjuvant vs salvage radiation therapy after radical prostatectomy*

No consensus was reached at APCCC 2017 on the use of adjuvant RT for the treatment of high-risk localised prostate cancer (pN0 or pN1). It was noted that no trial has compared 'pure' adjuvant RT at undetectable PSA levels with salvage RT at 'appropriately' low PSA levels. There was also no consensus on the most appropriate radiation field, with responses split between the prostatic bed and the prostatic bed plus whole pelvis.

While EAU and AUA guidelines recommend use of RP plus RT and ADT for high-risk prostate cancer [33,36], RT use is reported to be in decline [37]. APAC APCCC 2018 panellists reflected on data showing the benefits of RT in men with node-positive prostate cancer [38], noting that RT has been mandatory in STAMPEDE for men with N1 M0 disease since 2011.

A range of factors were identified that would influence the decision to use adjuvant or salvage RT after RP, including likelihood of cure as well as the potential to exacerbate complications of surgery. Regardless, the importance of the patient seeing a radiation oncologist to discuss the option of adjuvant RT was noted.

In relation to the optimal radiation field, radiation oncology panellists reflected on the lack of definitive evidence to guide field selection but noted that the evidence base is evolving as improved imaging technologies such as $^{68}$Ga-PSMA-PET become available [39].

As with APCCC 2017, no clear agreement was reached on whether ADT should be added to adjuvant RT in high-risk pN0 disease, noting the absence of high-level evidence to inform practice in this area.

**4. Management of 'oligometastatic' prostate cancer**

APCCC 2017 highlighted the lack of an agreed definition of oligometastatic disease and different treatment preferences for synchronous or metachronous oligometastatic disease. The considerable variation in practice reflected the choice of imaging technique used to define oligometastatic disease.

APAC APCCC 2018 panellists also reflected on the variation in definitions [40,41] and lack of a definitive cut-off for what constitutes oligometastatic prostate cancer. Some APAC APCCC 2018 panellists expressed different views to APCCC 2017 findings about management of oligometastatic disease. Variation was noted in the approach to treatment of newly diagnosed patients with an untreated primary, including whether to add docetaxel to local treatment plus ADT and the choice of local treatment. Some differences in preference for treatment of oligometastatic recurrent CNPC after local treatment were also noted.

The role of prostate-directed and metastasis-directed therapy was also discussed. Retrospective trial data exist but prospective data are emerging.

Factors identified as influencing the approach to management of oligometastatic disease in the APAC region included:

- limited availability in many APAC countries of imaging technologies such as $^{68}$Ga-PSMA-PET required to detect oligometastatic disease (see Table 2b)
- the challenge of recommending metastasis-directed treatments that carry additional cost (such as surgery or stereotactic body RT) in the context of metastatic disease in the absence of evidence for a survival benefit
- whether treatment is being undertaken with long term control / curative intent.

It was noted that this is an area in which registry data and collaboration in the APAC region is likely to be helpful.

**5. Global access to prostate cancer drugs and treatment in countries with limited resources**

Voting at APCCC 2017 occurred on the basis of no restrictions in access and no issues with cost.

At APAC APCCC 2018, access and cost were strong themes for each of the topics discussed and were often cited as having the greatest influence on prescribing decisions. The high cost of newer drugs such as abiraterone and enzalutamide was noted, with an estimated cost of USD $2.8bn expenditure in the USA alone if abiraterone plus prednisone is used in CNPC [42]. Availability of generic treatments, and country-level price negotiations result in a variable picture across the APAC region, meaning a region-wide statement on access cannot be made. However, there was strong agreement with the APCCC 2017 that "*it is a sub-optimal clinical achievement to show that new treatments can improve the duration and quality of survival of men with APC but to have such treatments unavailable to a large segment of the global population of men with APC*" [1].

***5.1 Lower cost options in countries with limited resources***

APCCC 2017 panellists voted on appropriate alternative options for treatment of advanced prostate cancer in countries with limited resources. There was consensus for the use in the setting of limited health care resources of:

- orchidectomy as ADT in the metastatic setting (90%) (noting socio-cultural and psychological barriers that may need to be considered)
- use of platinum-based chemotherapy in men with mCRPC progressing on or after docetaxel (77%).

APAC APCCC 2018 panellists noted that addressing the issue of limited resources is not as simple as choosing a lower cost option. For example, the choice of orchidectomy over a luteinising hormone-releasing hormone (LHRH) agonist or antagonist requires consideration of patient preference and follow-up requirements as well as cost. Many panellists indicated that patients in the APAC region would be more likely to choose medical ADT over surgery and emphasised the need to provide men with clear information about options that includes potential benefits, side effects and cost.

Dose reduction as a means of reducing cost and the likely requirement for supportive therapies was noted [30,31]. Resource-stratified guidelines were identified as a means of providing recommendations for treatment based on differing levels of health-care resources [43,44].

***5.2 What can be done to address resource limitations?***

APAC APCCC 2018 panellists recognised the requirement for universal health coverage as highly relevant in the APAC region. Opportunities for consideration include the World Health Organisation (WHO) Sustainable Development Goals (*Goal 3: Ensure healthy lives and promote well-being for all at all ages*) [45] as well as the Union for International Cancer Control (UICC) City Cancer Challenge [46]. Panellists noted that collaboration between academia, government, industry (pharmaceutical), non-government organisations and other sectors will be key to achievement of universal health coverage for cancer.

Given the inequalities in the standard and availability of cancer treatments in the APAC region, a 'one-size fits all' approach to guidelines and recommendations will not work. Resource-stratified recommendations and frameworks are therefore urgently needed to reflect the diversity of health systems in APAC countries at different stages of development. There was strong support from the panellists for a review and update of the *Management of prostate cancer in Asia: resource stratified guidelines from the Asian Oncology Summit 2013* [43].

The likely value of further development of local registries such as the Prostate Cancer Outcomes Registry – ANZ [47] and contributions to the A-CaP registry [48] in identifying differences in access and variation in practice was also noted.

**Discussion**

APAC APCCC 2018 was convened to review how statements of consensus and non-consensus from APCCC 2017 apply in everyday practice in the APAC region. The aim was to provide real-world insight into the application of the statements, focusing on the five issues most relevant to the APAC region. The meeting generated significant interest, with all invitees attending and contributing to discussions. This included one panellist participating via videoconference because of last minute travel issues.

APAC APCCC 2018 differed in format to APCCC 2017. The panel included a higher number of urologists, reflecting how treatment for men with prostate cancer is frequently managed in the APAC region. While there is likely to be some variation in views based on which disciplines are

consulted, it is worth noting, that in several APAC countries, urologists have responsibility for prescribing and managing systemic therapy including intravenous chemotherapy. RT is usually administered by radiation oncologists, although in some countries (e.g. Malaysia), both chemotherapy and radiation therapy are administered by clinical oncologists.
No formal voting mechanism was used at APAC APCCC 2018. Discussion focused instead on practical considerations relating to the areas of consensus and non-consensus from APCCC 2017. The views of the APAC APCCC 2018 panellists highlighted several caveats related to implementation of the APCCC 2017 statements, as well as some differences in opinion. As was the case with the APCCC 2017, differences in opinion do not reflect a failure of the process but highlights areas of controversy and evolving evidence where further research may be beneficial.

***Real-world implications of APCCC 2017 statements in the Asia Pacific region***

There was clear value in the process of discussion and in consideration of the real-world application of the APCCC 2017 consensus statements. A number of consistent themes emerged from the APAC APCCC 2018 discussions (see Box 1).

Access, cost of treatments and toxicity concerns influence prescribing decisions in the management of advanced prostate cancer and have a significant influence on the sequencing and timing of treatment. Specific examples include:

- a lack of established safety data for docetaxel in Asian men and concerns about febrile neutropenia influencing prescribing, particularly in men with poorer performance status
- increased use of G-CSF in men receiving docetaxel, with the associated cost having a significant impact in terms of health economics and prescribing even in presence of generic docetaxel
- while abiraterone may be more acceptable for Asian men than docetaxel due to lower toxicity, the cost is prohibitive in some countries and concerns exist about the toxicity of concomitant steroids.

Variation in the availability of imaging technologies may limit the ability of clinicians in some APAC countries to prescribe according to precise definitions. Within the APAC region, the question of whether more sensitive imaging results in changes to treatment and ultimately improved outcomes is of particular interest. In the meantime, alternative imaging technologies such as whole-body MRI may need to be considered.

As is the case in all countries, a multidisciplinary approach and provision of best practice care by clinicians with appropriate expertise are the cornerstones of treatment for high-risk localised prostate cancer. While multidisciplinary teams can be a challenge to set up in some APAC regions, the view of the APAC APCCC 2018 panellists is that options to support multidisciplinary team consultation, including virtual participation, should be encouraged. While it was noted that cultural factors may affect individual patient preferences to participate in shared decision making, the importance of informed patient choice was also a strong theme.

To address issues of cost, a collaborative approach to driving universal health coverage in the APAC region is likely to reap benefits and create greater parity across the region. However, access and cost are not the only considerations, with the discussions also pointing to the need to consider long-term therapeutic benefit before widely adopting new technologies and treatments in countries with limited resources.

In the era of evidence-based medicine, the importance and value of prospective clinical research to address areas of limited or conflicting evidence is significant. APAC APCCC 2018 highlights the opportunity for studies in APAC populations where genetics / epidemiology may result in different responses. The value of registries as a mechanism to collect real world data was noted, with strong support for collaborative input into the A-CaP registry.

APAC APCCC 2018 was the first region-wide meeting to discuss the management of advanced prostate cancer. Panellists noted a commitment to ongoing discussion and collaboration across the region to ensure that as evidence of benefit emerges for new treatments and technologies in improving outcomes in advanced prostate cancer, the benefits can be realised for all men.

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**Conflict of interest statement**

Associate Professor Chiong reports support for manuscript preparation from the Australian and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group during the conduct of the submitted work. Associate Professor Murphy reports grants and personal fees from Astellas Pharma Ltd, personal fees from Janssen Pharma Ltd, personal fees from Ipsen Pharma Ltd, and grants and personal fees from Ferring Pharma Ltd, outside the submitted work. Professor Davis reports being a member or chair of industry advisory boards for Pfizer, BMS, Astellas, Roche and AstraZeneca, some of which relate to products relevant to this paper. Professor Davis receives no remuneration for this work. All payments or honoraria are invoiced by and paid directly to ANZUP Cancer Trials Group. Professor Davis is Director and Chair of the Board of ANZUP Cancer Trials Group, a not-for-profit charity undertaking cooperative cancer clinical trials in genitourinary cancers. He receives no remuneration for this work. ANZUP is performing clinical trials in prostate and other genitourinary cancers, with funding support from industry. Dr Kanesvaran reports honoraria from Astellas, grants and honoraria from Johnson & Johnson, honoraria from Novartis, grants from Sanofi and honoraria from Amgen outside the submitted work. Dr Letran reports honoraria as an advisory board member or key opinion leader for Janssen, Astellas, Takeda, Ferring, Novartis, Menarini and Transmedic International. Dr Ng reports payment for consultancy from Janssen, payment for consultancy and as an investigator from Astellas and honoraria from Amgen outside the submitted work. Professor Pu reports grants and personal fee from Johnson & Johnson outside the submitted work. Dr Saad reports grants and honoraria from Johnson & Johnson, and honoraria from Astellas, Sanofi and Novartis outside the submitted work. Professor Umbas reports grants and honoraria from Astellas, and honoraria from Johnson & Johnson, Takeda and AstraZeneca outside the submitted work. All remaining authors report no conflicts of interest in relation to this manuscript.

**Table 1** APAC APCCC 2018 panel members

| Name | First name | Specialty | Chemotherapy prescriber† | | Country |
|---|---|---|---|---|---|
| | | | Oral agents | Intravenous | |
| Akaza | Hideyuki | Urologist | ✓ | ✓ | Japan |
| Buchan | Nick | Urologist | – | – | New Zealand |
| Chiong | Edmund | Urologist | ✓ | – | Singapore |
| Chung | Byung Ha | Urologist | ✓ | ✓ | South Korea |
| Davis | Ian | Medical oncologist | ✓ | ✓ | Australia |
| Kanesvaran | Ravindran | Medical oncologist | ✓ | ✓ | Singapore |
| Khochikar | Makarand | Urologist | – | – | India |
| Letran | Jason | Urologist | – | – | Philippines |
| Lojanapiwat | Bannakij | Urologist | ✓ | ✓ | Thailand |
| Murphy | Declan | Uro-oncologist | – | – | Australia |
| Ng | Anthony CF | Urologist | – | – | Hong Kong |
| Ong | Teng Aik | Urologist | ✓ | – | Malaysia |
| Pu | Yeong-Shiau | Urologist | ✓ | ✓ | Taiwan* |
| Saad | Marniza | Clinical oncologist | ✓ | ✓ | Malaysia |
| Schubach | Kathryn | Urology nurse practitioner | – | – | Australia |
| Türkeri | Levent | Urologist | ✓ | ✓ | Turkey |
| Umbas | Rainy | Urologist | ✓ | ✓ | Indonesia |
| Vu | Le Chuyen | Urologist | ✓ | – | Vietnam |
| Williams | Scott | Radiation oncologist | – | – | Australia |
| Ye | Ding-wei | Urologist | ✓ | ✓ | China |

† Refers to prescribing of oral agents (abiraterone and enzalutamide) and IV chemotherapy (docetaxel) for prostate cancer

* A review of prescribing practices among urologists in Taiwan suggests that about half of all urologists has prescribed IV chemotherapy but not on a regular basis

**Table 2a** Access in APAC countries to drugs used in the management of advanced prostate cancer

| Country | abiraterone | | | enzalutamide | | | docetaxel | | | radium-223 | | | G-CSF | | | bone loss therapy | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | reg | reimb | gen | reg | reimb | gen | reg | reimb | gen | reg | reimb | gen | reg | reimb | gen | zoledronic acid | denosumab |
| Australia | ✓ | ✓ | – | ✓ post-docetaxel | ✓ | | ✓ | ✓ | ✓ | ✓ | – | – | – | – | – | registered / reimbursed for CRPC | |
| China | ✓ | ✓ CRPC | – | – | – | – | ✓ | ✓ CRPC | – | – | – | – | ✓ | ✓ | – | registered/ reimbursed | – |
| Hong Kong | ✓ | ✓ part | – | ✓ | ✓ part | – | ✓ | ✓ CRPC | – | ✓ | – | – | ✓ | – | – | registered but not reimbursed | |
| India | ✓ | ✓ part | x | ✓ | ✓ part | ✓ | ✓ | ✓ part | ✓ | – | – | – | – | – | – | ✓ | – |
| Indonesia | ✓ | ✓ part | – | ✓ | – | – | ✓ | ✓ | ✓ | – | – | – | ✓ | ✓ part | – | ✓ part | – |
| Japan | – | ✓ | – | – | ✓ | – | – | ✓ | – | – | ✓ | – | – | ✓ | – | ✓ | ✓ |
| Malaysia | ✓ | ✓ part | – | ✓ | ✓ part | – | ✓ | ✓ part | ✓ | – | – | – | ✓ | ✓ part | ✓ | registered / partially reimbursed for mCRPC | |
| New Zealand | ✓ | ✓ | – | ✓ | – | – | ✓ | ✓ | – | – | – | – | – | – | – | ✓ | ✓ |
| Philippines | ✓ | – | – | ✓ | – | – | ✓ | – | – | – | – | – | ✓ | – | ✓ | registered but not reimbursed | |
| Singapore | ✓ | ✓ part | – | ✓ | ✓ part | – | ✓ | ✓ part | – | ✓ | – | – | ✓ | ✓ part | – | registered / partially reimbursed for metastatic CRPC | |
| South Korea | ✓ | ✓ | – | ✓ | ✓ | – | ✓ | ✓ | ✓ | ✓ | – | – | ✓ | ✓ | ✓ | ✓ | registered not reimbursed |
| Taiwan | ✓ | ✓ | – | ✓ | ✓ | – | ✓ | ✓ mCRPC | ✓ | ✓ | – | – | ✓ | ✓ | – | registered / reimbursed for bone metastases | |

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Thailand | ✓ | ✓ part | – | ✓ | ✓ part | – | ✓ | ✓ part | – | ✓ | – | – | ✓ | ✓ part | – | registered / partially reimbursed for mCRPC | – |
| Turkey | ✓ | ✓ post-chemo | – | ✓ | ✓ post-chemo | – | ✓ | ✓ | – | ✓ | – | – | ✓ | ✓ | – | ✓ | ✓ |
| Vietnam | ✓ | – | – | – | – | – | ✓ | ✓ | ✓ | – | – | – | – | – | – | registered/ reimbursed for mCRPC | – |

reg: registered; reimb: reimbursed; gen: generic version available; part: partially reimbursed / reimbursed with some limitations; CRPC: castration resistant prostate cancer; post-chemo: post-chemotherapy

**Table 2b** Access and use in APAC countries to imaging technologies relevant to in the management of advanced prostate cancer

| **Country** | **bone scanner** | | **whole body MRI** | | **choline PET-CT** | | **PSMA-PET** | |
|---|---|---|---|---|---|---|---|---|
| | **available** | **reimbursed** | **available** | **reimbursed** | **available** | **reimbursed** | **available** | **reimbursed** |
| Australia | ✓ | ✓ | ✓ | – | – | – | ✓ | – |
| China | ✓ | ✓ | ✓ | ✓ | ✓ | – | ✓ | – |
| Hong Kong | ✓ | – | ✓ | – | ✓ | – | ✓ | – |
| India | ✓ | ✓ | ✓ | ✓ | ✓ part | – | ✓ | ✓ |
| Indonesia | ✓ | ✓ | ✓ | ✓ part | – | – | – | – |
| Japan | ✓ | ✓ | ✓ | ✓ | ✓ | – | – | – |

| Country | bone scanner | | whole body MRI | | choline PET-CT | | PSMA-PET | |
|---|---|---|---|---|---|---|---|---|
| | available | reimbursed | available | reimbursed | available | reimbursed | available | reimbursed |
| Malaysia | ✓ | ✓ part | ✓ | ✓ part | ✓ | ✓ part | ✓ | ✓ part |
| New Zealand | ✓ | ✓ | ✓ | – | – | – | ✓ | ✓ with restrictions |
| Philippines | ✓ | – | ✓ | – | ✓ | – | ✓ | – |
| Singapore | ✓ | ✓ part | ✓ | ✓ part | ✓ | – | ✓ | – |
| South Korea | ✓ | ✓ | ✓ | – | ✓ | – | – | – |
| Taiwan | ✓ | ✓ | ✓ | – | ✓ | Free under trials at a few centres | ✓ | Free under trials at a few centres |
| Thailand | ✓ | ✓ part | ✓ | ✓ part | ✓ | – | – | – |
| Turkey | ✓ | ✓ | ✓ | – | – | – | ✓ | ✓ part |
| Vietnam | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ part | – | – |

reg: registered; reimb: reimbursed; CRPC: castration resistant prostate cancer

**Table 3** Areas of consensus from APCCC 2017 regarding management of mCRPC[1]

| Statement | % agreement |
|---|---|
| ***First-line CRPC*** | |
| Abiraterone or enzalutamide for:<br>• asymptomatic men without docetaxel for CNPC<br>• asymptomatic men with docetaxel for CNPC<br>• asymptomatic men with docetaxel for CNPC and progressed within ≤6 months after completion of docetaxel in the CNPC setting | <br>86%<br>90%<br>77% |
| Not to combine radium-223 and docetaxel | 88% |
| ***Second-line CRPC*** | |
| Taxane in men with:<br>• symptomatic mCRPC with progressive disease as best response to first-line abiraterone or enzalutamide<br>• symptomatic mCRPC and secondary (acquired) resistance after first use of first-line abiraterone or enzalutamide | <br>96%<br>90% |
| Abiraterone or enzalutamide in men with:<br>• asymptomatic mCRPC progressing on or after docetaxel for mCPRC (without prior abiraterone or enzalutamide)<br>• symptomatic mCRPC progressing on or after docetaxel for mCPRC (without prior abiraterone or enzalutamide) | <br>92%<br>76% |
| ***Third-line CRPC*** | |
| No randomised prospective data<br>Use of platinum-based chemotherapy in a range of situations if all approved treatments are exhausted and no clinical trial available | <br>96% |

**Box**

**Box 1: Management of advanced prostate cancer in the APAC region: real world challenges in implementing the St Gallen APCCC recommendations**

1. **Differences in toxicity**: Safety data for docetaxel are not fully established in Asian men and concerns

about the toxicity profile and risk of neutropenia may influence prescribing.

2. **Disparities in access to imaging technology:** variable access to imaging technology may limit prescribing according to precise definitions
3. **Disparities in access and cost of treatment:** availability and cost of treatments is the most significant factor influencing prescribing decisions in the region; lower-cost alternatives are not always culturally acceptable and informed choice is important
4. **Variability in multidisciplinary team (MDT) approaches**: The importance of multidisciplinary input to treatment recommendations is understood but MDTs are a challenge in some APAC countries; virtual MDT participation should be encouraged
5. **Variability in demographics**: genetics and epidemiology in Asian men with prostate cancer may result in different treatment responses; collaborative registry studies and trials in APAC populations are likely to be valuable

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