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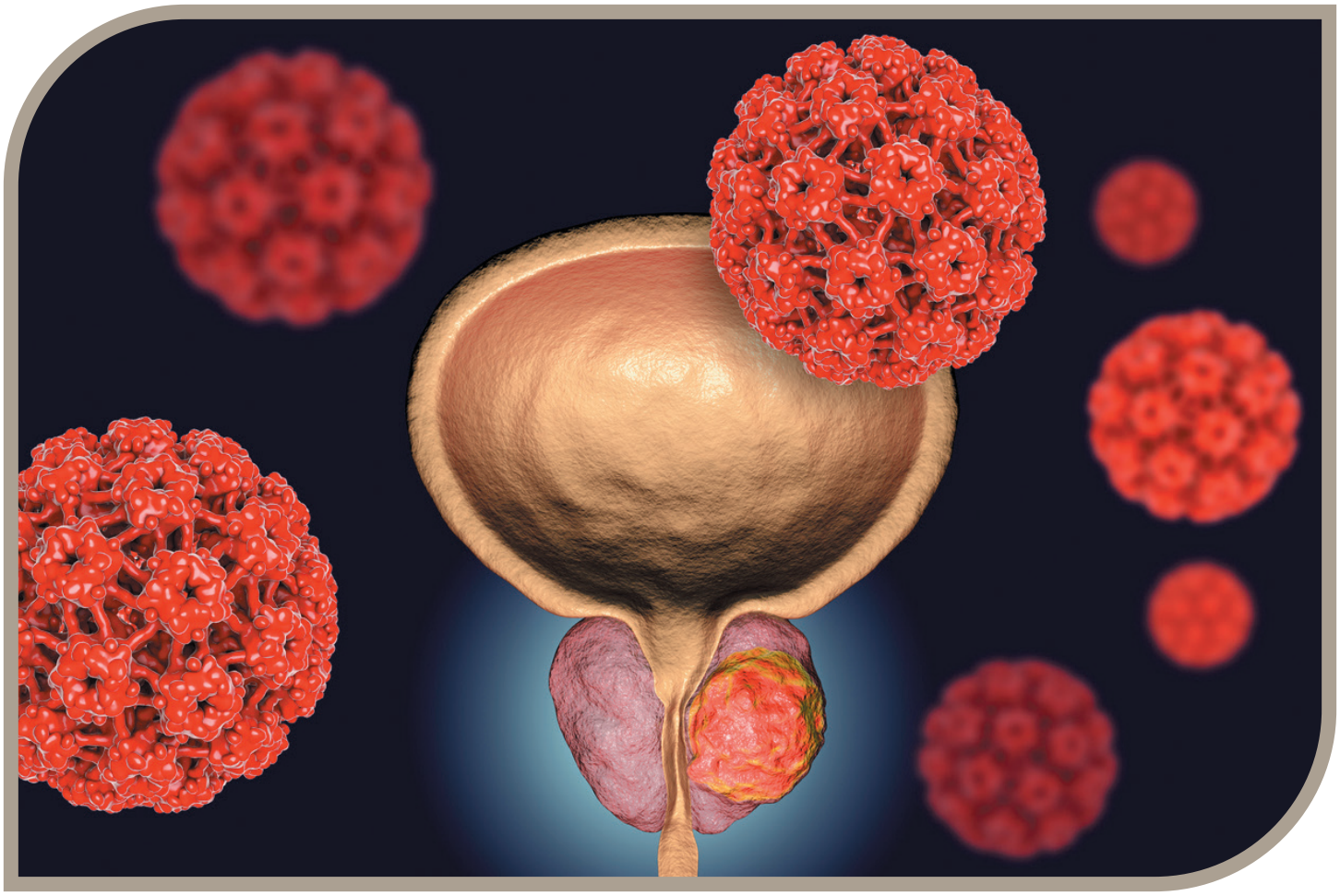
2023 Asia-Pacific Advanced Prostate Cancer Consensus Satellite Symposium Program

Wednesday 5 July, Fairmont Swissotel Singapore



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Welcome

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2023 Asia-Pacific Advanced Prostate Cancer Consensus Satellite Symposium Program

On behalf of ANZUP Cancer Trials Group (ANZUP), the host organisation, welcome to the 3rd Asia-Pacific (APAC) Advanced Prostate Cancer Consensus (APCC) Satellite Symposium.

As you may know from previous involvement, the Advanced Prostate Cancer Consensus Conference (APCCC) was initiated to provide a forum to discuss and debate current questions on the clinical management of individuals with advanced prostate cancer, with a special focus on these unclear situations.

In 2018, ANZUP hosted the inaugural APAC APCC Symposium, to test the ten priority areas within a group of APAC experts and determine any differences compared to the main St Gallen meeting. The Symposium brought together 25 experts from 15 APAC countries to discuss the real-world application of consensus statements from the second APCCC held in St Gallen in 2017 (APCCC 2017). The meeting highlighted that cost and access to contemporary treatments and technologies are key factors influencing therapeutic decision-making in the APAC region. Outcomes of the meeting included a BJUI publication Chiong et al **https://bjui-journals.onlinelibrary.wiley.com/doi/10.1111/bju.14489*** as well as oral presentations both at the 2018 USANZ and ANZUP Cancer Trials Group Annual Scientific Meetings.

In 2020, despite the impact of the global pandemic, the experts were keen to come together so we transformed the symposium into a 'virtual' meeting in October. Once again, the objective of the Symposium was to review recommendations from the 2019 St Gallen APCCC and to consider their relevance and applicability in the context of healthcare in the APAC region. Once again outputs included the publication Chiong et al **https://onlinelibrary.wiley.com/doi/full/10.1111/ajco.13722*** and virtual presentations at USANZ, ANZUP, and across the APAC regions.

A paper will be drafted by our medical writer Dr. Alison Evans, based on the summary of the discussions at the 2023 APAC APCC Consensus Symposium with input from our experts, and will be submitted for publication in the BJUI. The findings will be presented at the UROFAIR conference on 6-8 July in Singapore as well as the ANZUP Annual Scientific Meeting in Melbourne on 9-11 July. Thank you to convenors Ian Davis, Edmund Chiong and Declan Murphy for their expertise and for coordinating this important meeting.

Thank you also to our wonderful sponsors, Platinum Sponsor – Bayer, and Gold Sponsors – Astellas, AstraZeneca, and Pfizer. Without their support, we would be unable to organise this important meeting.

*Past papers can be found from page 17.

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Agenda

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Time	Wednesday 5 July, 2023	Presenter/s
8.00am	Welcome and Introductions.	Ian Davis, Edmund Chiong, Declan Murphy
8.10am	Overview of the APCCC consultation process.	Ian Davis
8.30am	**Priority Area One – Intermediate and high-risk and locally advanced prostate cancer (Paper 1).** • TNM – include imaging? • How to include PSMA PET or other information in the initial evaluation • How to act on findings of next-gen imaging, including what to do if it does not equate to conventional imaging • (Nature of tracers) • Management of nodes • Radiation regimen to primary • Adjuvant vs salvage RT • Role of additional systemic therapy • What additional regional clinical or research questions still need to be addressed?	Declan Murphy, Makarand Khochikar, Scott Williams, Jeremy Tey
9.15am	**Priority Area Two – Management of newly diagnosed metastatic hormone-sensitive prostate cancer (mHSPC) (Paper 2).** • Who should get combination treatment, who should get triplet, who should get ADT alone • Relevance of synchronous vs metachronous presentation; volume of disease; imaging modality to define disease volume • Sequencing of therapy • Other mutations • Age and frailty • Optimal follow-up regimen • Note section 2/6 limited resources section • What additional regional clinical or research questions still need to be addressed?	Ian Davis, Teng Ong, Bannakij Lojanapiwat, Marniza Saad
10.00am	**Priority Area Three – Management of nonmetastatic castration-resistant prostate cancer (nmCRPC). (Paper 2).** • Risk stratification e.g., by PSADT • Imaging issues • Treatment selection • How to monitor • What additional regional clinical or research questions still need to be addressed?	Kiyoshi Takahara, Yeong – Shiau Pu, Chi Fai (Anthony) Ng,Indranil Mallick
10.45am	**Morning tea**	

Continued over

Agenda

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Continued from previous page

Time	Wednesday 5 July, 2023	*Presenter/s*
11.15am	**Priority Area Four – Management of metastatic CRPC. (Paper 2).** • Initial treatment selection, with consideration of prior treatment • Treatment sequencing • Monitoring of treatment • LuPSMA • What additional regional clinical or research questions still need to be addressed?	Darren Poon, Sue-Ping Thang
12.00pm	**Priority Area Five – Regional consensus statements – HRR testing? (Paper 2).** • Impact of mutation testing/results – local policies, practices, access • PARP inhibition specifically • What additional regional clinical or research questions still need t o be addressed?	Ravi Kanesvaran, Edmund Chiong
12.45pm	**Lunch**	
1.30pm	Consensus discussion – identify key issues	Edmund Chiong, Ian Davis, Declan Murphy
2.25pm	**Working afternoon tea**	
2.30pm	Summary and close	Ian Davis
3.00pm	Delegates depart	

Convenors

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Ian Davis | Australia

Medical Oncologist

Professor Ian Davis is chair of the ANZUP Board and of its Scientific Advisory Committee. He is a medical oncologist and Professor of Medicine and Head of the Eastern Health Clinical School, Monash University and Eastern Health, in Melbourne, Australia. Heis an Associate Professor of the University of Melbourne, and Associate of the University of Sydney. His primary clinical interests are in urologic cancers, and his primary research interests are in cancer immunology and the biology of urologic cancers. Prof Davis is a member of the Medical & Scientific Committee and of the Standing Subcommittee on Research for the Cancer Council Victoria. He founded the Urologic Oncology Group of the Clinical Oncology Society of Australia (COSA), is a member of COSA Council, and was previously a COSA Board director.

Edmund Chiong | Singapore

Urologist

Head & Senior Consultant, Department of Urology, National University Hospital and Associate Professor, Department of Surgery, Yong Loo Lin School of Medicine, National University of Singapore. A/Prof Chiong's interests include managing and performing surgery for prostate cancers, bladder cancers, kidney cancers, testes cancers, penile cancers, and performing robotic surgery and prostate cancer high-dose rate brachytherapy.

Declan Murphy | Australia

Urologist

Declan Murphy is Consultant Urologist, Director of Genitourinary (GU) Oncology, and Director of Robotic Surgery at the Peter MacCallum Cancer Centre, Melbourne, Australia, and Professorial Fellow at the Sir Peter MacCallum Department of Oncology, University of Melbourne. He has previously been Consultant Urologist at Guys & St Thomas' NHS Foundation Trust in London. Declan specialises full-time in GU Oncology, prostate cancer in particular, and his private practice is based at Cancer Specialists in Melbourne.

Experts

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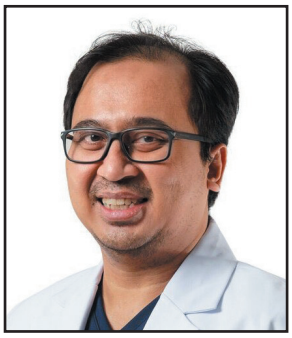

Agus Rizal Hamid | Indonesia

Urologist

Dr. Agus Rizal Ardy Hariandy Hamid, Sp.U (K), PhD is a Urologist with more than 10 years of experience. Currently, he practices at Siloam Hospitals Asri Mampang and RSU Bunda, Jakarta. He completed his General Medical Science education at the University of Indonesia in 2001, then continued his Urology Specialist education at the University of Indonesia in 2008. He last completed his Doctor of Medical Sciences at Radboud University Nijmegen in 2016.Dr. Agus Rizal Ardy Hariandy Hamid, Sp.U(K), PhD is a member of the Indonesian Medical Association (IDI), the Indonesian Surgeons Association (IKABI) and the Indonesian Association of Urologists (IAUI). The health services provided by him are consultations on urology.

Bannakij Lojanapiwat | Thailand

Urologist

Dr Bannakij Lojanapiwat, MD is a Surgical Urologist at The Chiangmai University. He received a medical degree from Chiangmai University. He is board-certified in Endocrinology. His research interests are Urology, Surgical Urology, Aging Male, Erectile Dysfunction, Surgery, Endocrinology, Transplantation.

Chi Fai (Anthony) Ng | Hong Kong

Urologist

Dr NG Chi Fai, Anthony is Professor of Division of Urology, Department of Surgery. He has research interests in stone diseases and prostate diseases. He has more than 200 peer-reviewed publications and nearly twenty book chapters written over the years. Besides his effort in basic and clinical research, he is also devoted to improving the care of his patients and urology care in Hong Kong and the region.

Experts

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Darren Poon | Hong Kong

Medical Oncologist

Dr Darren Poon is the Honorary Clinical Associate Professor at the Chinese University of Hong Kong and the Honorary Consultant in Clinical Oncology at both the Hong Kong Sanatorium & Hospital and Prince of Wales Hospital, Hong Kong.
Dr Poon has several specialist areas of expertise, which include genitourinary (GU) cancer, neuro-oncology, hepato-pancreatic cancer, and head and neck cancer. His research interests include novel therapies for GU cancers, image-guided radiotherapy and stereotactic body radiotherapy (SBRT) for prostate, central nervous system tumor, pancreatic and liver cancer.

Dingwei Ye | China

Urologist

Prof Dingwei Ye, Director of the Multi-disciplinary Team for GU cancer, Director of Fudan University Prostate Cancer Institute, President of genitourinary cancer committee of Chinese Anti-Cancer Association, Standing Committee member of Chinese Society of Clinical Oncology(CSCO), Vice chairs of RCC committee and Immunotherapy committee of CSCO, Vice chair of Chinese Anti-Cancer Association Family Hereditary Oncology group, deputy leader of writing group of NCCN Guidelines for diagnosis and treatment of renal cancer (Chinese edition), committee member of NCCN Asia consensus of prostate cancer and bladder cancer, Vice chair of Shanghai Medical Doctor Association urology branch decisive reviewer of National Scientific Foundation of China, executive member of Asian Pacific Prostate Society, Vice President of Asia Cry-surgery Society.

Indranil Mallick | India

Radiation Oncology

Dr Indranil Mallick is a Radiation Oncologist working at Tata Medical Center, a large tertiary care cancer hospital in Kolkata, India. He specializes in cancers of the head and neck, gastrointestinal tract and genitourinary tract, and is responsible for the treatment of more than 500 patients a year. He has a special interest in Image Guidance (IGRT) in External Beam Radiation Therapy, and he is responsible for several audits and publications on IGRT in selected sites.
The other focus of both his clinical and research work is on the use of hypofractionated radiotherapy. He is currently leading a clinical trial assessing the safety and efficacy of extreme hypofrationated radiotherapy in locally advanced prostate cancer.

Experts

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Jason Letran | Philippines

Urologist

Dr Letran finished his Residency Training in Urology at University of Santo Tomas Hospital in 1996. The following year, he was accepted as a Senior Fellow in Urologic Oncology at University of Washington School of Medicine, Seattle, Washington, USA. He further trained as a Scholar of the Japanese Foundation for Promotion of Endoscopy and Research, Fujieda Municipal General Hospital, Shizuoka, Japan in 1998. He is currently the Chief of the Section of Urology at Cardinal Santos Medical Center and the Director of the Cancer Institute and Head of Clinical Services Integration Department at Chinese General Hospital and Medical Center.

Jeremy Tey | Singapore

Radiation Oncologist

Adjunct Associate Professor Jeremy Tey graduated from the National University of Singapore Yong Loo Lin School of Medicine, and obtained his fellowship from the Royal Australian and New Zealand College of Radiologists. A/Prof Tey is currently practising as a Senior Consultant in the Department of Radiation Oncology at the National University Cancer Institute, Singapore and serves as the Clinical Director of the Department. He completed his training in high dose rate endorectal brachytherapy for rectal cancer at the Jewish General Hospital, Montreal, Canada. A/Prof Tey's sub-specialty interests are in Gastrointestinal and Genitourinary cancers. He has published in peer review journals and written book chapters.

Kathryn Schubach | Australia

Nurse

Kath Schubach is a GU Nurse Practitioner working in private practice in metropolitan Melbourne and rural Victoria. She has had 25 years of experience and qualifications working across two-core disciplines cancer and urology. Kath has expertise in managing sexual dysfunction in oncology/urology patients. She has a master's in Nursing Science and postgraduate qualifications in oncology, urology, and continence, nursing. She is currently enrolled in her Ph.D.

Experts

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Kenneth Chen | Singapore

Urologist

Dr Chen obtained membership of the Royal College of Surgeons (MRCS Edinburgh) in 2010 and Fellowship of the Royal College of Surgeons (Glasgow) and more recently has completed the Masters of Clinical Investigation (MCI) course with National University of Singapore on a NMRC MOH Healthcare Research Scholarship. He has completed his 6-year residency in Urology with SingHealth and has cleared his specialist exit exams with distinction, having obtained the College of Surgeons GOLD medal for best performing advanced surgical trainee in Urology. Dr Chen's research interest comprises a mix of basic science as well as translational and clinical components in the area of uro-oncology as well as novel device development and is currently under the Nurturing Clinician Scientist Scheme under SingHealth Surgery ACP grant working on developing a novel drug-eluting ureteral stent for ureteric strictures and upper tract urothelial cancers. His other area of interest is in the field of metastatic prostate cancer and he is developing the department's dedicated metastatic prostate cancer service.

Kiyoshi Takahara | Japan

Urologist

Dr. Kiyoshi Takahara is a senior lecturer in the Department of Urology at Fujita Health University School of Medicine in Aichi, Japan. He obtained his M.D. degree from Osaka Medical College in 1999 and earned a Ph.D. from the same institution in 2013. Dr. Takahara's research interests encompass various areas within urology, including prostate cancer basic research, regenerative medicine, stem cell research, and neutron capture therapy. His dedication to advancing the field is evident through his active memberships in professional societies, including the Japanese Urological Association (JUA), Japanese Society of Endourology, Japan Society for Endoscopic Surgery, Japan Society of Clinical Oncology, Japanese Society of Neutron Capture Therapy, and the Society for Reconstruction and Regeneration in Urologic Surgery.

Levent Turkeri | Turkey

Urologist

Dr Levent Turkeri is a Professor of Urology. His main expertise is Uro-oncology involving robotic, laparoscopic and open surgery. His research focuses on molecular biology of urological malignancies along with clinical trials. Currently, he is serving at Board of Urooncology Association and Director of School of Urology at Society of Urological Surgeons (Turkey). Also actively involved in a number of national and international urological societies (AUA, EAU, ESU, URS, AAEU, EORTC, ESOU).

Experts

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Makarand Khochikar | India

Urologist

Dr Makarand Khochikar qualified as a surgeon in 1988 (Miraj), completed his residency in urology in 1992 (Mumbai) and then had further training in urology, urologic oncology at Bedford and Addenbrooke's hospital, Cambridge (UK) from 1993-1998. He returned to India in 1998 to establish a state of the art Uro-oncology unit at Siddhi Vinayak Ganapati Cancer Hospital, Miraj. This department undertakes large amount of uro-oncological work and has made its presence felt nationally and internationally.

Marniza Saad | Malaysia

Clinical Oncologist

Prof Marniza is a Consultant Oncologist who has been involved in medical education and an advisor in creating the framework for Masters of Clinical Oncology in Malaysia. Her area of expertise includes urogenital cancer, breast cancer and gastro-intestinal cancer.

Melvin Chua | Singapore

Radiation Oncology

Dr Melvin Chua is the Head of Department and Senior Consultant for Head and Neck and Thoracic Cancers, Division of Radiation Oncology, and Director of the Data and Computational Science Core at the National Cancer Centre Singapore. He is also a Clinician-Scientist and Principal Investigator of the Tan Chin Tuan Laboratory of Optical Imaging, Photodynamic and Proton Beam Therapy – Precision Radiation Oncology Programme. His research is supported by the NMRC Clinician-Scientist award, and is focused on discovery and translational cancer genomics, and the development of biomarker-directed clinical trials in nasopharyngeal (NPC) and prostate cancers.

Experts

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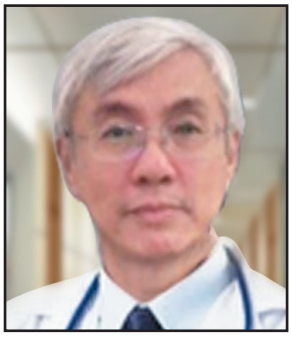

Nguyen Tuan Vinh | Vietnam

Urologist

Dr. Nguyen Tuan Vinh is an Associate Professor, PhD, and accomplished urologist. He serves as the Head of Urology B Department at Binh Binh Hospital and collaborates with the Department of Urology at Hoan My Hospital in Saigon.
Dr. Nguyen Tuan Vinh is also the Vice President of the Ho Chi Minh City Urology and Nephrology Association. With extensive experience, he runs his own Urology Clinic and contributes to the High-tech Treatment Area at Binh Dan Hospital. Dr. Nguyen Tuan Vinh is dedicated to providing excellent urological care and improving patient outcomes.

Nick Buchan | New Zealand

Urologist

Nick joined the practice from Vancouver in Canada, where he undertook a fellowship in uro-oncology and robotic surgery at the Prostate Centre based at Vancouver General Hospital and affiliated with the University of British Columbia. It is one of the largest research and clinical centres in the world that focuses on translational research into prostatic diseases and in particular prostate cancer. Prior to his fellowship in Canada, Nick undertook his urology training in Brisbane, Australia following his medical school and house surgeon years in Dunedin and Christchurch.

Ravi Kanesvaran | Singapore

Medical Oncologist

Associate Professor Ravindran Kanesvaran is a Deputy Chair and Senior Consultant in the Division of Medical Oncology of the National Cancer Centre Singapore (NCCS). He is also an Associate Professor at Duke-NUS Graduate Medical School and clinical senior lecturer at the Yong Loo Lin School of Medicine, National University of Singapore. He did his medical oncology training at NCCS and a post exit fellowship in GU cancers and geriatric oncology at the Duke Cancer Institute , North Carolina, USA. His research interests include genito-urinary oncology and geriatric oncology.

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Sarah Chen | Singapore

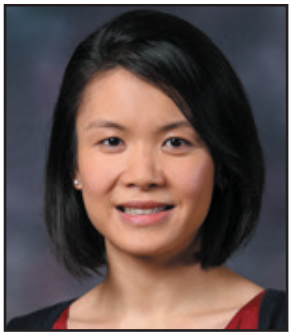
Nurse Clinician

Sarah has been providing complex nursing assessment and management to patients with Urological / Continence Conditions in Tan Tock Seng Hospital for more than 15 years. She attained her Diploma in Nursing in 2005, BSc in Nursing in 2012 and in 2022, graduated from a short course in Nursing Management in Urology / Continence and Prostate Nursing Care, La Trobe University. Imparting knowledge and supporting the community are both very strong passions of hers. She has participated both as a speaker and as a moderator in multiple Urological and Continence symposiums. To support the prostate cancer population, Sarah is part of Singapore Cancer Society's Prostate Cancer Advisory Panel Committee. She ends her week with a few sporting activities, refreshing her mind and body for the coming work week.

Scott Williams | Australia

Radiation Oncologist

Professor Scott Williams is a consultant Radiation Oncologist and Professor with the Peter MacCallum Cancer Centre Uro-Oncology service in Melbourne where he has a special interest practice made up almost exclusively of prostate cancer patients. He is heavily involved in research, managing several national and international randomised trials in prostate cancer and is a member of PeterMac ethics as well as several national research and advisory committees. He holds a USA prostate cancer foundation creativity award, their highest individual honour for innovative research ideas. This award relates to novel translational research, while he is also a collaborator on active research grants for work ranging from clinical trials to functional imaging to mathematical modelling to genetics, with national and international collaborations.



Sue-Ping Thang | Singapore

Nuclear Medicine

Dr Sue-Ping Thang graduated from the University of Edinburgh in 2006. She obtained her Membership of the Royal College of Physicians, U.K in 2009. She started her Advanced Specialty Training in Nuclear Medicine at Singapore General Hospital in 2010 and completed training in March 2013. In 2016, she was awarded the HMDP fellowship from the Ministry of Health, Singapore and underwent further training at the Peter MacCallum Cancer Centre, Melbourne, Australia, with a special emphasis on theranostics and oncology imaging. She currently works as a Consultant at Singapore General Hospital.

Experts

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Teng Ong | Malaysia

Urologist

Prof Ong is currently the President of the Malaysian Urological Association (MUA). He is also the head of the Department of Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur. Prof Ong was the BJUI Scholar from 2005 to 2007 during his training period in urology. Since then, he has been active in promoting international collaboration in education and research. At the moment, he is a board member of the Urological Association of Asia (UAA) and Societe Internationale d'Urologie (SIU). Uro-oncology is the focus of the clinical and research activities of Prof Ong. He was instrumental in establishing the first uro-onco clinic in Malaysia, in collaboration with the oncologists. He championed the M-CaP prostate cancer registry for Malaysia (working together with the A-CaP group). His group had recently published the survival data of patients with prostate cancer in Malaysia.

Toh Poh Choo | Singapore

Nurse Clinician

Ms Toh is currently a Nurse Clinician in Urology and Colorectal Centre, National University Hospital, with 28 years of experience in Urology Nursing. As a nurse, Poh Choo is very involved in daily running of the Centres, ensuring the high quality and safe care to her patients. Ms Toh was conferred the Outstanding Nurse Leader Award 2018 at Stars @ NUH Award Ceremony in recognition of her outstanding performance and significant contributions to the nursing profession and most recently in 2022, she was awarded Singapore's National Day Award Efficiency Medal 2022.

Yeong – Shiau Pu | Taiwan

Urologist

Dr. Yeong-Shiau Pu is a world-renowned specialist in prostate cancer and a professor at the Graduate Institute of Medical Medicine, NTU's College of Medicine. Dr. Pu has dedicated his academic career to clinical research and related studies on urologic oncology. Besides publishing numerous crucial papers in internationally prestigious journals, Dr. Pu has headed joint academic collaborations between Taiwan and multiple international research centres. He is also the president of the Taiwan Urology Association (TUA) and the former director of NTU Hospital's Department of Urology.

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Past papers / references

Managing advanced prostate cancer in the Asia Pacific region: "Real-world" application of Advanced Prostate Cancer Consensus Conference 2019 statements

See page 18 or visit:

https://onlinelibrary.wiley.com/doi/full/10.1111/ajco.13722

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

See page 28 or visit:

https://bjui-journals.onlinelibrary.wiley.com/doi/10.1111/bju.14489

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ORIGINAL ARTICLE

WILEY

Managing advanced prostate cancer in the Asia Pacific region: "Real-world" application of Advanced Prostate Cancer Consensus Conference 2019 statements

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Correspondence
Professor Ian D. Davis, Professor of Medicine, Monash University and Eastern Health; Head, Eastern Health Clinical School, Level 2, 5 Arnold St, Box Hill, VIC 3128, Australia.
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Abstract

Aim: The second Asia-Pacific Advanced Prostate Cancer Consensus Conference (APAC APCCC 2020) gathered insights into the real-world application in the Asia-Pacific (APAC) region of consensus statements from the 3rd Advanced Prostate Cancer Consensus Conference (APCCC 2019).

Methods: The 4-h our virtual meeting in October 2020 brought together 26 experts from 14 APAC countries to discuss APCCC 2019 recommendations. Presentations were prerecorded and viewed prior to the meeting. A postmeeting survey gathered views on current practice.

Results: The meeting and survey highlighted several developments since APAC APCCC 2018. Increased access and use in the region of PSMA PET/CT imaging is providing additional diagnostic and staging information for advanced prostate cancer and influencing local and systemic therapy choices. Awareness of oligometastatic disease, although not clearly defined, is increasing. Novel androgen receptor pathway antagonists are expanding treatment options. Cost and access to contemporary treatments and technologies continue to be a significant factor influencing therapeutic decisions in the region. With treatment options increasing, multidisciplinary treatment planning, shared decision making, and informed choice remain critical. A discussion on the COVID-19 pandemic highlighted challenges for diagnosis, treatment, and clinical trials and new service delivery models that will continue beyond the pandemic.

Conclusion: APAC-specific prostate cancer research and data are important to ensure that treatment guidelines and recommendations reflect local populations and resources. Facilitated approaches to collaboration across the region such as that achieved through APAC APCCC meetings continue to be a valuable mechanism to ensure the relevance of consensus guidelines within the region.

KEYWORDS
Asia-Pacific, consensus, guideline, metastasis, prostate cancer

1 | INTRODUCTION

The second Asia-Pacific Advanced Prostate Cancer Consensus Conference (APAC APCCC 2020) was convened in October 2020 following the 2019 Advanced Prostate Cancer Consensus Conference (APCCC 2019).[1] APCCC recommendations take an "ideal-world" perspective with no resource constraints and where patients reflect trial populations. In the Asia-Pacific (APAC) region, populations often differ from "idealized" clinical trial populations, and resources vary. APAC APCCC meetings consider the real-world application of international consensus statements for the APAC region.

Advanced prostate cancer is a significant issue for the APAC region. Patients present with advanced disease at much higher rates than in the United States (50% vs. 10%),[2,3] driven by differences in ethnicity and access to screening, testing, and treatment.

Access to and reimbursement of imaging modalities, radiation therapy, systemic therapies, and genomic testing varies in the APAC region (Figure 1A–D). Some newer systemic therapies are more available in generic form in some APAC countries. The increased likelihood of systemic treatment toxicities among some Asian populations[4,5] also influences management.

2 | METHODS

APAC APCCC 2020 brought together 26 advanced prostate cancer experts from 14 APAC countries (Table 1). The 4-h virtual meeting was hosted by the Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP). Panelist presentations on evidence, key issues, and APCCC 2019 recommendations were prerecorded and viewed prior to the meeting. A postmeeting electronic survey captured views on current practice (see Supplementary Data for survey responses).

APAC APCCC 2020 covered six topics most relevant for the APAC region:

- Management of locally advanced prostate cancer
- Management of the primary tumor in metastatic disease
- Management of newly diagnosed metastatic hormone-sensitive prostate cancer (mHSPC), including oligometastatic prostate cancer
- Management of nonmetastatic castration-resistant prostate cancer (CRPC)
- Management of metastatic CRPC sequencing
- Managing prostate cancer in a pandemic

3 | RESULTS

3.1 | Management of locally advanced prostate cancer

3.1.1 | Use of prostate-specific membrane antigen positron emission tomography/computed tomography

APCCC 2019 reported consensus for prostate-specific membrane antigen (PSMA) positron emission tomography (PET)/computed tomography (CT) imaging in patients with rising prostate-specific antigen (PSA) after radical radiation therapy to the prostate (80%) and radical prostatectomy (87%).

While the use of PSMA PET/CT is increasing in the APAC region, access and reimbursement varies (Figure 1A). APAC APCCC 2020 panelists discussed the influence of greater sensitivity of PSMA PET/CT compared with conventional imaging on treatment recommendations for locally advanced prostate cancer. The potential for under or overtreatment, depending on the interpretation of PSMA PET/CT findings, was noted.

3.1.2 | Local prostate-directed treatment for cN1M0 disease

APCCC 2019 reported strong consensus (98%) for radical locoregional treatment (radiation therapy or surgery) with or without systemic therapy for cN1 (pelvic lymph nodes) M0 prostate cancer (defined by conventional imaging).

APAC APCCC 2020 achieved consensus (92% of 26 panelists) for use of locoregional treatment as part of multimodal treatment for cN1M0 disease with consensus (83%) for use of radiation therapy. Panelists identified a range of factors influencing locoregional treatment choice (Box 1A), noting that systemic therapy improvements may influence future decision making.

Box 1: Considerations influencing the choice of local prostate-directed treatment (surgery/radiation therapy) for cN1M0 disease

- Primary tumor volume
- Likelihood of resection with a clear margin
- Number, size, and location of involved lymph nodes
- Patient age and performance status
- Requirement for pathology/genetic information to assist with treatment planning
- Whether cN1 disease is diagnosed de novo or after definitive prior therapy

B: Considerations influencing the decision to treat the primary tumor in low-risk/low-volume metastatic disease

- Local symptoms such as local obstruction (noting that these may resolve with systemic treatment, so review of local treatment is warranted after initial systemic therapy)
- Locally advanced disease
- Baseline PSA and/or PSA kinetics
- Variant histologies associated with reduced sensitivity to AR-directed therapies and have a poorer prognosis
- Performance status, frailty, and comorbidities

3.1.3 | Systemic treatment for cN1M0 disease

APCCC 2019 reported strong consensus (98%) for addition of systemic therapy to locoregional treatment with radiation therapy for patients with cN1M0 prostate cancer.

APAC APCCC 2020 panelists agreed with the addition of systemic therapy to locoregional treatment for node-positive prostate cancer. No consensus was reached on preferred systemic therapy (73% of 26 panelists use androgen-deprivation therapy [ADT] alone rather than in combination with abiraterone). Decisions about postprostatectomy systemic therapy in patients with node-positive disease are influenced by PSA levels. Patients with low-volume node-positive disease and undetectable PSA may be observed for biochemical recurrence.

Panelists noted the stronger evidence base for adjuvant systemic therapy in pN1 disease compared with cN1 disease and noted that neoadjuvant systemic treatment benefits have not yet been demonstrated in locally advanced disease.

3.2 | Management of the primary tumor in metastatic disease

APCCC 2019 reported strong consensus (98%) for overall survival benefit of local treatment of the primary tumor in low-volume/low-burden M1 disease.

Radiation therapy access in the APAC region (Figure 1C) influences choice of prostate-directed treatment in metastatic disease. In some low- and middle-income countries, lack of access to high-quality radiation therapy preferences surgery over radiation therapy, particularly

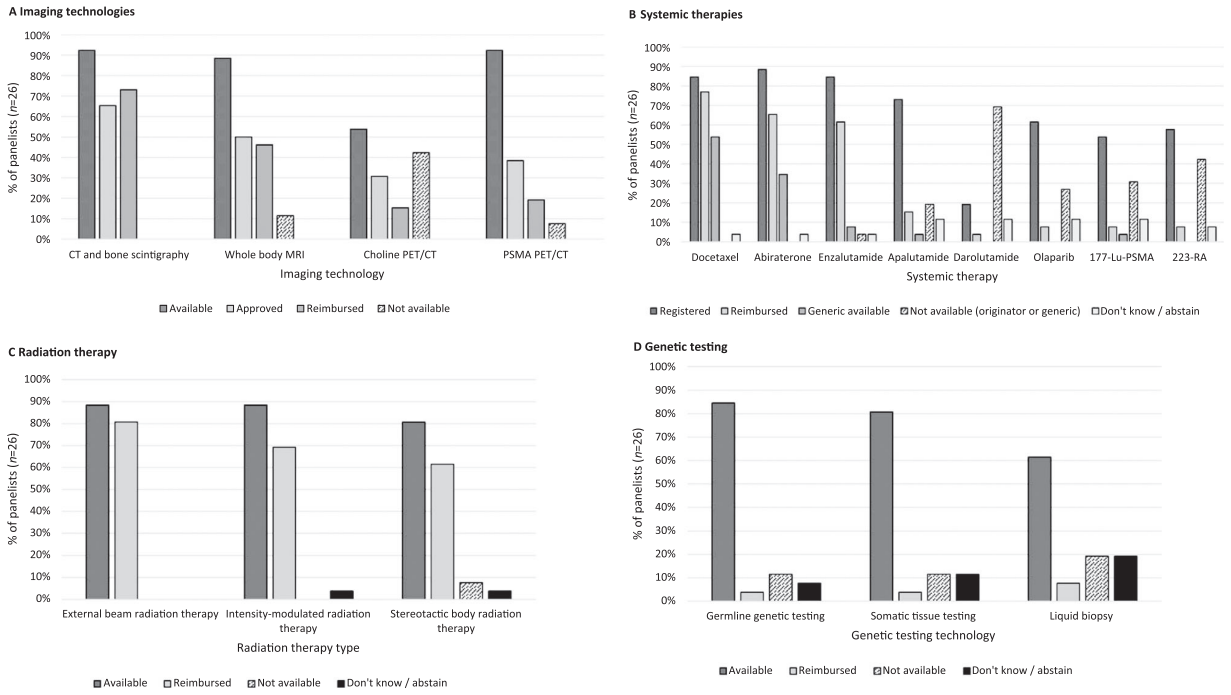

FIGURE 1 Access, approval, and reimbursement of technologies and treatments in the APAC region ($n = 26$).[a] (A) Imaging technologies, (B) systemic therapies, (C) radiation therapy, and (D) genetic testing. Abbreviations: CT, computed tomography; Lu, Lutetium; MRI, magnetic resonance imaging; PET, positron emission tomography; PSMA, prostate-specific membrane antigen; RA, radium. [a]Question was asked based on availability in each panelist's country, but some responses suggest that panelists replied on the basis of availability at their institution

TABLE 1 APAC APCCC 2020 panelists and survey respondents: disciplines and countries ($n = 26$)

	Urology	Uro-oncology	Medical oncology	Radiation oncology	Clinical oncology	Hematology /oncology	Nursing
Australia	1		2	1			1
China[a]	1						
Hong Kong	1				1		
India		1					
Indonesia	1	1					
Japan	1						
Korea	1						
Malaysia	2				1		
New Zealand	1						
Philippines	1						
Singapore	1		1	1		1	
Taiwan	1						
Thailand	1						
Turkey		1					
Vietnam	1						
Total	14	3	3	2	2	1	1

[a]Survey response only.

in patients with low-volume/low-burden M1 disease. Healthcare reimbursement policies also influence treatment decisions. Type of radiation therapy depends on available technologies, with use of stereotactic body radiation therapy (SBRT), and ultra-hypofractionation limited across the region.[6]

3.2.1 | Criteria influencing the decision to treat the primary tumor

Factors influencing APAC APCCC 2020 panelist decisions to treat the primary tumor in patients with low-volume disease are listed in Box 1B. Local treatment of the primary tumor may be considered in patients with high-volume disease where the only evidence of progression is within the prostate.

APAC APCCC 2020 panelists highlighted that choice of imaging modality can influence decision making. This mirrors the APCCC 2019 view that low-volume states on conventional and novel imaging are likely to differ clinically. APAC APCCC 2020 panelists agreed that a consistent definition of low disease burden would be useful. The most common definition (73% of 26 panelists) is disease that does not meet the CHAARTED criteria for high-volume disease (≥4 bone metastases with ≥1 beyond the axial skeleton or visceral metastases).[7]

3.2.2 | Selection of local prostate-directed treatment in low-burden/low-volume M1 prostate cancer

APCCC 2019 reported consensus (84%) for radiation therapy as local treatment for low-volume/low-burden M1 castration-sensitive/naive prostate cancer. Consensus (75%) was also reported for including primary and pelvic lymph nodes in radiation therapy of the primary tumor in newly diagnosed low-volume/low-burden M1 castration-sensitive/naive prostate cancer and clinical pelvic N1 disease.

APAC APCCC 2020 panelists agreed with radiation therapy use in patients with low-burden/low-volume M1 disease, noting that the use of surgery should be restricted to clinical trials. The heterogeneity of radiation therapy mode, dose, and fractionation was discussed, with a preference for fewer fractions of higher dose radiation or SBRT (where available) to limit hospital visits, particularly during the COVID-19 pandemic. Views differed on the role of SBRT in high-volume tumors with some panelists concerned about the risk of normal tissue toxicity and justification for palliative SBRT use.

3.3 | Management of newly diagnosed mHSPC, including oligometastatic disease

3.3.1 | Management of mHSPC

APCCC 2019 reported consensus (81%) not to combine docetaxel, an androgen receptor (AR) pathway inhibitor and ADT for newly diagnosed mHSPC. No consensus was reached on the use of high-/low-volume or high-/low-risk to guide systemic treatment in addition to ADT.

APAC APCCC 2020 panelists noted that the use and choice of an additional systemic agent with ADT in patients with mHSPC depends on treatment availability and reimbursement, disease extent, and patient factors (including potential for chemotherapy-induced toxicity, age, comorbidities, and patient preference). Docetaxel may be used instead of an AR pathway inhibitor when access and cost are barriers. In some APAC countries, an AR pathway inhibitor plus ADT is used instead of docetaxel because of the higher risk of chemotherapy-related toxicity among Asian populations and patient concerns about chemotherapy.

Around two-thirds of APAC APCCC 2020 panelists (65% of 26 panelists) indicated that they would not add docetaxel to ADT in patients with low-volume disease (de novo or metachronous metastases). Almost one quarter (23%) would consider adding docetaxel in people with low-volume disease only if they had de novo metastases.

APCCC 2019 reported consensus (78%) for no additional imaging modalities in newly diagnosed high-volume mHSPC (based on CT and bone scan). No consensus was reached on additional imaging modalities in newly diagnosed low-volume mHSPC (based on CT and bone scan).

APAC APCCC 2020 panelists agreed that the use of PSMA PET/CT is unlikely to change treatment recommendations if conventional imaging has identified high-volume mHSPC. PSMA PET/CT is likely to be more useful to confirm disease extent in patients with mHSPC for whom conventional imaging has identified low-volume disease.

3.3.2 | Management of oligometastatic prostate cancer

The concept of oligometastatic disease has emerged more strongly since APCCC 2017 and APAC APCCC 2018. However, oligometastatic disease is still not clearly defined.

At APCCC 2019, no consensus was reached on the number of metastases or location (bone, lymph nodes, viscera, and lung) of metastases that qualify as oligometastatic disease. Consensus (79%) was reported that CT and bone scan are not sufficient to define an oligometastatic state for treatment planning. Consensus (75%) was also reported for use of PSMA PET/CT or MRI to confirm a diagnosis of metachronous oligometastatic prostate cancer if detected on CT and bone scan.

No consensus was reached at APAC APCCC 2020 on the number of metastases that qualify as oligometastatic disease. Seventy-three percent of 26 panelists indicated that imaging by CT and bone scintigraphy is not sufficient to define the oligometastatic state for treatment planning. Almost all survey respondents (96% of 26 panelists) indicated that, if available, they would undertake additional imaging with PSMA PET/CT to confirm oligometastatic disease identified on conventional imaging.

Consensus was reached at APAC APCCC 2020 (77% of 26 panelists) for the need to distinguish de novo treatment-naïve (synchronous) oligometastatic prostate cancer from oligometastatic prostate cancer recurring after an initial diagnosis of M0 disease (metachronous metastases). There was also consensus that, in untreated de novo oligometastatic prostate cancer, it is important to distinguish lymph

node-only disease (including distant lymph node metastases) from disease that includes metastatic lesions at other sites (81% of 26 panelists).

APAC APCCC 2020 panelists discussed the difficulty of obtaining a differential diagnosis between true oligometastatic disease and metastatic disease that is not yet evident, and the impact of this on decision making about local prostate-directed treatment. It was suggested that including time since diagnosis in the definition of oligometastatic disease can increase confidence in identifying disease that may be amendable to radical therapy, with time allowing subclinical metastases to become evident.

APAC APCCC 2020 panelists discussed the use of treatment to the primary/metastases to manage symptoms, improve quality of life, and slow disease progression in patients with low metastatic burden. Data from STAMPEDE were referenced, showing that local prostate-directed treatment in metastatic disease affects progression-free and overall survival but not metastasis.[8] In the subgroup analysis, overall survival advantage was observed in patients with low-volume metastatic disease.

At APCCC 2019, consensus was almost reached (74%) for use of systemic therapy plus local prostate-directed therapy of all lesions in metachronous oligometastatic prostate cancer.

No consensus was reached among APAC APCCC 2020 panelists about preferred treatments for de novo synchronous or metachronous oligometastatic prostate cancer. Responses to the postmeeting survey reflect a range of treatment goals and combinations (Table 2A–E). Panelists noted European Association of Urology and National Comprehensive Cancer Network guideline recommendations[9,10] about the use of radiation therapy to treat the primary tumor in oligometastatic disease and agreed that surgery should be considered investigational in this setting. The potential for phase II trials to provide further information on the role of metastasis-directed therapy in patients with oligometastatic disease was discussed.[11–14]

3.4 | Management of nonmetastatic (M0) CRPC

APAC APCCC 2020 panelists reflected on the potential for PSMA PET/CT to change a diagnosis from M0CRPC (diagnosed using conventional imaging) to M1 metastatic CRPC (mCRPC). The high likelihood of PSMA PET/CT detecting metastases in patients at high risk of progression was noted.

Panelists agreed that additional information from PSMA PET/CT is unlikely to change treatment recommendations or outcomes for most patients with M0CRPC if newer AR pathway inhibitors are available. However, in countries where novel agents are not available, PSMA PET/CT may provide information to inform metastasis-directed therapy or local prostate-directed therapy. A change in diagnosis from M0CRPC to mCRPC can increase access to AR pathway inhibitors in countries where these agents are not indicated/reimbursed for M0CRPC disease.

APCCC 2019 reported consensus (86%) for use of an AR antagonist (apalutamide, enzalutamide, and darolutamide) as the preferred choice of treatment in addition to ADT in M0CRPC with PSA≥2 mg/mL and PSA doubling time ≤10 months. Consensus was also reported (86%) for not extrapolating data from ARAMIS, PROSPER, and SPARTAN to M0CRPC with a PSA doubling time > 10 months.

APAC APCCC 2020 panelists discussed whether the cost and potential side effects of novel AR antagonists can be justified in asymptomatic patients with M0CRPC, noting the need to balance these issues with effects on symptoms and survival. Panelists agreed that data on novel AR pathway inhibitors should not be extrapolated to abiraterone to address the high cost of novel therapies. Concerns about side effects of long-term steroid use with abiraterone were also noted. However, two-thirds of APAC APCCC 2020 panelists (65% of 26 survey respondents) indicated that they would consider using abiraterone for treatment of M0CRPC to address issues of access and cost of novel AR antagonists. Some panelists also consider older therapies (bicalutamide, nilutamide, fosfestrol, diethylstilbestrol, finasteride/dutasteride, and dexamethasone) when access and cost are an issue. It was noted that the use of older agents should be limited to patients with M0CRPC with a longer PSA doubling time (> 10 months).

3.5 | Sequencing of therapies in mCRPC

A range of treatment options are available for mCRPC, including second-, third-, and fourth-line options, influenced by local regulatory restrictions.[9,10] In some APAC countries, access and cost issues increase reliance on older drugs or cheaper drugs in the same treatment category. Increased toxicity risk also limits chemotherapy use in some Asian patients. This may result in use of an AR pathway inhibitor instead of switching to docetaxel or another type of chemotherapy. Again, some panelists highlighted that access and cost issues mean older therapies are still used despite limited evidence of benefit.

APAC APCCC 2020 panelists discussed factors influencing treatment sequencing decisions in patients with mCRPC, noting that PSA doubling time alone is insufficient for decision making. Other factors indicative of clinical progression, such as changes in imaging and symptoms, and type, duration, and response to previous treatments, should be considered.

No consensus was reached at APCCC 2019 about switching to enzalutamide when disease progresses on abiraterone or vice versa.

APAC APCCC 2020 panelists reflected on the high degree of AR pathway inhibitor cross-resistance, noting little benefit in switching to another AR pathway inhibitor following disease progression on an AR pathway inhibitor. Panelists noted that switching from abiraterone to enzalutamide generally has a higher probability of PSA response than vice versa. However, there is no high-level evidence to substantiate this practice, with the only data from a single, randomized, phase II trial.[15]

Steroid dosage should be tapered when discontinuing abiraterone, with an associated increased risk of diabetes. Panelists noted that the higher risk of diabetes among some Asian populations means additional caution is needed for these patients.

Use of ^{177}Lu-PSMA was discussed. Panelists noted that cost (including the cost of pretreatment imaging and follow-up) is a key factor

TABLE 2 APAC APCCC views on management of oligometastatic disease ($n = 26$)

A) Treatment goal when recommending local treatment of all lesions instead of systemic therapy in oligometastatic prostate cancer			B) Treatment goal when recommending adding local treatment of all lesions to systemic treatment in oligometastatic prostate cancer		
Goal	**%**	***N***	**Goal**	**%**	***N***
Delay start of ADT	8%	2	Prolong progression-free survival	23%	6
Prolong progression-free survival	12%	3	Prolong overall survival	12%	3
Prolong overall survival	4%	1	Prolong both progression-free and overall survival	50%	13
All three of the above	50%	13	Cure	0%	0
Cure	0%	0	None of the above	0%	0
None of the above	4%	1	I do not recommend local treatment of all lesions in oligometastatic prostate cancer	12%	3
I do not recommend local treatment of all lesions in oligometastatic prostate cancer	19%	5	Abstain	4%	1
Abstain	4%	1			
C) Treatment recommended for majority of patients with synchronous oligometastatic prostate cancer (based on conventional imaging) with an untreated primary tumor			**D) Treatment recommended for the majority of patients with newly diagnosed oligometastatic prostate cancer on novel imaging (but no metastases on conventional imaging) with an untreated primary tumor**		
Treatment	**%**	***N***	**Treatment**	**%**	***N***
Systemic therapy only	4%	1	Systemic therapy only	8%	2
Systemic therapy plus treatment of the primary tumor	62%	16	Local/regional therapy only	4%	1
Systemic therapy plus treatment of the primary tumor and focal treatment of all lesions	27%	7	Systemic therapy plus treatment of the primary tumor	39%	10
Treatment of the primary tumor and focal treatment of all lesions without systemic therapy	4%	1	Systemic therapy plus treatment of the primary tumor and focal treatment of all lesions	44%	11
Abstain	4%	1	Treatment of the primary tumor and focal treatment of all lesions without systemic therapy	4%	1
			Abstain	4%	1
E) Treatment recommended for the majority of patients with oligorecurrent (metachronous) oligometastatic prostate cancer					
Treatment	**%**	***N***			
Systemic therapy alone	38%	10			
Systemic therapy and local treatment of all lesions	58%	15			
Abstain	4%	1			

influencing use. Examples were cited of patients self-funding treatment, even when ^{177}Lu-PSMA therapy is not recommended. Panelists agreed that ^{177}Lu-PSMA should only be considered as a last line of treatment when all approved options have been exhausted. The challenge of managing patient expectations about new treatments and not offering treatment based only on an individual's ability to self-fund was highlighted.

Panelists reflected on access and cost in the APAC region of sequencing, genetic testing, and access to biomarker-based therapies, such as olaparib. It was suggested that biomarker testing is limited to patients whose disease progresses after multiple treatment lines.

3.6 | Managing prostate cancer in a pandemic

APAC APCCC 2020 included discussion about the impact of COVID-19 on prostate cancer clinical care and research in the region. Concern has been raised about the impact of the pandemic on cancer diagnosis and treatment, due to diversion of resources for pandemic

TABLE 3 Impact of COVID-19 on prostate cancer management and research in APAC countries ($n = 26$)

	No noticeable issue		Some effect		Significant issue		Don't know/abstain	
Impact	%	N	%	N	%	N	%	N
Fewer new patients presenting for diagnosis	8%	2	65%	17	23%	6	4%	1
Fewer patients presenting for follow-up appointments	4%	1	54%	14	38%	10	4%	1
Postponed/cancelled diagnostic services	19%	5	54%	14	23%	6	4%	1
Postponed/cancelled treatment services–surgery	19%	5	46%	12	23%	6	12%	3
Postponed/cancelled treatment services–radiation therapy	19%	5	42%	11	15%	4	23%	6
Fewer patients accessing support services	15%	4	46%	12	27%	7	12%	3
Less access to imaging technologies	35%	9	54%	14	4%	1	8%	2
Change in systemic therapy regimen	28%	7	54%	14	12%	3	12%	3
Delayed/postponed clinical trial recruitment	12%	3	38%	10	42%	11	8%	2

management, health service protocols to minimize transmission risk, and public concern about accessing health services.[16,17] Clinical trial activity has also been affected, with some clinical trials suspended.[18,19]

APAC APCCC panelists highlighted a range of impacts of COVID-19 on prostate cancer management (Table 3) including:

- fewer patients presenting for diagnosis, follow-up, and support, with concern expressed about the impact on delayed diagnosis
- postponement or cancellation of diagnostic and treatment services
- changes to systemic treatment regimens (e.g., reduced use of treatments with a potential impact on immunity and use of longer acting treatments to limit hospital visits)
- delayed or postponed clinical trials
- changes in planning and delivery of prostate cancer care, including increased use of telehealth and home delivery of medications by pharmacies

Panelists highlighted the value of rapid prostate cancer guidelines during the pandemic,[20,21] and reflected on how long services should expect to be working under revised guidelines. Reference was made to the importance of local treatment in locally advanced and low-volume metastatic disease and how long such treatment should be postponed as the pandemic continues.

Panelists noted that changes in service delivery, such as the use of telehealth, are likely to continue beyond the pandemic and will be useful alongside face-to-face consultations.

4 | DISCUSSION

APAC APCCC 2020 was convened to review how ideal-world consensus recommendations from APCCC 2019 apply in everyday practice in the APAC region. Discussion focused on five issues most relevant to the APAC region with an additional discussion on the impact of COVID-19 on prostate cancer management in the region. Insights were gathered from a real-world perspective to better understand practical considerations in the APAC region for management of advanced prostate cancer.

A number of themes from APAC APCCC 2020 are consistent with APAC APCCC 2018.[22] Differences in access to and cost of therapeutic agents and imaging technologies (including availability of generic products) influence management and treatment choices. The toxicity profile of chemotherapy among some Asian populations also influences treatment. Later stage at diagnosis of prostate cancer is an issue among some Asian populations, and there is a risk this will be exacerbated by the COVID-19 pandemic.

Panelist views highlight some differences in practice compared with APCCC 2019 consensus recommendations and some differences within the region. Such differences reflect evolving evidence and the influence on practice of resource constraints.

A key theme was the rapidly evolving role of novel imaging (PSMA PET/CT). APAC APCCC 2020 panelists agreed that, in an ideal-world scenario (disregarding cost and access issues), PSMA PET/CT would be the first choice of imaging modality for patients with suspected metastatic disease. However, access and reimbursement limitations currently restrict use. While almost all 26 panelists (92%) indicated that PSMA PET/CT is available in their country, only 38% indicated approval for use in advanced prostate cancer and only 19% indicated that it is reimbursed for this indication.

PSMA PET/CT is changing definitions of staging, with clear differences compared with conventional imaging. APAC APCCC 2020 panelists noted the need to understand the impact of PSMA PET/CT staging on disease management and whether this translates into improved patient outcomes. The significance of low-volume disease diagnosed using conventional imaging that has a high-volume pattern on PSMA PET/CT is unknown. Preferred uses by APAC APCCC 2020 panelists for PSMA PET/CT (where available) included diagnosis and staging of high-risk clinically localized prostate cancer, to confirm low-volume metastatic disease diagnosed on conventional imaging, and to resolve discordant findings, such as high PSA with no evidence of metastasis on conventional imaging.

Recognition of the concept of oligometastatic disease and biological differences between de novo and metachronous metastatic disease has increased since APAC APCCC 2018. However, there is still no consensus on a clear definition for oligometastatic disease.

The role of novel systemic and radiation treatments also featured in discussions, particularly in relation to low-volume mHSPC and M0CRPC. Variability in access and cost of treatments across the APAC region continues to influence treatment choices.

A common theme was the importance of multidisciplinary management of advanced prostate cancer. Panelists also emphasized the importance of shared decision making with patients noting the need for informed choice underpinned by clear communication about benefits, risks, and costs of available treatment options. Areas requiring careful communication included:

- the distinction between "life-extending treatment" and "curative treatment"
- the risk of systemic treatment side effects in asymptomatic patients
- the significant level of "PSA anxiety" that exists for patients
- the complexity of explaining how differences between PSMA PET/CT and conventional imaging findings may influence treatment options

Areas of nonconsensus at APCCC meetings often reflect emerging evidence. Examples at APAC APCCC 2020 included:

- the lack of a consistent definition of "low disease burden" in the metastatic setting
- the need for clarity in the definition of M0CRPC
- the impact of newer radiation therapy techniques such as SBRT on outcomes for patients with locally advanced (cT3/4 and/or cN1) or metastatic disease
- the evolving field of biomarker testing in identifying treatment targets in metastatic disease

APAC APCCC 2020 was conducted against the backdrop of a global pandemic. Panelists described effects on clinical service delivery and clinical trials and highlighted the likely longer term impact on stage at diagnosis and outcomes. Postpandemic implications for service delivery were discussed, including standardization of telehealth and sense-checking the number and frequency of hospital visits for clinical trials.

APAC APCCC 2020 was the second region-wide meeting to discuss management of advanced prostate cancer. The value of shared insights and collaboration across the region were once again apparent, with an ongoing commitment to translating innovations in technologies and treatments into improved outcomes for men with advanced prostate cancer across the region.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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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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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 second APCCC 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-naïve 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. Whilst 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. The 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

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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.

Keywords

advanced prostate cancer, castration-naïve prostate cancer, castration-resistant prostate cancer, high-risk localised prostate cancer, oligometastatic prostate cancer, cost and access to treatment

Introduction

The 2018 Asia Pacific Advanced Prostate Cancer Consensus Conference (APAC APCCC 2018) was convened to reflect on consensus statements from the 2017 APCCC (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 the 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 the 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 are 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 1-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 10 topic areas discussed during the APCCC 2017 and agreed on the five

Table 1 The APAC APCCC 2018 panel members.

Name	First name	Specialty	Chemotherapy prescriber*		Country
			Oral agents	i.v.	
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	Urologist	✓	–	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 i.v. chemotherapy (docetaxel) for prostate cancer. †A review of prescribing practices among urologists in Taiwan suggests that about half of all urologists has prescribed i.v. chemotherapy but not on a regular basis.*

most contentious areas to discuss at the APAC APCCC 2018, based on their relevance for the APAC region:

- Management of castration-sensitive/naïve prostate cancer (CNPC).
- Management of castration-resistant prostate cancer (CRPC).
- Management of high-risk localised and locally advanced prostate cancer.
- Management of oligometastatic prostate cancer.
- 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 amongst the 20-strong panel.

Management of advanced prostate cancer in the APAC region

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

The PREVAIL study (a multinational phase 3, randomised, double-blind, placebo-controlled efficacy and safety study of oral Mdv3100 in chemotherapy-naïve patients with progressive metastatic prostate cancer who have failed androgen-deprivation therapy) 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 of ≥8 and a higher percentage with bone disease (likely a result of less frequent 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].

Whilst 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 the APAC APCCC 2018.

Another factor influencing advanced prostate cancer management is the status of registration and reimbursement for diagnostic technologies and treatments. Tables 2 and 3 provide a summary of the status of prostate cancer drugs (Table 2) and imaging technologies (Table 3) as reported for the countries represented at the APAC APCCC 2018 in early 2018.

The APAC APCCC 2018 outcomes

Management of metastatic CNPC (mCNPC)

Addition of docetaxel to androgen-deprivation therapy (ADT) in mCNPC

The APCCC 2017 reported strong consensus (96%) for the addition of docetaxel (3 weekly at 75 mg/m^2) to ADT in men with *de novo* mCNPC and high-volume disease, as defined in the chemohormonal therapy versus androgen ablation randomised trial for extensive disease in prostate cancer (CHAARTED) (visceral [lung or liver] and/or ≥4 bone metastases, at least one beyond the pelvis and vertebral column) [6]. Whilst not reaching the threshold 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).

The APAC APCCC 2018 panellists reflected on the recently published 53-month follow-up data from CHAARTED showing an overall survival (OS) benefit for the addition of docetaxel (3 weekly at 75 mg/m^2) in patients with high-volume disease (hazard ratio [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

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

Country	Abiraterone			Enzalutamide			Docetaxel			^{223}Ra			G-CSF			Bone loss therapy	
	Reg	Reimb	Gen	Reg	Reimb	Gen	Reg	Reimb	Gen	Reg	Reimb	Gen	Reg	Reimb	Gen	Zvoledronic 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; post-chemo, post-chemotherapy.

Table 3 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	✓	✓	✓	✓	✓	–	–	–
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.

be considered in low-volume mCNPC. This contrasts with practice in the USA, 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 the following:

- increased toxicity of docetaxel in Asian men, specifically a higher incidence of febrile neutropaenia.
- 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 (Table 2).

The issue of increased toxicity of docetaxel in Asian men was notable during discussions about mCNPC and metastatic CRPC (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 the APAC APCCC 2018. The USA and European guidelines state that G-CSF prophylaxis should be considered in men with risk factors [12–14]. No consensus was reached at the 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 of the 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 75 mg/m^2 has been reported in men with CRPC [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 60 mg/m^2. A similar finding was reported from the Taiwan consensus meeting held after the APCCC 2017: only 50% of participating doctors indicated that they use a starting dose of docetaxel of 75 mg/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.

Addition of abiraterone to ADT in mCNPC

Panellists at the APCCC 2017 did not vote on the addition of abiraterone to ADT in mCNPC as data from the randomised, double-blind, comparative study of abiraterone acetate plus low-dose prednisone plus ADT vs ADT alone in newly diagnosed subjects with high-risk, metastatic hormone-naive prostate cancer (LATITUDE) [16] and systemic therapy in advancing or metastatic prostate cancer: evaluation of drug efficacy (STAMPEDE) [17] trials were not yet available. European Association of Urology (EAU) 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 the 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 (Table 2).

Imaging to determine therapeutic strategies

The APCCC 2017 focused on the use of increasingly sensitive imaging techniques, such as ^{68}Ga- prostate-specific membrane antigen (PSMA)-positron emission tomography (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 (Table 3). 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 amongst panellists in the potential to use other imaging techniques, such as MRI, as a means of determining stage of disease [21,22].

Other issues related to management of mCNPC

Other issues discussed in relation to mCNPC included the following:

- 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.

Management of mCRPC

The 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

Table 4 Areas of consensus from the APCCC 2017 regarding the management of mCRPC.

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

sequencing and treatment combinations in the management of mCRPC for which evidence is limited and clinical trials underway.

Sequencing of treatment for mCRPC

Table 4 summarises the areas of consensus at the APCCC 2017 related to sequencing of treatment for mCRPC.

The APAC APCCC 2018 panellists reflected on the large number of trials that have shown an OS advantage for survival-prolonging agents in mCRPC when used before and after 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. The APAC APCCC 2018 panellists agreed with the APCCC 2017 conclusions that clinical factors, such as performance status, symptoms, comorbidities, 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 the following:

- 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 the APAC APCCC 2018 was the impact of cost and access on prescribing habits (Table 2). 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 was 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.

Combined treatment

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

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

Other issues related to the management of mCRPC

Other issues discussed in relation to mCRPC included the following:

- whether the clinical benefits of starting treatment for mCRPC earlier (e.g. whilst 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. The panellists noted inconsistency in clinical uptake of information about benefits of exercise programmes offering advice on resistance training or access to an exercise physiologist, to mitigate loss of bone density associated with ADT.

High-risk localised and locally advanced prostate cancer

The APCCC 2017 highlighted discipline-specific variation in the definition of 'high risk' as it relates to prostate cancer. The EAU, European Society for Radiation Therapy and Oncology, and International Society of Geriatric Oncology (EAU-ESTRO-SIOG) definition was used at the APCCC 2017 meeting (localised disease: PSA level >20 ng/mL, or Gleason score >7 or cT2c; locally advanced disease: any PSA level, 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 level >20 ng/mL) [12].

Treatment preferences for high risk and locally advanced prostate cancer

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

The panellists at the APAC APCCC 2018 discussed primary treatment for high risk and locally advanced disease. It was noted that the use of radical prostatectomy (RP) with or without radiation therapy (RT) and ADT depends on a range of factors, including patient age and fitness, comorbidities, and the 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 the APAC APCCC 2018 was the importance of a multidisciplinary team (MDT) approach to developing treatment recommendations for advanced prostate cancer. Whilst geography and access to specialist cancer centres can be a significant barrier to MDTworking, the benefits of virtual participation in MDT 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].

Pelvic lymph node dissection (PLND) for high risk and locally advanced prostate cancer

At the APCCC 2017, there was consensus for the use of PLND in most men with cN0cM0 high-risk prostate cancer undergoing RP (84%), and for removal of >10 lymph nodes (76%). European [33] and NCCN guidelines [12] recommend RP with an extended PLND (ePLND) for men with high risk and locally advanced prostate cancer.

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

The panellists noted differing preferences regarding standard or ePLND. Concerns were noted about possible complications following ePLND and their potential to limit opportunities for further treatment such as RT. The 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.

Use of adjuvant vs salvage RT after RP

No consensus was reached at the 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.

Whilst EAU and AUA guidelines recommend the use of RP plus RT and ADT for high-risk prostate cancer [33,36], RT use is reported to be in decline [37]. The 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 N1M0 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 the 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.

Management of 'oligometastatic' prostate cancer

The 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.

The APAC APCCC 2018 panellists also reflected on the variation in definitions [40,41] and the lack of a definitive threshold for what constitutes oligometastatic prostate cancer. Some APAC APCCC 2018 panellists expressed different views to the APCCC 2017 findings about the 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 and prospective data are emerging.

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

- limited availability in many APAC countries of imaging technologies, such as ^{68}Ga-PSMA-PET, required to detect oligometastatic disease (Table 3).
- 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 of 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 are likely to be helpful.

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

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

At the 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 $2.8 billion (American dollars) 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 suboptimal clinical achievement to show that new treatments can improve the duration and quality of survival of men with advanced prostate cancer but to have such treatments unavailable to a large segment of the global population of men with advanced prostate cancer' [1].

Lower-cost options in countries with limited resources

The 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 healthcare resources of:

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

The 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 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 healthcare resources [43,44].

What can be done to address resource limitations?

The APAC APCCC 2018 panellists recognised the requirement for universal health coverage as highly relevant in the APAC region. Opportunities for consideration include the 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]. The panellists noted that collaboration between academia, government, industry (pharmaceutical), non-government organisations, and other sectors will be key to the 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 – Australia and New Zealand [47] and contributions to the Asian Prostate Cancer Study Group (A-CaP) registry [48] in identifying differences in access and variation in practice was also noted.

Discussion

The APAC APCCC 2018 was convened to review how statements of consensus and non-consensus from the 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.

The APAC APCCC 2018 differed in format to the APCCC 2017. The panel included more urologists, reflecting how treatment for men with prostate cancer is frequently managed in the APAC region. Whilst 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 i.v. chemotherapy. RT is usually administered by radiation oncologists, although in some countries (e.g. Malaysia), both chemotherapy and RT are administered by clinical oncologists.

No formal voting mechanism was used at the APAC APCCC 2018. Discussion focused instead on practical considerations relating to the areas of consensus and non-consensus from the 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 highlight areas of controversy and evolving evidence where further research may be beneficial.

Real-world Implications of the APCCC 2017 statements in the APAC 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 (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 the following:

- a lack of established safety data for docetaxel in Asian men and concerns about febrile neutropaenia 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 the presence of generic docetaxel.
- whilst 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

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 neutropaenia 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 are 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 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.

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 MDTs can be a challenge to set up in some APAC regions, the view of the APAC APCCC 2018 panellists is that options to support MDT 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 are significant. The 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.

The APAC APCCC 2018 was the first region-wide meeting to discuss the management of advanced prostate cancer. The 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

Dr Ong reports grants and honoraria from Johnson & Johnson, and honoraria from Astellas, Sanofi and Novartis outside the submitted work Associate Professor Williams reports being a member of industry advisory boards for Astellas, Bayer and Janssen outside the submitted work, with all remuneration for this work being retained by his employer. Dr Nicholas Ruchan is on the Board of ANZUP Cancer Trials Group, Associate Professor Chiong reports support for manuscript preparation from the ANZUP Cancer Trials Group during the conduct of the submitted work, and honoraria from Astellas, Johnson & Johnson, Amgen, Bayer, Astra Zenica, Sanofi, Menarini and Transmedic International outside the submitted work.

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Abbreviations: (e)PLND, (extended) pelvic lymph node dissection; (m)CNPC, (metastatic) castration-naïve prostate cancer; (m)CRPC, (metastatic) castration-resistant prostate cancer; A-CaP, Asian Prostate Cancer Study Group; ADT, androgen-deprivation therapy; ANZUP, Australian and New Zealand Urogenital and Prostate (Cancer Trials Group); APAC, Asia Pacific; APCCC, Advanced Prostate Cancer Consensus Conference; ASIR, age-standardised incidence rate; CHAARTED, chemohormonal therapy versus androgen ablation randomised trial for extensive disease in prostate cancer; EAU, European Association of Urology; G-CSF, granulocyte colony-stimulating factor; MDT, multidisciplinary team; NCCN, National Comprehensive Cancer Network; PET, positron emission tomography; PSMA, prostate-specific membrane antigen; RP, radical prostatectomy; RT, radiation therapy; SDI, sociodemographic index; STAMPEDE, Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy.

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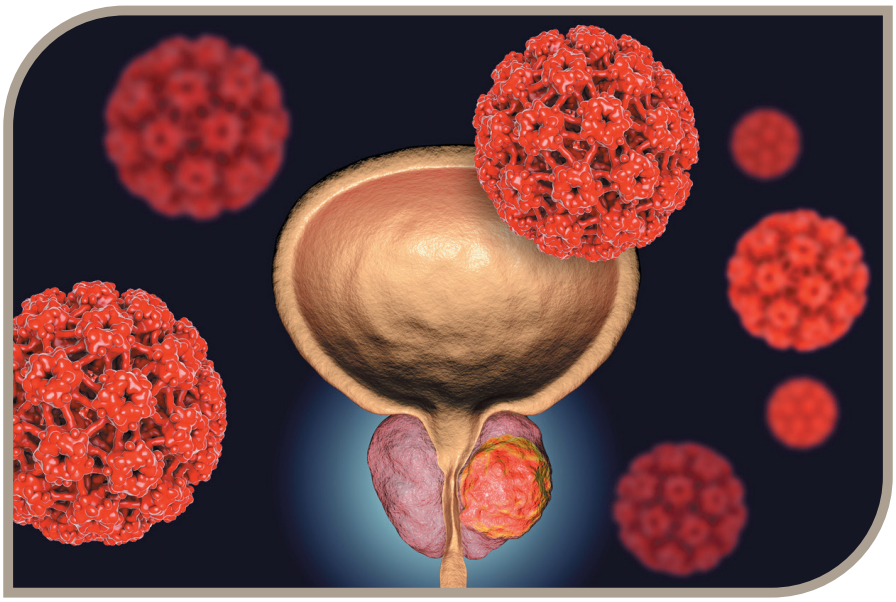

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