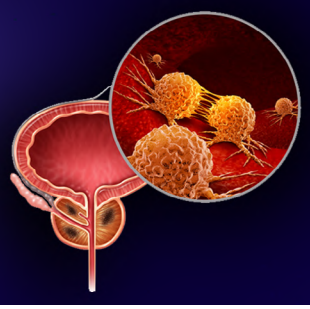
Prostate Cancer Practice Review™



Making Education Easy

Issue 31 - 2025

In this issue:

Abbreviations used in this issue:

ADT = androgen-deprivation therapy; **ARPI** = androgen receptor pathway inhibitor; **FDA** = US Food & Drug Administration; **HRR** = homologous recombinant repair; **mCRPC** = metastatic castration resistant prostate cancer; **mCSPC** = castration-sensitive prostate cancer; **NCCN** = US National Comprehensive Cancer Network; **PARP** = poly (ADP-ribose) polymerase; **PBAC** = Pharmaceutical Benefits Advisory Committee; **PBS** = Pharmaceutical Benefits Scheme; **PSA** = prostate-specific antigen; **PSMA** = prostate-specific membrane antigen.

Earn CPD

Nursing and Midwifery Board of Australia (NMBA) Journal reading and watching videos (including Research Reviews') may be considered a self-directed activity set out in the NMBA Registration Standard: Continuing Professional Development. One hour of active learning will equal one hour of CPD. Details at NMBA CPD page.

Welcome to the 31st issue of Prostate Cancer Practice Review.

This Review covers news and issues relevant to clinical practice in prostate cancer. It will bring you the latest updates, both locally and from around the globe, in relation to topics such as new and updated treatment guidelines, changes to medicines reimbursement and licensing, educational, professional body news and more. Finally, on the back cover you will find a summary of upcoming local and international educational opportunities including workshops, webinars and conferences.

We hope you enjoy this Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,

Dr Janette Tenne
Editor
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Clinical Practice

Prostate Cancer Foundation White Paper on combination therapy for metastatic hormone-sensitive prostate cancer

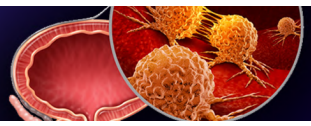
A collaborative multi-organisation effort aimed to identify factors contributing to the disparity between established optimal care for patients with metastatic hormone-sensitive prostate cancer (henceforth referred to as castration-sensitive prostate cancer [CSPC]) and that employed in routine care across the globe and offer practical solutions to align the two. Organised by the US Prostate Cancer Foundation in collaboration with key representatives from academia, community practices, industry and patient advocacy groups, a comprehensive review of real-world clinical practice was first undertaken to elucidate the extent of deviation from gold standard guideline-recommended care and key factors contributing to this disparity before examination of ways to navigate through the complex situation and development of fundamental strategies to mitigate major obstacles and improve care delivery.

Despite the clear clinical trial evidence demonstrating the superior efficacy of doublet or triplet combination therapy comprised of androgen deprivation therapy (ADT) plus an androgen receptor pathway inhibitor (ARPI) ± docetaxel, versus ADT alone, for mCSPC - establishing combination therapy as the recommended gold standard initial treatment for all but the small proportion of patients with contraindications due to frailty or limited life expectancy - in routine clinical practice worldwide more than half of clinically indicated patients receive discordant treatment. Disturbingly, analysis of contemporary real-world evidence revealed that there was a significant problem with translation of trial research into access to combination therapy in this patient population, with estimates of the proportion of patients treated with combination therapy ranging overall from < 10% to 38%, with an ARPI employed in less than half of patients and most patients (90%) not receiving docetaxel.

Lack of adherence to optimal therapy in this space was attributed to multiple challenges including racial and geographic disparities in access to treatment, financial barriers and variability in standard care approaches across different practice settings. Underutilisation of evidence-based therapies in mCSPC due to clinical practice and care delivery issues was primarily due to concerns about medication tolerability, lack of knowledge of trial evidence, reimbursement and other financial issues and doubt about whether combination therapy should be utilised earlier or later in the disease course.

Pivotal strategies suggested to improve care delivery for mCSPC included dissemination of targeted educational programs, development of resources and prioritisation of standardised and equitable access to evidence-based treatment. The White Paper concludes that concerted application of the suggestions proposed through this expert discussion may contribute to the improved survival and quality of life for patients with mCSPC.

JCO Oncol Pract. 2025;21(9):1240-46



Updates to NCCN Guidelines

NCCN Clinical Practice Guidelines in Oncology® - Prostate Cancer

Recent updates to the US National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for prostate cancer have been published (version 2.2026). Aimed at urologists, medical oncologists and other physicians involved in the care of patients with prostate cancer, the guidelines provide a framework to optimise and personalise treatment. Since their inception in 1996 the guidelines have undergone at least one annual update to reflect changes in regulatory regulations, the introduction of novel therapeutic or diagnostic agents and greater understanding of the responsiveness of various disease states to different therapeutic strategies. Advice covers initial diagnosis, initial risk stratification and staging workup for clinically localised, regional or metastatic disease, primary therapy according to risk group, prostate-specific antigen (PSA) persistence/recurrence following radical prostatectomy and/or radiation therapy, workup and treatment for second biochemical recurrence, and therapy for progressive disease according to castration-sensitivity status and the presence/absence and volume of metastasis.

Salient revisions and updates in recent iterations include the removal of the very-low-risk group from the guidelines and replacement of "other hormonal agents" with ARPIs. Treatment recommendations for recurrent disease after radical prostatectomy or radiotherapy and for metastatic castration resistant prostate cancer (mCRPC) were also modernised this year.

The following treatment algorithm summarises the current recommendations for the systemic treatment of mCRPC according to prior therapy from the 2026 iteration of the NCCN guidelines.

	Pre-ARPI	**Post-ARPI/ Pre-docetaxel**	**Post-ARPI and docetaxel**
Preferred	• Abiraterone • Enzalutamide	• Docetaxel	• Cabazitaxel • Docetaxel rechallenge
Other recommended	Docetaxel		
Useful in certain circumstances:			
BRCA1/2-positive	• Niraparib + abiraterone • Olaparib + abiraterone • Talazoparib + enzalutamide	• Olaparib • Rucaparib • Niraparib + abiraterone • Talazoparib + enzalutamide	• Olaparib • Rucaparib
Non-*BRCA* HRR-positive	• Talazoparib + enzalutamide	• Olaparib • Talazoparib + enzalutamide	• Olaparib • Other FDA approved agents for tissue agnostic indications
Bone metastases	• Radium-233 + enzalutamide		
PSMA-positive		• ^{177}Lu-PSMA-617	• ^{177}Lu-PSMA-617
Aggressive variant		• Cabazitaxel + carboplatin	• Cabazitaxel + carboplatin
Additional options irrespective of prior ARPI or docetaxel (useful in certain circumstances)			
Asymptomatic without visceral metastases	Sipuleucel-T		
Oligometastatic/ oligoprogressive disease	Metastasis-directed therapy with mCRPC systemic therapy		
Symptomatic bone-predominant metastases	Radium-223		
MSI-H/dMMR	Pembrolizumab		

^{177}Lu-PSMA-617 = lutetium-177-PSMA-617; ***BRCA*** = BReast CAncer gene; **dMMR** = mismatch repair-deficient; **HRR** = homologous recombinant repair; **MSI-H** = microsatellite instability-high; **PSMA** = prostate-specific membrane antigen.

The complete and most recent versions of these guidelines are available free of charge at www.NCCN.org (register to access) and a new interactive digital guideline tool (NCCN Guidelines Navigator™) is also available. Guidelines for patients are available in English, Arabic, Chinese and Spanish and can be downloaded here.

New NCCN guideline digital navigator tool

In a concerted effort to make NCCN Guidelines more accessible for clinicians and facilitate easy access to search, filter and highlight relevant content a novel interactive, virtual platform – called the NCCN Guidelines Navigator™ - has been launched. The tool supports the provision of guideline-concordant care by enabling access from mobile devices and simplifying the subject matter via advanced search functionality and filter capability. New in this platform are colour-coded navigation links, integrated footnotes, tutorial and frequently asked question sections, as well as links to patient versions and the guideline in PDF format. Currently, the NCCN Guidelines Navigator™ platform is available for 17 of the 88 NCCN Guidelines including prostate cancer, renal cancer and rectal cancer and the rest will become available in stages.

The NCCN Guidelines Navigator™ is available at no charge to registered users. More information is available here.

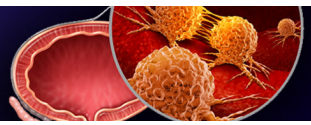
American Cancer Society cancer reports, 2025

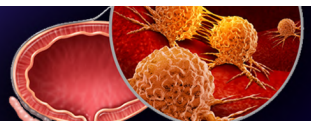
Prostate cancer statistics

The American Cancer Society (ACS) has analysed US population-based data to explicate the current status of prostate cancer incidence and outcomes, as well as changes over time. Analysis of statistics from the National Cancer Institute and the Centres for Disease Control and Prevention revealed an increase in prostate cancer incidence over the most recent eight-year period (2014-2021) with a 3% annual growth annually, a reversal in trend from the previous period (2007-2014) where a 6.4% annual decline was found. This increased incidence was primarily due to increases in diagnoses of advanced-stage disease with distant disease dissemination in all age groups, as well as a slight increase in early-stage diagnosis in elderly men (≥ 70 years). Over a similar timeframe, prostate cancer mortality has continued to decline but at a slower rate in the last decade (0.6% per year) compared to the 3%-4% annual decline in the 1990s and 2000s.

Other pertinent findings from the study included persistent racial disparities with significantly higher prostate cancer incidence and mortality in Black versus White men, and elevated mortality despite a lower incidence in American Indian/Alaska Native compared to White Americans. Advocacy is given to optimisation of early detection and to addressing barriers to equitable outcomes.

CA Cancer J Clin. 2025: 2 September. Online ahead of print





Cancer treatment and survivorship statistics

This analysis of up-to-date cancer data in the US estimates that almost 19 million individuals are currently living with a history of cancer and that this figure will increase by at least three million over the next decade to surpass 22 million. According to data collated from the Surveillance, Epidemiology, and End Results cancer registries, the Centres for Disease Control and Prevention's National Centre for Health Statistics, and the United States Census Bureau, prostate cancer is the most prevalent malignancy in males, accounting for over 3.5 million cases, while breast cancer is the most common cancer in females with over 4.3 million cases. Just over half of cancer survivors received their diagnosis in the last decade. Older adults accounted for the large majority of cancer cases (79%).

A companion to this article titled *Fast Facts: Cancer Treatment and Survivorship* can be found at cancer.org.

CA Cancer J Clin. 2025;75(4):308-40

Regulatory News

PBAC recommendations

At its July 2025 meeting the Pharmaceutical Benefits Advisory Committee (PBAC) recommended that a new composite abiraterone acetate/prednisolone pack (Andriga-10®; 56 tablets each of abiraterone acetate 500 mg and prednisolone 5 mg; Actor Pharmaceuticals) be subsidised through the Pharmaceutical Benefits Scheme (PBS) for patients with mCRPC.

Equi-effective doses of Andriga-10® and alternative therapies were determined to be:

- Andriga-10® abiraterone 1000 mg and prednisolone 10 mg (2 x tablets of each) = abiraterone 1000 mg (500 mg tablet x 2 or 250 mg tablet x 4) and prednisolone 10 mg (5 mg tablet x 2)
- Yonsa Mpred™ abiraterone acetate tablets (fine particle formulation) 500 mg + methylprednisolone 8 mg = abiraterone acetate 1000 mg + prednisolone/prednisone 10 mg
- enzalutamide 160 mg = abiraterone 1000 mg

Clinicians are cautioned to carefully disseminate information about dosing to patients changing between Yonsa Mpred™, Andriga-10® or single abiraterone acetate products.

A proposal from Merck Sharp & Dohme to expand the current PBS listing of pembrolizumab (Keytruda®) to a broad multi-indication listing for Therapeutic Goods Administration (TGA)-approved unresectable advanced and metastatic cancers was not supported by the PBAC. Uncertainty in the ability to achieve a cost-effective listing in combination with the prices suggested for the extended circumstances of use (additional indications, extended treatment duration and retreatment) were cited as attributing to the negative decision.

PBAC recommendations will be provided to the Federal Government for a final decision on public funding.

Read more here

Expanded indication for Akeega® under consideration in Europe and the US

Akeega®, an orally administered, dual action tablet containing the poly (ADP-ribose) polymerase (PARP) inhibitor niraparib and the novel hormonal therapy abiraterone acetate, has been approved in Europe and the US for the treatment of *BRCA*-mutated mCRPC since 2023. Now, regulatory bodies in both places are evaluating the merit of expanding the indications for Akeega® to include mCSPC in patients harbouring mutations in *BRCA* or other homologous recombination repair (HRR) genes.

The European Medicines Agency (EMA) accepted an extension of indication application for the hormone-sensitive indication in July, while the US Food & Drug Administration (FDA) granted Priority Review status to a supplemental New Drug Application more recently (in October) to expedite its evaluation. Both applications are supported by data from the global phase 3 AMPLITUDE trial, the first trial to demonstrate efficacy for a doublet regimen with a PARP inhibitor plus ARPI in this population. Briefly, AMPLITUDE revealed that the addition of niraparib to therapy with abiraterone acetate with prednisone plus ADT (niraparib and abiraterone acetate administered as a dual-action tablet formulation) outperformed abiraterone acetate with prednisone plus ADT, significantly prolonging radiographic progression-free survival, as well as improving other efficacy endpoints, in a cohort of 696 patients with germline or somatic HRR-altered mCSPC.

Data from AMPLITUDE was presented at the 2025 American Society of Clinical Oncology Annual Meeting. Abstracts have been published as a Special Issue online supplement to *The Journal of Clinical Oncology* and can be accessed on the journal's website here.

Relevant press releases from the trial sponsor Johnson & Johnson can be found here and here.

Voro® urologic scaffold under investigation in the US for postprostatectomy incontinence

Earlier this year the FDA authorised initiation of a phase 3 clinical trial to evaluate the investigational Voro® Urologic Scaffold medical device for the management of post-prostatectomy incontinence based on promising data from a feasibility study. Per a press release from the trial's sponsor - Levee Medical - the bioabsorbable device is designed to mitigate stress urinary incontinence in men undergoing radical prostatectomy by supporting the bladder neck and preserving urethral length. Currently underway, the ARID II trial (NCT06873581) aims to demonstrate that implantation of the device during robotic assisted radical prostatectomy is safe and improves early and long-term continence rates in men at least 45 years of age with Gleason Grade Group 4 or lower prostate cancer with prostate sizes < 80 g and plans to enrol 266 patients. To aid in the FDA evaluation process and possible eventual reimbursement approval, the device has also recently been issued a category III Current Procedural Terminology (CPT) add-on code from the American Medical Association. This temporary code expedites transition to a Category 1 code by enabling tracking of the device use. The Voro® Urologic Scaffold is also now covered by a Foundational US Patent.

Primary and final completion of ARID II is estimated for February 2027 and February 2028, respectively.

A relevant press release can be read here.

Earn CPD

Royal Australasian College of Physicians (RACP) MyCPD participants can claim the time spent reading and evaluating research reviews as CPD in the online MyCPD program. Please contact MyCPD@racp.edu.au for any assistance.

Royal Australian & New Zealand College of Radiologists (RANZCR) members can claim reading related to their practice as a CPD activity under the category 'journal reading and web based no certificate *reflection required'. More info.

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Australian Prostate Centre apc

ANZUP Cancer Trials Group Limited

News in Brief

First data from cell therapy INKmune in mCRPC

Promising preliminary results have been reported for a novel off-the-shelf cell therapy, INKmune™, for mCRPC in the CaRe Prostate trial (ClinicalTrials.gov ID NCT06056791). The therapy consists of replication-incompetent tumour cells designed to activate the patient's own natural killer cells into a tumour killing state. In the multicentre US trial adults with progressive mCRPC after ADT and at least one ARPI received three infusions of INKmune™ over roughly two weeks (dose levels, 1 x10^8, 3 x10^8 and 5 x 10^8 cells). According to a press release from the trial's sponsor, INKmune™ successfully demonstrated proof of concept, activating natural killer cells in a proportion of patients, and exhibited a safe profile. Preliminary anti-tumour activity was also reported. The tumour-agnostic cell therapy may have application across a range of natural killer-resistant malignancies, including multiple myeloma and leukaemia as well as lung, ovarian, breast, renal and nasopharyngeal cancers. Patient accrual to CaRe Prostate has now concluded but further trials in prostate cancer are planned for later this year.

More information can be found in a news release from INmuneBio

Update on current prostate cancer trials

ASPIRE trial to evaluate triplet therapy for mCSPC

The phase 3 US ASPIRE trial (Alliance A032302) plans to enrol 1,200 patients with mCSPC to assess whether early treatment intensification with the addition of chemotherapy to hormonal therapy and apalutamide, improves survival. Chemotherapy-naïve patients enrolled to the trial will receive ADT and apalutamide ± docetaxel and be monitored for 10 years. The researchers also aim to refine the optimal patient population for this triplet regimen by utilising genetic profiling to elucidate subgroups who derive the greatest clinical benefit from treatment. The projected primary study completion is November 2031.

A relevant press releases from Alliance can be read here

Trial of dual-masked T-cell engager with ARPIs commences

A press release from Vir Biotechnology has announced that their phase 1 trial of an investigational prostate-specific membrane antigen (PSMA)-directed dual-masked T-cell engager for metastatic prostate cancer has progressed to part 3 . The PSMA and CD3-specific bispecific – named VIR-5500 – is masked using the PRO-XTEN® technology to optimise tumour specificity and mitigate off-target toxicity. The four-part trial is evaluating VIR-5500 as a monotherapy in patients who have received at least one prior taxane-based regimen (Parts 1 & 2) and in combination with ARPIs in the first-line setting (Parts 3 & 4). To date, promising interim safety and efficacy data has been reported from a small heavily pre-treated cohort who received VIR-5500 as a single-agent, including a PSA reduction of ≥50% in roughly 60% of patients (n=7/12).

Full eligibility criteria for both trials can be found at clinicaltrials.gov (NCT05997615 & NCT06931340).

BALANCE: First biomarker for prediction of benefit from hormone therapy in prostate cancer

Results from the prospective biomarker-driven BALANCE trial - presented at the recent American Society for Radiation Oncology (ASTRO) Annual Meeting - suggest utility of the PAM50 biomarker to personalise post-prostatectomy hormone therapy in men with recurrent non-metastatic prostate cancer. The trial evaluated salvage radiotherapy ± apalutamide in a cohort of 295 men with PSA levels 0.1-1.0 ng/mL after radical prostatectomy without nodal or distant disease dissemination, stratified by luminal B status as determined by PAM50 molecular subtyping. Results showed that while patients with luminal B tumours derived significant clinical benefits from the addition of apalutamide to salvage radiotherapy, with lowered risks of both disease recurrence and metastatic disease, the addition of apalutamide did not improve outcomes in patients with non-luminal B type tumours.

The abstract from the conference can be found online (Abstract LBA 04).

Conferences, Workshops, and CPD

Please click on the links below for upcoming local and international prostate cancer meetings, workshops and CPD.

AUA - Meetings & Education
COSA – Events
MOGA – Events
USANZ – Events

Research Review Publications

Genitourinary Cancer Research Review with Associate Professor Andrew Weickhardt

Prostate Cancer Research Review with Professor Niall Corcoran

Urology Research Review with Professor Eric Chung

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