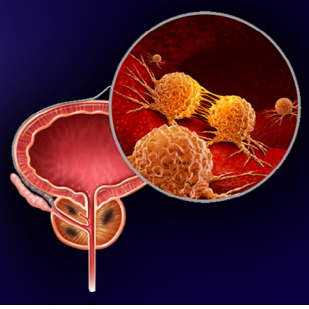
Prostate Cancer Practice Review™



Making Education Easy

Issue 27 - 2025

In this issue:

Abbreviations used in this issue:

^{177}Lu = lutetium-177; **ADT** = androgen-deprivation therapy; **ARPI** = androgen receptor pathway inhibition; **ASCO** = American Society of Clinical Oncology; **AusPAR** = Australian Public Assessment Report; ***BRCA*** = BReast CAncer gene; **CRPC** = castration-resistant prostate cancer; **CT** = computed tomography; **EMSN** = Extended Medicare Safety Net; **FDA** = US Food & Drug Administration; **HSPC** = hormone-sensitive prostate cancer; **MBS** = Medicare Benefits Schedule; **mCRPC** = metastatic castration-resistant prostate cancer; **MRI** = magnetic resonance imaging; **NCCN** = US National Comprehensive Cancer Network; **PARP** = poly-ADP ribose polymerase; **PET** = positron emission tomography; **PSA** = prostate-specific antigen; **PSMA** = prostate-specific membrane antigen; **TGA** = Australian Therapeutic Goods Administration.

Welcome to the 27th 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 our COVID-19 resources, and 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
janette.tenne@researchreview.com.au

Clinical Practice

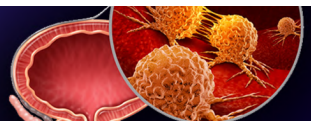
Should *BRCA* testing be expanded to relatives of men with hereditary prostate cancer?

A cost-utility analysis of genetic testing for the presence of pathogenic BReast CAncer (*BRCA*) gene variants in men with prostate cancer reveals that expanding testing to include the first-degree relatives of men with hereditary disease offers substantial benefits, including significantly improving healthcare costs. Researchers developed a semi-Markov multi–health-state transition model to compare from the Australian payer perspective the cost-effectiveness of germline *BRCA* testing only in patients diagnosed with prostate cancer versus a cascade strategy of also testing the families of men harbouring genetic mutations in *BRCA1* or *BRCA2*, who may therefore be predisposed to a range of hereditary cancers such as breast and ovarian cancer, as well as prostate cancer.

While genetic testing in patients diagnosed with prostate cancer is essential to tailor therapy, determine suitability for efficacious targeted therapeutics including poly-ADP ribose polymerase (PARP) inhibitors such as olaparib (and be eligible for government subsidy of treatments) and optimise outcomes, expanding the scope of genetic testing to the families of men - both male and female relatives - with hereditary risk factors enables early detection of malignancy and preventative actions that could save lives.

Results showed that while a stand-alone strategy of *BRCA* testing in men with advanced prostate cancer was very unlikely to have a cost benefit, cascade testing of family members was cost-effective. The data suggests that providing access to subsidised genetic testing for families at risk of hereditary cancer in Australia may be an economic way to detect cancer early and improve cancer-related mortality rates.

Value Health. 2024;27(11):1515-27



Updates to NCCN Guidelines

This year the US National Comprehensive Cancer Network (NCCN) have published updates to several guidelines relevant to physicians treating patients with prostate cancer that provide evidence-based expert consensus recommendations on treatment and early detection of malignancy. These updated guidelines - as well as the evidence supporting them – were presented at the recent NCCN Annual Conference held in Florida.

NCCN Clinical Practice Guidelines in Oncology® – Prostate cancer

Version 1.2025 of the NCCN Clinical Practice Guidelines in Oncology for the management of prostate cancer is now available.

Key revisions have been made to treatment recommendations to reflect novel drug approvals as well as clinical trial data, specifically in the radiation therapy and radical prostatectomy pathways and the initial therapy algorithm for asymptomatic disease.

Other changes include removal of the word "conventional" to describe computed tomography (CT) or bone scan imaging modalities, advice to utilise prostate-specific membrane antigen (PSMA)- positron emission tomography (PET)/CT or PSMA-PET/magnetic resonance imaging (MRI) as front-line imaging modalities for both initial staging and at biochemical recurrence, and a note that approved biosimilars can be substituted for biologics listed in the guidelines. Refinement of guidelines on targeted therapies including PARP inhibitors is provided as well as the use of bone protective agents for patients on long-term androgen deprivation therapy (ADT).

NCCN Clinical Practice Guidelines in Oncology® - Prostate Cancer Early Detection

The latest iteration of the NCCN Prostate Cancer Early Detection guidelines has just been published (version 1.2025). The recommendations are specifically for individuals with a prostate (including transgender women and other gender-diverse individuals with a prostate, regardless of gender affirmation surgery) who have chosen to undergo early screening following appropriate advice regarding the risks and benefits. Emphasis is given to optimising the identification of clinically significant aggressive disease that would benefit from early initiation of treatment while curtailing morbidity associated with the over treatment of slower-growing indolent disease. This publication is intended to accompany the NCCN Guidelines for Prostate Cancer treatment. As in previous versions, advocacy is given to making decisions regarding screening and treatment utilising shared patient-physician decision making processes and considering personalised risk assessment. Endorsement is also given to utilisation of genetic risk assessment and counselling.

The guidelines clarify that the higher incidence of prostate cancer and related mortality in African American versus Caucasian men is primarily attributable to a greater risk of developing preclinical disease and of disease dissemination plus disparities in access to treatment, rather than race, but that early screening may be more beneficial in this population. It is, therefore, suggested that screening be initiated earlier and be conducted at more regular intervals in African American men (from 40 years of age and annually, respectively). The standard of care for further pre-biopsy assessment of individuals with elevated prostate-specific antigen (PSA) levels (> 3 ng/mL) and/or a suspicious digital rectal exam is multiparametric MRI, if available, in combination with biomarker evaluation and risk calculators. For biopsy in individuals at high clinical suspicion for clinically significant malignancy, a transrectal or transperineal approach with MRI targeting is preferred.

The complete and most recent version of these guidelines is available free of charge at www.NCCN.org (register to access).

Earn CPD

CPD Home. Subscribers can claim the time spent reading and evaluating research reviews as an Educational Activity: Professional Reading in the CPD Tracker. Please Contact Us for support.

Guidelines for detection, prevention, & risk reduction: Genetic/familial high-risk assessment: Breast, ovarian, pancreatic, and prostate

Prostate Cancer has just been added to the NCCN Guidelines for the detection, prevention and risk reduction of genetic/familial high-risk malignancy, joining breast, ovarian and pancreatic cancer. Version 3.2025 of the guidelines became available in early March. Expert evidence-based consensus recommendations provide guidance for clinicians on genetic testing to enhance screening practices and inform targeted therapy options. In four main sections, advice covers the appropriate clinical situations to propose genetic testing and which test/s to use. Genetic mutations and hereditary conditions associated with predisposal to malignancy are detailed, as well as ways to manage this risk through means such as screening and preventative interventions in both patients with cancer and their families, according to degree of risk.

Optimal strategies to manage prostate cancer risk in patients harbouring pathogenic/likely pathogenic genetic variants according to genetic test results can be found in the NCCN Guidelines for Prostate Cancer Early Detection and include early initiation of screening (recommended from 40 years of age for carriers of *BRCA2* variants and to be considered in individuals harbouring *BRCA1* variants). The absolute elevated risk of developing prostate cancer for carriers of pathogenic variants of various genes follows:

GENE	MAGNITUDE OF PROSTATE CANCER RISK
ATM	Emerging evidence for association with increased risk
BRCA1	Absolute risk: 7%–26%
BRCA2	Absolute risk: 19%–61%
CHEK2	Emerging evidence for association with increased risk
TP53	Risk associated with Li-Fraumeni syndrome

Per the latest iteration of the guideline, genetic testing for prostate cancer susceptibility genes is indicated in the following situations:

- General tumour criteria are met
- A personal history of metastatic, node-positive, high-risk or very high-risk prostate cancer
- Ashkenazi Jewish ancestry
- A family history with:
    - One or more close blood relatives with breast cancer diagnosed before 50 years of age, male breast cancer, ovarian cancer, pancreatic cancer or metastatic, node-positive or high-risk prostate cancer OR
    - Three or more close blood relatives on the same side of the family with any-grade prostate cancer

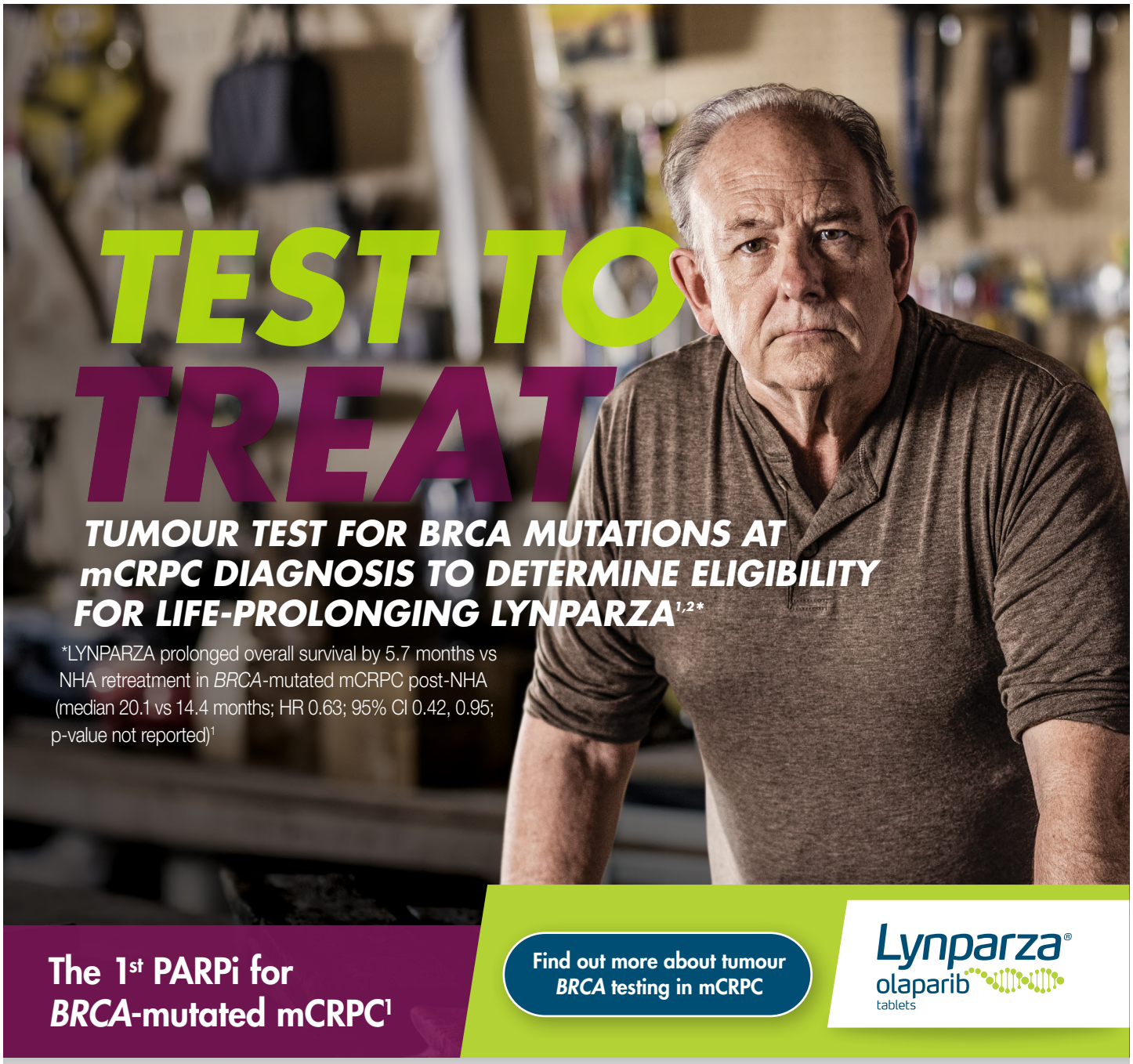
Genetic testing may also be considered in individuals who do not meet the above criteria with a personal history of prostate cancer diagnosed at 55 years or younger or those with a personal history of intermediate-risk prostate cancer with intraductal/cribriform histology at any age.

NCCN Guidelines for Patients® with prostate cancer

A free library of resources is also available to inform patients about their options and to assist them to navigate through their treatment journey (NCCN Guidelines for Patients). For men with prostate cancer, guidelines are available specifically for patients with advanced-stage and early-stage disease in multiple languages including English, Arabic, Chinese, Hindi and Spanish. Other patient resources inform on detection, prevention, & risk reduction (Genetic Testing for Hereditary Breast, Ovarian, Pancreatic, and Prostate Cancers), and multiple publications detail advice for various aspects of supportive care such as Survivorship Care for Cancer-Related Late and Long-Term Effects, Palliative Care and Fatigue and Cancer.

A collaboration between Outcomes4Me and NCCN now also provides patients with access to the most comprehensive and up-to-date NCCN guidelines and resources, empowering them to make informed treatment decisions, through a single digital cancer navigation platform. The Outcomes4Me app can be downloaded on iOS or Android through the App Store or Google Play and in addition to treatment options, lists potentially relevant clinical trials and genetic and genomic testing opportunities plus enables tracking of medications and symptoms and storage of health records.

The latest iteration of all NCCN Guidelines can be viewed and downloaded free-of-charge online at www.NCCN.org or via the Virtual Library of NCCN Guidelines App. The option to order free print copies of patient guidelines will also be available soon.

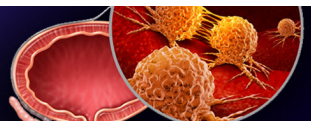


PBS Listed: LYNPARZA® Tablets. Authority Required. Refer to PBS Schedule for full information.

PLEASE CLICK HERE TO REVIEW FULL PRODUCT INFORMATION BEFORE PRESCRIBING.
FURTHER INFORMATION AVAILABLE ON REQUEST FROM ASTRAZENECA.

BRCA: BReast CAncer; CI: confidence interval; HR: hazard ratio; mCRPC: metastatic castration-resistant prostate cancer; NHA: novel hormonal agent; PARPi: poly (ADP-ribose) polymerase inhibitor. "*BRCA*-mutated" refers to patients with a mutation in *BRCA*1 or *BRCA*2.

References: 1. LYNPARZA® (olaparib) Tablets Product Information. **2.** NCCN Clinical Practice Guidelines in Oncology. Prostate Cancer: NCCN Evidence Blocks™. Version 1.2025 – December 4, 2024. Accessed March 2025. https://www.nccn.org/guidelines/category_1.



Regulatory News

TGA registration for enzalutamide expanded

The Australian Therapeutic Goods Administration (TGA) recently approved a fifth indication for **enzalutamide** (Xtandi®), enabling it to be employed in an earlier prostate cancer treatment setting for patients with non-metastatic hormone-sensitive (HSPC) disease with biochemical recurrence at high-risk for metastasis.

This novel prostate cancer indication was based on demonstration of a significantly reduced risk of metastasis (improved metastasis-free survival) with enzalutamide ± leuprolide versus leuprolide monotherapy in over 1,000 patients with high-risk biochemical recurrence (a PSA doubling time of ≤ nine months) after primary therapy with/without salvage local treatment in the global phase 3 EMBARK trial. Both the US Food & Drug Administration (FDA) and the European Medicines Agency have also approved enzalutamide for this indication.

Enzalutamide is now indicated for the treatment of:

- non-metastatic HSPC with high-risk biochemical recurrence
- metastatic HSPC
- non-metastatic castration-resistant prostate cancer (CRPC)
- metastatic CRPC (mCRPC) following failure of ADT in patients in whom chemotherapy is not yet indicated
- mCRPC in patients who have previously received docetaxel

The novel Prescription medicine registration can be viewed here

New indication for darolutamide under evaluation

The non-steroidal androgen receptor inhibitor **darolutamide** (Nubeqa®; Bayer Australia Ltd) currently has two TGA approved prostate cancer indications, namely:

- the treatment of patients with metastatic HSPC in combination with docetaxel

AND

- the treatment of patients with non-metastatic CRPC

Relevant Australian Public Assessment Reports (AusPARs) can be found here and here

Now, the TGA are evaluating the evidence for the safety and efficacy of **darolutamide plus ADT regimens**, with or without docetaxel, for metastatic HSPC. Two phase 3 trials – ARANOTE and ARASENS – have demonstrated the improved efficacy of standard of care ADT ± docetaxel regimens with the addition of darolutamide, finding significant delays in disease progression and improved survival versus standard of care regimens without darolutamide, without adversely impacting quality of life.

The application for this new indication was accepted by the TGA in December 2024 and an outcome is awaited (Prescription medicines under evaluation).

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.

Updates to US approvals & designations

The US FDA have recently granted several novel approvals and designations relevant to prostate cancer.

The Ibex Prostate Detect software

This *in vitro* digital diagnostic pathology device - developed and validated by Ibex Medical Analytics - that aims to ensure the accuracy of pathologist's prostate cancer diagnosis was granted FDA 510(k) Clearance in February. The program employs artificial intelligence to recognise small and rare prostatic malignancies from scanned histopathology whole slide images of prostate core needle biopsies that may have been misdiagnosed as benign by the pathologist. On identification of potentially malignant tissue, the application generates a heatmap to indicate the suspicious region/s and sends case alerts. Unpublished data from precision and clinical validation studies in the US and Europe submitted to the FDA as part of the clearance process reported a substantial benefit to use of the software versus current standard diagnostics, finding a 99.6% positive predictive power and identification of misdiagnosed tumours in 13% of patients originally cleared.

A press release from Ibex can be found here

^{67}Cu-SAR-bisPMSA granted Fast Track Designation in mCRPC

In order to expedite the development and regulatory review of the dual-targeted bisPSMA radiopharmaceutical ^{67}Cu-SAR-bisPMSA for mCRPC, it has been granted Fast Track Designation from the FDA. This designation was granted based on positive preliminary data from the ongoing phase 1/2a SECuRE trial of 4-12 GBq ^{67}Cu-SAR-bisPMSA that showed significant decreases in PSA levels in patients with PSMA-positive mCRPC who have been previously treated with androgen receptor pathway inhibition (ARPI), with a favourable safety profile.

Clarity Pharmaceuticals previously received two fast track designations for its diagnostic ^{64}Cu-SAR-bisPSMA product for use in patients with suspected prostate cancer metastasis eligible for initial definitive therapy and in patients with biochemical recurrence post-definitive therapy. The CLARFIY and AMPLIFY phase 3 registrational trials of ^{64}Cu-SAR-bisPSMA aim to support final approval.

More information can be found in a press release from Clarity Pharmaceuticals here

^{177}Lu 177 vipivotide tetraxetan approved for mCRPC before chemotherapy

In the US, the therapeutic radiopharmaceutical lutetium-177 (^{177}Lu) vipivotide tetraxetan (Pluvicto™; Novartis Pharmaceuticals) is now indicated for the treatment of PSMA-positive mCRPC after ARPI therapy in adult patients in whom postponement of taxane-based chemotherapy is deemed appropriate. Previously, it was approved for use after both ARPI and taxane-based chemotherapy. The benefit of use earlier in the treatment continuum prior to chemotherapy was demonstrated in the PSMAfore trial, where ^{177}Lu vipivotide tetraxetan significantly delayed radiographic disease progression compared to a change in ARPI in patients with progression on the first ARPI.

The recommended schedule of ^{177}Lu vipivotide tetraxetan is six doses of 7.4 GBq, administered intravenously every six weeks, or until disease progression or unacceptable toxicity.

More information is available on the FDA website

Next-generation PSMA-PET imaging agent for prostate cancer approved

A second-generation gallium (Ga)-based imaging and diagnostic agent with an extended shelf-life and improved distribution radius was recently FDA approved for use in PET scans to evaluate disease dissemination in patients with PSMA-positive lesions suitable for initial definitive therapy and for patients with suspected recurrence based on elevated PSA level. Precision medicine scans with either the new agent - Gozellix® (TLX007-CDx, kit for the preparation of ^{68}Ga gozetotide injection), - as well as the first-generation imaging agent Illuccix®, will both be available for suitable patients.

A relevant press release from Telix can be read here

Recent amendments to the MBS

Several changes to the Medicare Benefits Schedule (MBS) came into effect on the 1st March including:

- The removal of the 85% out of hospital benefit from over 800 MBS items to restrict benefit payment for specific services to a hospital setting
- Clarification of 'telehealth' as an umbrella term for video and phone services
- The addition of two new items for participating nurse practitioner attendance of at least 60 mins (82216 and 91206)
- The amendment of telehealth and some subsequent in-patient consultation items for admission of patients to a psychiatric facility to restrict claiming to within one week (92478, 92479, 92480, 92481 and 92482)

More information can be found on the MBS website

Extended Medicare Safety Net

The Extended Medicare Safety Net (EMSN) allows for additional government subsidy of out-of-hospital services - including specialist practitioner appointments plus pathology and diagnostic imaging services - for individuals who exceed the annual Original Medicare Safety Net threshold. Both Medicare Safety nets are indexed every year on the 1st of January to correspond with the previous year's September quarter consumer price index.

This calendar year everyone registered in Medicare is entitled to:

- 100% reimbursement of the schedule fee for out of hospital services up to a gap threshold of $576
- 80% remuneration of out-of-pocket costs (or the EMSN benefit caps) for additional out of hospital services up to $2,615.50 (or $834.50 for concessional and Family Tax Benefit Part A recipients)

More information can be found on the MBS website

News in Brief

POPSTAR II recruiting in Australia

The POPSTAR II trial (NCT05560659) of stereotactic ablative radiotherapy ± ^{177}Lu-PSMA radionuclide therapy for oligometastatic prostate cancer is still recruiting at sites in NSW and Victoria. Trial eligibility restrict enrolment to adult patients with histologically confirmed prostate adenocarcinoma with 1-5 sites of nodal or bony metastases who have undergone definitive curative-intent treatment to the primary tumour.

Full trial details are available at ClinicalTrials.gov

Phase 2 trial of darolutamide + opaganib for poor prognosis mCRPC commences

A phase 2 trial evaluating whether adding the first-in-class, orally administered sphingosine kinase-2 (SPHK2) selective inhibitor opaganib to darolutamide improves efficacy in advanced ARPI treatment-resistant mCRPC has commenced. The trial will utilise a companion lipid biomarker test (PCPro®) to identify patients resistant to ARPI therapy predicted to have poor prognosis with standard therapy.

More information is available in a press release from RedHill Biopharma

New Medicare handbook for health professionals

A resource for Australian medical providers – the Understanding Medicare: Provider Handbook – is available online to assist clinicians navigate the Medicare system. Available to download as a word or PDF document areas such as Medicare programs, Safety News, the MBS, Medicare claiming and MBS online are covered.

The Understanding Medicare Handbook can be downloaded here

2025 ASCO Annual Meeting

Early registration for the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting - scheduled to be held in Chicago and Online between May 30 and June 3, 2025 – closes on the 23rd April.

Attendees can register online here

ASCO Genitourinary Cancers Symposiums

The 2026 ASCO Genitourinary Cancer Symposium will be held in California next February. Online participation is also available. Abstracts from this year's symposium are available online here

COVID-19 Resources

Royal Australasian College of Surgeons
European Urology Journal
British Association of Urological Surgeons
American Urological Association
European Society of Medical Oncology

Conferences, Workshops, and CPD

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

COSA – Events
MOGA – Events
USANZ – Events

Research Review Publications

Prostate Cancer Research Review with Professor Niall Corcoran
Urology Research Review with Professor Eric Chung

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.

Follow us at:

Kindly Supported by

Australian Prostate Centre

ANZUP Cancer Trials Group Limited

Australian Research Review subscribers can claim CPD/CME points for time spent reading our reviews from a wide range of local medical and nursing colleges. Find out more on our CPD page.