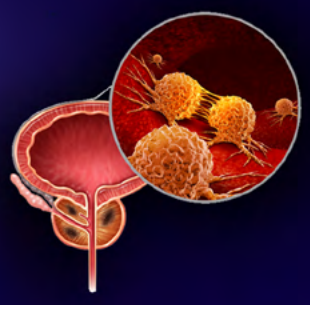
# Prostate Cancer Practice Review™



Making Education Easy

Issue 22 - 2024


## In this issue:



### Abbreviations used in this issue:

**ADT** = androgen deprivation therapy; **ASCO** = American Society of Clinical Oncology; **CDC** = Centres for Disease Control and Prevention; **CT** = computed tomography; **CTV** = clinical target volume; **EAU** = European Association of Urology; **GFRU** = the Groupe Francophone de Radiothérapie Urologique; **MRI** = magnetic resonance imaging; **PARP** = poly ADP ribose polymerase; **PBAC** = Pharmaceutical Benefits Advisory Committee; **PBS** = Pharmaceutical Benefits Scheme; **PET** = positron emission tomography; **PSA** = prostate-specific antigen; **PSMA** = prostate-specific membrane antigen.

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## Welcome to the 22nd 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. And 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**
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## Clinical Practice

### Prostate-specific membrane antigen positron emission tomography/computed tomography-based clinical target volume delineation guideline for postprostatectomy salvage radiation therapy: The PERYTON guideline

Several guidelines regarding prostate bed delineation for postoperative radiation therapy have been published from various groups including the Radiation Therapy Oncology Group, the European Organisation for Research and Treatment of Cancer (EORTC) Radiation Oncology Group, the Groupe Francophone de Radiothérapie Urologique (GFRU), the European SocieTy for Radiotherapy and Oncology - Advisory Committee for Radiation Oncology Practice (ESTRO-ACROP) and the Australian and New Zealand Radiation Oncology Genito-Urinary Group. All provide detailed contouring principles for delineation of regions of residual microscopic disease in the prostate bed (prostatic fossa) which should be included in the clinical target volume (CTV) for postoperative prostate radiotherapy in the adjuvant or salvage settings for immediate therapy or following biochemical relapse post-prostatectomy.

A Dutch research group have now developed the PERYTON guideline employing prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT), rather than conventional, less sensitive imaging modalities, to refine the treatment area for salvage external beam radiation therapy in patients with biochemical recurrent prostate cancer post-prostatectomy. To optimise the CTV, expert nuclear medicine physicians in collaboration with radiation oncologists adapted boundaries of prostatic fossa local recurrence defined per GFRU guidelines in 83 patients using PSMA PET-CT imaging. The study authors reported that compared to the GFRU definition, the novel PERYTON CTV improved the accuracy of radiation treatment, increasing the coverage of PSMA PET/CT–detected local recurrences from 67% to 96% and reduced the total target volume significantly by minimising the unnecessary irradiation of normal tissue. Determination of CTV per PERYTON guidelines was also reported to be highly reproducible.

Updated consensus delineation guidelines for pelvic lymph node radiation therapy of prostate cancer in various therapeutic settings are also available from the GFRU and were discussed in Issue 19 of *Prostate Cancer Practice Review*.

Int J Radiat Oncol Biol Phys. 2024;118(3):688-96

## EAU-EANM-ESTRO-ESUR-ISUP-SIOG guidelines on prostate cancer -2024 update

### Part I: Screening, diagnosis, and local treatment with curative intent

The European Association of Urology (EAU)-European Association of Nuclear Medicine (EANM)-European Society for Radiotherapy and Oncology (ESTRO)-European Society of Urogenital Radiology (ESUR)-International Society of Urological Pathology (ISUP)-International Society of Geriatric Oncology (SIOG) published an inaugural prostate cancer guideline in 2021 and have updated it annually. The 2024 update is now available and aims to provide up-to-date recommendations to assist clinicians in the evidence-based management of prostate cancer. Summaries of changes have been published in two parts to individually cover screening, diagnosis and treatment with curative intent of localised and locally advanced disease, and treatment of relapsing and metastatic prostate cancer.

A structured appraisal of novel additions to the literature published in English between May 2022 and May 2023 was undertaken and changes to the recommendations from the 2023 iteration of the guidelines were made, based primarily on high-level evidence from systematic reviews with meta-analysis, randomised controlled trials and prospective comparative studies, and assigned a strength rating.

**The up-to-date guidelines advocate for:**

- Initiation of a multi-step risk-adapted screening strategy in men from around 50 years of age to optimise identification of "curable" prostate cancer prior to disease dissemination
- The use of multiparametric magnetic resonance imaging (MRI) over biopsy for diagnosis
- A combination of targeted and systematic biopsies when biopsy is indicated
- PSMA-PET/CT imaging to detect metastatic spread
- Management via active surveillance for low-risk disease and selected patients with favourable intermediate-risk disease with International Society of Urological Pathology grade group 2 lesions. Shared-decision making should inform decisions regarding active treatment modality (i.e., surgery, radiotherapy) for all other risk classes
- Consideration of hypofractionation in patients with intermediate-risk disease
- Intensification of localised treatment with long-term intensified hormonal treatment in cases of clinically lymph node-positive (cN1) disease

The guideline authors note that the treatment landscape for localised prostate cancer is changing rapidly and novel evidence with clinical implications for diagnosis and staging is continually emerging. This rapid growth is reflected in the multitude of novel subsections including on tissue samples for homologous recombination repair (HRR)-testing, intra-operative assessment of surgical margin status and perilesional biopsy plus new summaries on the evidence supporting active surveillance and on controversies in the definitions of clinically relevant prostate-specific antigen (PSA) relapse.

Ongoing and new systematic reviews will inform guidelines regarding the performance of new stratification tools that consider imaging, biomarkers and biopsy versus classical risk classifications such as d'Amico, EAU, the Cancer of the Prostate Risk Assessment (CAPRA) and the National Comprehensive Cancer Network (NCCN) for predicting outcomes after primary curative-intent localised treatment. These will be included in the 2025 guideline iteration.

These guidelines have been endorsed by a range of Associations including the International Society of Geriatric Oncology, the European Society for Radiotherapy & Oncology, the European Society for Urogenital Radiology, the European Association of Nuclear Medicine and the International Society of Urological Pathology.

Eur Urol. 2024; Apr 12; Online ahead of print



### Part II: Treatment of relapsing and metastatic prostate cancer

The guidelines detail assessment and treatment of local and metastatic (including nodal) PSA-only disease recurrence/relapse after curative-intent treatment according to primary therapeutic modality and comment on controversies in the definitions of clinically relevant PSA relapse. Secondary therapies may include salvage radiotherapy with/without androgen deprivation therapy (ADT), nodal-directed treatment or lymph node dissection after primary radical prostatectomy or salvage radical prostatectomy, cryoablation of the prostate, re-irradiation, stereotactic ablative body radiotherapy or high-intensity focused ultrasound for PSA failure after radiation therapy. Systemic therapeutic options include hormonal therapy (pharmacological or surgical), cytotoxic drug treatment and non-hormonal non-cytotoxic drug treatments such as poly ADP ribose polymerase (PARP) inhibitors, AKT inhibitors and immune checkpoint inhibitors.

With regards to management of metastatic disease, advice is provided on front-line hormonal therapy (intermittent or continuous ADT) as a monotherapy or in combination with an older generation non-steroidal anti-androgen, chemotherapy or an androgen receptor pathway inhibitor ± docetaxel. Suggestions for metastasis-directed or primary tumour-directed therapy for disease according to status of hormone sensitivity is also detailed.

In this latest update, advocacy is given to guidance of salvage treatment decision by risk stratification of relapsing prostate cancer after primary therapy. In the metastatic disease setting, novel additions to the treatment armamentarium include androgen receptor–targeted agents with/without chemotherapy, PARP inhibitors as monotherapy and in combination regimens, and prostate-specific membrane antigen–based therapy.

The full guidelines, as well as a quick reference document (Pocket guidelines), can be downloaded from the EAU website here

Eur Urol. 2024; Apr 29; Online ahead of print

## Prostate cancer trials enrolling in Australia

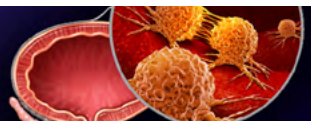
There are three clinical trials currently recruiting patients with prostate cancer at Australian research sites.

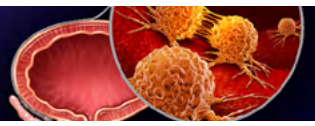
AstraZeneca's phase 3 EvoPAR-Prostate01 trial (ClinicalTrials.gov ID NCT06120491) will evaluate continued intensification of novel hormonal agent therapy with the selective PARP inhibitor saruparib in patients with *de novo* or recurrent metastatic castration-sensitive prostate cancer regardless of homologous repair status. The estimated global enrolment is 1,800 patients. Sites in Victoria, New South Wales, South Australia and Queensland are currently recruiting.

Macquarie University in New South Wales is looking for men with progressive metastatic castration-resistant prostate cancer after treatment with a next-generation hormonal agent to participate in one of two trials of the investigational androgen-receptor signalling pathway inhibitor opevesostat (MK-5684). Sponsored by Merck Sharp & Dohme, the trials will assess the efficacy of opevesostat ± hormone replacement therapy versus alternative abiraterone acetate or enzalutamide. The coordinator of the studies can be contacted on 0402 856 430. Full eligibility criteria are available through the ClinicalTrials.gov listings NCT06136624 & NCT06136650).

Other currently active clinical trials include a multi-centre US evaluation of shorter versus usual duration radiotherapy in patients with high-risk prostate cancer (NCT05946213) that has an estimated primary completion date of 2041, the open-label real-world MIRROR study of the radioactive PET-CT/MRI diagnostic agent piflufolastat F 18 (Pylarify) in newly diagnosed favourable intermediate-risk prostate cancer (NCT06074510) and a study of high-dose vitamin D for ADT-induced bone loss in patients with prostate cancer who are undergoing ADT (NCT05838716).

More information on each trial can be found by following the relevant ClinicalTrials.gov links.





## Vaccination of adults with cancer: ASCO Guideline

The American Society of Clinical Oncology (ASCO) have recently updated their clinical practice guidelines regarding vaccination of adult patients with solid cancers or haematological malignancies. Developed by an expert panel and emerging through a five-year cooperative agreement with the Centres for Disease Control and Prevention (CDC) and the Council of Medical Specialty Societies, *inter alia*, the document provides evidence-based recommendations for oncologists and cancer patients and replaces the advice given in the 2013 guideline by the Infectious Disease Society of America. Through this collaboration, as well as consultation with various US health systems, the overarching aim is to boost guideline-concordant vaccination in the oncology population and optimise infection protection and illness severity attenuation.

A rigorous review of over 100 systematic reviews, randomised controlled trials and nonrandomised studies published between 2013 and February 2023 was undertaken to inform the recommendations. In brief, the vital importance of vaccination and revaccination before and/or following cancer treatment in this population, as well as their household contacts, through multidisciplinary coordination is strongly emphasised. The guideline further details appropriate vaccination/revaccination plans and schedules according to the patient's underlying immune status, anticancer therapeutic and comorbidities and specifies contraindicated vaccines.

**Seven strong recommendations advocate for the following:**

- That clinicians determine vaccination status in all patients newly diagnosed with cancer and ensure that all seasonal and age- and risk-based vaccines are up to date
- That vaccines ideally be administered 2-4 weeks prior to cancer therapy. Non-live vaccines may be given during or after chemotherapy, immunotherapy, hormonal treatment, radiation or surgery
- Complete revaccination after haematopoietic stem-cell transplant, initiated with the following timings post-transplant:
  - Non-live vaccines 6-12 months
  - Live and live attenuated vaccines > two years (only in the absence of graft-versus-host disease or immunosuppression)
  - COVID-19, influenza and pneumococcal vaccines from three months
- Revaccination for COVID-19 only, six months after completion of B-cell–depleting therapy
- That despite possible attenuated response, recommended non-live vaccines be provided to long-term survivors of haematologic malignancy and or patients with long-standing B-cell dysfunction or hypogammaglobulinemia, regardless of active disease status
- Standard CDC recommendations for travel immunisations be adhered to. It is noted that hepatitis A, intramuscular typhoid vaccine, inactivated polio, hepatitis B, rabies, meningococcal, and non-live Japanese encephalitis vaccines are safe in patients with cancer
- Up to date vaccination of all household members and close contacts

A weak recommendation supports the provision of influenza and COVID-19 vaccines at least three months after chimeric antigen receptor (CAR) T-cell therapy directed against B-cell antigens such as CD19 or BCMA and non-live vaccines from at least six months.

**Individualised vaccination plans for adults with cancer can be based on the following recommended immunisation schedule:**

| VACCINE | RECOMMENDED AGE | SCHEDULE |
|---|---|---|
| **COVID-19** | All ages | Per CDC schedule for immunocompromised |
| **HEPATITIS B** | 19-59 years and ≥ 60 years with other risk factors | Three-dose Recombivax HB series (0, 1, 6 months) OR four-dose Engerix-B series (0, 1, 2, 6 months) |
| **HUMAN PAPILLOMAVIRUS (HPV)** | 19-26 years and up to 45 years with shared decision making | Three doses: 0, 1–2, 6-months |
| **INFLUENZA** | All ages | annually |
| **PNEUMOCOCCAL VACCINE** | ≥ 19 years | One dose pneumococcal conjugate vaccine; (PCV15) + 23 valent pneumococcal polysaccharide vaccine (PPSV23) eight weeks apart OR One dose PVC20 |
| **RECOMBINANT ZOSTER VACCINE** | ≥ 19 years | Two doses at least four weeks apart |
| **RESPIRATORY SYNCYTIAL VIRUS (RSV)** | ≥ 60 years | Once |
| **TETANUS AND DIPHTHERIA (TD) OR TETANUS, DIPHTHERIA AND PERTUSSIS (TDAP)** | ≥ 19 years | One dose of Tdap plus Td or Tdap booster every ten years |

Further elucidation of vaccine immunogenicity in patients with cancer undergoing various cancer therapies and the optimal timing of vaccination is still required.

The full guideline document is available on ASCO's Supportive Care and Treatment Related Issues webpage here

J Clin Oncol. 2024;42(14):1699-721

# Regulatory News

## PBAC recommendations

At its March 2024 meeting the Pharmaceutical Benefits Advisory Committee (PBAC) recommended against Pharmaceutical Benefits Scheme (PBS) subsidy of talazoparib (Talzenna®; Pfizer Australia Ptd Ltd) for the treatment of *BRCA1/2* mutated metastatic castration-resistant prostate cancer as part of a combination regimen with enzalutamide in patients who have not received prior treatment with a novel hormonal agent. While the PBAC acknowledged that the addition of talazoparib to enzalutamide therapy likely improved efficacy in this indication, the supporting evidence came from a small subgroup post hoc analysis rendering uncertainty regarding the magnitude of benefit. The PBAC suggested that Pfizer pursue subsidy of this regimen through the Early Re-Entry resubmission pathway and further proposed that talazoparib plus enzalutamide join the existing risk sharing arrangement for olaparib monotherapy.

Read more here

## Upcoming PBAC agendas

On the agenda for consideration at the July 2024 PBAC meeting is a request from Janssen-Cilag Ptd Ltd for a new PBS listing of a new strength of apalutamide (Erlyand®; 240 mg tablet) for the treatment of non-metastatic castration-resistant and metastatic castration-sensitive carcinoma of the prostate

## PBS listings

Following a positive recommendation from the PBAC in November 2022, abiraterone & methylprednisolone (Yonsa Mpred®) has been listed on the PBS for the treatment of metastatic castration-resistant prostate cancer. Effective from the 1st May this year a pack containing [120] 125 mg abiraterone acetate tablets and [30] 4 mg methylprednisolone tablets will be subsided with authority applications taken via the real-time Online PBS Authorities system or over the phone.

More information can be found on the PBS Medicine Status Website here

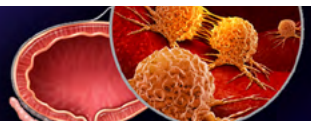
## Global regulatory update

### Enzalutamide approved for recurrent non-metastatic hormone-sensitive prostate cancer in Europe

Based on positive data from the phase 3 EMBARK trial of leuprolide ± enzalutamide (Xtandi™) in high-risk biochemically recurrent non-metastatic hormone-sensitive prostate cancer with rapidly rising PSA levels, the label indication for enzalutamide in the European Union has been extended to include this indication as a monotherapy or in combination with ADT for patients unsuitable for salvage radiotherapy.

A press release from the trial sponsor - Astellas Pharma Inc – can be read here

A full list of indications for enzalutamide in the European Union can be found here



## News in Brief

### United Against Racism initiative mitigates health care disparities in prostate cancer care

In an effort to curb racial disparities in health care in prostate cancer a large Boston-based hospital network – Mass General Brigham – implemented the United Against Racism initiative which included a Prostate Cancer Outreach Clinic. Central to the initiative is improved patient interactions and streamlined access to services for men with elevated PSA levels or those requiring prostate cancer screening.

More information on the program can be found on Mass General Brigham's website here

### Interim results from Australian ENZA-p trial

Interim data from the multi-centre Australian ENZA-p trial have been published in *The Lancet Oncology*. Results showed that a front-line doublet regimen of enzalutamide plus lutetium-177–labelled PSMA-617 significantly improved PSA progression-free survival versus enzalutamide monotherapy in men with metastatic castration-resistant prostate cancer.

The publication can be found here

### Urinary test may replace biopsy for detection of high-grade prostate cancer

A novel multiplex urine-based test may offer a non-invasive alternative to biopsy to distinguish indolent from aggressive prostate cancer. Developed by a US team of researchers, the urinary test – named 18-gene MyProstateScore 2.0 – demonstrated high sensitivity for the detection of grade group 2 or greater prostate cancer and according to the study authors, may improve PSA screening outcomes relative to existing biomarker tests.

Results from the diagnostic study can be found here

### *The Lancet* Commission on prostate cancer: planning for the surge in cases

Novel global annual prostate cancer diagnoses will more than double over the next 15 years - to an estimated 2.9 million in 2040 - and result in a rapid rise in prostate cancer mortality, according to projections from *The Lancet* Commission. The explosion in cases is attributed predominantly to increases in life expectancy and changing age structures and cannot be arrested by lifestyle changes or public health interventions. Suggestions to deal with this escalation in cases are provided.

Lancet. 2024;403(10437):1683-722

## 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.

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European Urology Journal
British Association of Urological Surgeons
American Urological Association
European Society of Medical Oncology
American Society of Clinical 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
COMS – Conferences and Meetings on Urology

## Research Review Publications

Prostate Cancer Research Review with Professor Niall Corcoran and Professor Nathan Lawrentschuk

Urology Research Review with Professor Eric Chung

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