

LuPSMA shows promise as first-line treatment for prostate cancer

A targeted radioactive infusion that is a game-changer in late-stage prostate cancer can also dramatically improve outcomes for patients in earlier stages of this disease, a co-badged Peter Mac and Australian and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group study has shown.

Lutetium-177 PSMA-617 – or LuPSMA – therapy had been shown in previous clinical trials to extend lives, and improve quality-of-life, in patients with advanced metastatic prostate cancers who have exhausted all other treatment options.

The UpFrontPSMA (ANZUP 1904) study was the first to test this treatment in patients with newly diagnosed prostate cancers that had spread. The trial's "remarkable" results were simultaneously published overnight in the leading journal *Lancet Oncology* and presented at Europe's major cancer conference - ESMO (European Society for Medical Oncology) Congress 2024, in Barcelona.

Peter Mac was the leading recruitment site for this Phase II clinical trial, which enrolled 130 people from 11 hospitals across Australia. All of the people received androgen deprivation therapy – starving their prostate cancer of the hormone it uses as fuel – and they were then randomised to receive chemotherapy alone (the standard-of-care) or chemotherapy plus LuPSMA.

"Adding LuPSMA therapy to the standard-of-care approach was seen to dramatically improve responses for the people compared to chemotherapy alone," explains Associate Professor Arun Azad, who presented the results at ESMO 2024.

"We looked for people who had undetectable PSA - a marker for prostate cancer - at 48 weeks after treatment and this was achieved in 41% of people who received LuPSMA compared to just 16% for people who received the standard-of-care.

"This is a remarkable result however before we can say this should change clinical practice we need to see this replicated in a larger Phase III clinical trial and, thankfully, a trial like this is already underway globally."

Benefits were also seen across a range of progression-free survival measures, while adverse events were equivalent in either treatment approach and linked mostly to chemotherapy.

UpFrontPSMA was funded by the Prostate Cancer Research Alliance (PCRA) - involving Movember and the Australian Government's Medical Research Future Fund, with support from Novartis and a US Department of Defense grant.

Movember's Director of Prostate Cancer Research, Sam McKeown says: "Movember are proud to have supported this research through the Prostate Cancer Research Alliance. With prostate cancer cases set to double by 2040, research into preventing high-risk prostate cancer from progressing to fatal disease is critical".

Professor Michael Hofman, who leads the Prostate Cancer Theranostics and Imaging Centre of Excellence (ProSTIC) at Peter Mac, adds: "The exciting results we have seen in the UpFrontPSMA trial validate the PCRA's approach of supporting high-risk, high reward clinical trials".

The trial was co-badged with the Australian and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group. ANZUP CEO A/Prof. Samantha Oakes says: "ANZUP is extremely proud of this world first study, and the results are clear that adding LuPSMA to standard of care is improving lives of people with advanced metastatic prostate cancer."

The paper, titled "Sequential [¹⁷⁷Lu]Lu-PSMA-617 and Docetaxel versus Docetaxel in Metastatic Hormone-Sensitive Prostate Cancer (UpFrontPSMA): a multicentre, open-label, randomised, phase 2 study" can be read in full [here](#).

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About Peter Mac

Peter MacCallum Cancer Centre is a world leading cancer research, education and treatment centre and Australia's only public health service dedicated to caring for people affected by cancer.

About ANZUP

ANZUP is the leading cancer-cooperative clinical trials group that brings together all of the professional disciplines and groups involved in researching and treating urogenital cancers and conduct high quality clinical research. ANZUP identifies gaps in evidence and areas of clinical need, collaborates with the best clinicians and researchers in GU cancer and communicates frequently and effectively with the broader community along the way. ANZUP receives valuable infrastructure support from the Australian Government through Cancer Australia.