ANZUP®
Cancer Trials Group Limited

A little below the belt

Conducting clinical trial research to improve outcomes for bladder, kidney, testicular, penile and prostate cancers

AN ANZUP CANCER TRIALS GROUP PUBLICATION

ISSUE 16, FEBRUARY 2022

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YOU VS CANCER

DISCOVER THE LATEST IN CUTTING EDGE CLINICAL TRIALS AND RESEARCH

Hear from world-renowned below the belt cancer experts

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- Ask a question in the interactive Q&A session with the panel of clinical experts and patients

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ADELAIDE CONVENTION CENTRE 1PM – 4PM

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research
trials
outcomes

What is ANZUP?

The Australian and New Zealand Urogenital and Prostate Cancer Trials Group was formed in 2008, bringing together a world-leading multidisciplinary team of doctors, nurses, other health care professionals, scientists, researchers, and community representatives, all working in areas related to urogenital cancer.

ANZUP has members in every state and territory in Australia and New Zealand, with an increasing international membership.

Urogenital cancers are those coming from the testicles, prostate, kidney, penis or bladder.

Australian
Registered Charity:
ACN 133 634 956

New Zealand
Registered Charity:
CC51217

ANZUP aims to improve outcomes for people affected by these cancers. We do this by performing clinical trials to generate new evidence for better treatments, or ways of providing other support.

Our members and investigators are widely dispersed and busy, working in a range of disciplines. A trial idea only comes to fruition when we are able to provide opportunities for people to meet, work through the science, develop the trial concepts, and write and work through all the other documentation and processes. Then it is necessary to initiate, run, monitor and report the trial results. All of this relies on the volunteered time of our members and is separate from the other needs ANZUP has to source the much larger amounts of funding to support the trials themselves.

"Every meaningful advance in treatment has been the result of testing a new idea in a clinical trial."

Professor Ian Davis, ANZUP Chair

ANZUP acknowledges the Traditional Owners of the lands on which our company is located and where we conduct our business. We pay our respects to ancestors and Elders, past and present. ANZUP is committed to honouring the First Peoples' unique cultural and spiritual relationships to the land, waters and seas and their rich contribution to society.

The paper used in this edition is called Maine Recycled Digital – Silk. It is made with fibre derived only from sustainable sources and produced with a low reliance on energy from fossil fuels. The purchase of carbon offsets compensates for emissions produced over an international supply chain, from seedling through to final delivery to the customer.

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What's inside

Message from the Chair, Professor Ian Davis

Welcome to this latest edition of "A little below the belt."

Whoever thought we would need to be familiar with Greek letters? Alpha, Delta, Omicron, ThreeBagsFull… I'm just waiting for Omega, because that designation isn't ominous at all! Honestly, I feel like giving a big ψ to all of it, although I do feel a little better now because that joke works on both an auditory and visual level.

I'm writing this just before the close of 2021, and the projections are scary. I've already seen the effects on health care services and, more importantly, the people who provide them. We are battening down for a storm that none of us really know how to weather. It's worrisome, demoralising, and frustrating because the best efforts of so many well-meaning people seem all too often to come to nothing. We can easily fall into the traps of saturating ourselves with the fear and uncertainty of it. Browsing becomes doomscrolling. Socialising becomes dangerous. Common courtesies, like wearing a mask to protect others, earn abuse. There have been some shocking failures of leadership, although there is also huge disagreement about which leaders have failed and which have not. People we thought were like-minded and reasonable members of society suddenly declare themselves as sociopaths. We hang on daily numbers, often fed to us by people who do not even understand concepts like exponential growth. We don't even know what numbers we should be concerned about: Cases? Hospitalisations? R? Doubling times? Variant characteristics? Antibody tests? What booster to get? Will life ever be back to normal? We're all tired but there is no escape.

Must it be like this all the time? Every bit of news, every conversation, every aspect of life: it's all disrupted and nothing is as it should be. A huge part of the problem is the uncertainty. Not all of the predictions have panned out. Unexpected events have occurred, and the pace of change can leave us breathless. We get used to one situation and then suddenly everything changes. A treatment that previously worked seems like it might be less useful in the current situation. We hear pronouncements apparently based on evidence that are seemingly contradicted when more information comes to hand. Misinformation abounds and it's hard to know whose authority to trust. We are told we need to take "personal responsibility" and that this is the only way to fix the problem; the people we trusted and put in place to fix the problem seem unable to do so. Our usual anchor points all seem to have come loose.

On the other hand, look at how far we have come. We know way more about it than we did at the start. The science continues to move rapidly (although never as fast as we would like), and our approaches to management and prevention are much more rational and effective now. The situation changes day by day but our long familiarity with it means that we can rapidly adapt and make changes to our everyday lives when and as we need to do so. We can find ways to experience joy even in the midst of extreme constraints on what we are able to do. There is hope despite it all.

Lots of good things have come out of all of this. We have all had to increase our health literacy. We have had to learn how to identify reliable sources of information. I think we all have more respect for the science and the scientists, and I'm personally amazed sometimes by the work they do. We've had to modify our behaviour, often unwillingly, but also often for the good – remember when we all blithely came to work with a bit of a sniffle? We've learned that just because things were always done a certain way doesn't mean they should continue to be done that way. We've definitely learned to value our freedoms, acknowledge our privileges, and appreciate the most important things in our lives, especially those we love.

Does all this sound a bit familiar? It should, because if you look carefully you'll see I haven't mentioned COVID since paragraph 2. What we are all experiencing at the moment is what people affected by cancer have to manage every day, and their challenges are magnified when you add a pandemic to it.

Cancers, and certain viruses, are terrorists: they can disrupt life profoundly for everyone concerned, even if they don't affect us directly. But they are also like terrorists in another very important way: vigilance and alertness are important, and yes they might end up harming or killing us despite our best efforts, but the point of life is to live it as well as we can for as long as we can.

That doesn't mean we stop trying. None of us are satisfied with our current approaches to dealing with cancer (or pandemics, but let's focus a bit more now!) Outcomes for people affected by cancer have generally continued to improve, but too many people still experience illness, disability, disruption, or death, and we cannot allow that to continue. How do we make a difference?

"Basic" research is important, of course. Basic research is what happens in laboratories and other places where people try to understand why things like cancer or viruses behave as they do. This gives clues as to how we might affect those processes to improve outcomes, leading to development of treatments that are new or better (not always the same thing…) The problem is that if that is as far as it goes, then we haven't helped anyone. We need to know several more key pieces of information: does this treatment actually help humans? How do we give it? What side effects can it cause? Does the treatment actually leave people in a better situation? How does it stack up against what we've been doing before?

This is where clinical trials come in. Clinical trials take that basic science information and use it to test the interventions that have been developed from it. The only way we make any progress in improving outcomes is through completing the cycle by answering those key questions in clinical trials. If we don't, then we're back in that earlier paragraph: uncertainty, no reliable guidance, no anchor points, can't tell misinformation from accurate information, and we will be constantly taken by surprise as the disease does what it does. The reason your health professionals are able to give you information you can rely upon and use to make decisions is that they have evidence to back them up. There are some uncomfortable corollaries of this too, though: if they don't have evidence, or the evidence is unreliable, or too good to be true, or someone stands to benefit personally by pushing you down a particular path, then that should raise red flags for you.

ANZUP is the Australian and New Zealand Urogenital and Prostate Cancer Trials Group. That's a mouthful, but what it means is that we work with people affected by genitourinary cancers (cancers of the prostate, kidney, bladder, testicle, or penis). ANZUP is made up of people working in the field of genitourinary cancers, either in treatment, research, or support; and also includes people with direct experience of these cancers. This gives us several important perspectives. We understand the clinical needs, and we are constantly kept informed and up to date about them by our work with people affected by these cancers, and the direct input of our community representatives.

We understand the science, as it exists and as it is unfolding. We see potential new interventions as they are being developed. We are not constrained by corporate priorities, but instead we can devise research questions that are directly and specifically relevant to the areas of clinical need. We perform clinical trials that generate the evidence that you, your families, and your health professionals need, in order to help you make the best decisions.

ANZUP has been in existence since 2008 and since then we have performed clinical trials involving thousands of patients from various parts of the world. We have done small scale trials to test various questions before going into a big trial. We've also performed the big trials, that have changed practice around the world. We also know that our job is nowhere near complete, so long before a trial finishes we are already planning what we should be doing next.

This is a complex, difficult, time-consuming, and expensive process. ANZUP's researchers are all volunteers: we do this on top of our usual jobs, because we are uplifted when we see something making a positive difference, and even if it doesn't then we know we have learned something that will help all of us to make better treatment decisions in the future.

Frustrations that we all share is that research seems to take a very long time, and is very expensive. A clinical trial that changes practice can take years to plan and many more years to perform, before the results are available. ANZUP must find the resources for every trial that it does.

Sometimes this comes from grant funding, although that is increasingly scarce and hard to obtain. Sometimes it comes from industry support, although we are careful to keep at arms' length to preserve our independence and to ensure the trial is not affected by commercial interests. Sometimes we are able to support some work through our fundraising activities; ANZUP is registered as a charity in all Australian states and territories and in New Zealand.

How can you help? Firstly, thanks for your interest – if you've read this far then congratulations in getting through my rambling! Perhaps you've been personally affected by cancer, or it has affected someone close to you. We need to increase people's awareness of these cancers, some of which are uncomfortable for some people to talk about (although imagine how uncomfortable it might be to be affected by one). We need to increase people's understanding of the importance of clinical research, like the trials ANZUP does. And of course, we need to continue to raise resources to do the actual work.

You might be interested in making a donation. Every donation helps, and we are very careful to direct them to support research activities. You might be able to help us in our various fundraising activities, like our #YourWay campaign or our Below the Belt Pedalthons – you will read about all these opportunities in the pages of this publication. You might be interested in participating in a clinical trial, if one is suitable for you – we have information in here about our trials, with more on our web site. Your doctors will also be aware of these trials and can direct you to more information if it is relevant to you.

Whatever it might be: thank you for your interest and support. Please tell someone about us, the work we do, and why it is important. And now, if you'll excuse me, I beta eta mince pi and iota have a kappa coffee, or alpha-all over. Oh, come on!

Please enjoy this edition of "A Little Below the Belt."

IAN DAVIS
CHAIR, ANZUP

A message from the CEO, Margaret McJannett

As we welcome in the new year, we reflect on some of the challenges and achievements we faced over the past 12 months in order to meet ANZUP's mission: to improve the lives of people affected by Below the Belt (bladder, kidney, testicular, penile and prostate) cancers through practice-changing clinical trials.

Despite the impact of COVID, ANZUP continued to build on and develop high quality cutting edge clinical trials. Our current trial portfolio continued to expand and now includes nine ANZUP-led open and recruiting trials, seven trials in development and three trials due to open very soon. We are very grateful to all our researchers, trial staff and the many thousands of patients who support and participate in our ANZUP trials. You can find more information about our trials on our **website**.

9 ANZUP-led open & recruiting trials

7 Trials in development

3 Trials due to open early 2022

In December we were delighted to learn that we were successful with our Cancer Australia infrastructure grant application for the next 2 1/2 years. Whilst we value this financial and in-kind support from the Federal Government through Cancer Australia, independent funding is required for every clinical trial we undertake. It is therefore critical for ANZUP to continue to build greater financial independence and self-sufficiency through our fundraising activities. You can read more about this funding on page 17.

Last year we undertook a review of ANZUP's Strategic Plan for the next three years. Following a series of interviews and focus groups with our members, we identified five Strategic Goals:

- Conduct high-quality, multidisciplinary, practice-changing clinical trials in urogenital cancers
- Maintain a portfolio of trials relevant to and accessible by all people with urogenital cancers in Australia and New Zealand
- Strengthen ANZUP's capacity for practice-changing clinical trials
- Forward plan to maintain a vibrant and active urogenital cancer trials community
- Provide leadership in collaborative cancer clinical trials

An implementation plan with deliverables underpins these Goals.

In terms of fundraising: Our ANZUP Below the Belt #YourWay campaign again featured in 2021, due to the postponement of our Pedalthon events in Sydney and Melbourne. It was a great way for the community to get moving their way and run, walk, swim, ride as many kilometres or hours as they could. This was a great initiative to keep our community united and raised over $75,000 for ANZUP's Below the Belt Research Fund which directly supports our members to develop research projects with the potential to lead to future ANZUP trials.

You can join us, get involved, and help raise funds when **#YourWay** returns from **1-31 May 2022**. **www.belowthebelt.org.au**

You can also support ANZUP and help develop new trial ideas. For lots of ideas about how you can get involved and fundraise visit: **www.belowthebelt.org.au/getinvolved.**

Education and mentoring remain an important focus for ANZUP. Our Concept Development Workshops continued and are designed to support and encourage our members to bring new concepts forward for development. These are where the seeds for many of ANZUP's clinical trials are sown.

Our major annual educational event is our Annual Scientific Meeting (ASM). It was due to be held in Adelaide, but sadly was postponed (again!). As in 2020, we switched it to be a hybrid event across two days with local hubs in Queensland, South Australia, Western Australia and New Zealand. Despite being virtual, over 400 members came together to hear the latest in "below the belt" cancer research and an update on ANZUP's pipeline of new and existing trials. As always, the event allowed our members to continue to engage, discuss challenges and explore new and innovative ways of delivering the best healthcare to people living with below the belt cancers.

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We invite you to join "Friends of ANZUP" and stay connected with the work we do. It's free and you can join by visiting **https://anzup.org.au/join-us-friends-of-anzup/.** You will also receive your free copy of this magazine delivered to your door.

We acknowledge and thank our extraordinarily hard-working members (~2000), our donors, sponsors and corporate supporters for your ongoing support and generosity. With your help, together we will find better treatments and outcomes for people affected by these below the belt cancers.

To the many thousands of patients who participate in ANZUP trials, thankyou. Each and every one of you help us improve treatment and outcomes for patients and their families affected by these below the belt cancers.

On behalf of the ANZUP team I hope you enjoy this edition of our magazine.

MARGARET MCJANNETT
CEO, ANZUP

Consumer Advisory Panel (CAP) update

By Belinda Jago, CAP Chair

The ANZUP Consumer Advisory Panel (CAP) is a group of dedicated volunteers who have had a cancer diagnosis themselves or have cared for a family member/loved one with cancer. We demonstrate a commitment to clinical trials research as a key strategy for improving the outcomes of those affected by below the belt cancers, and provide the voice to consider 'what is the value of this clinical trial to the community?'

As we head into 2022 we can only hope that COVID-19 settles down soon. It continues to be a very anxious time for patients, carers and their families who have already had a cancer diagnosis to then also deal with the added complexity of the pandemic. Cancer patients are certainly in good hands with the health professionals doing their utmost to look after the community, often ahead of themselves. They are now heading into the third year of this pandemic, and we can play our part by living safely, wearing masks and being vaccinated and boosted.

For the ANZUP CAP, technology continues to allow us to participate in all ANZUP activities and in some respects it gave us the opportunity to attend additional meetings as budgets for travel costs and personal time are greatly reduced with virtual meetings.

The last 6 months has seen us participate in the virtual ASM for 2021. We are hoping for 2022 we may be able to meet together in Adelaide – only time will tell. We had CAP members participate in several sessions and this meeting is always valuable and informative for us.

We continued to provide advice on a number of new Patient Information and Consent forms for new trials that will be starting in 2022. We also had the lead investigators for these trials attend our meetings as part of our feedback discussions and the 360 review at the time is very useful.

Well, here's to 2022 and whatever it may have in store for us. We know we can rise to the challenges presented, and be as positive as possible, by living each day as it comes in a safe way.

BELINDA JAGO
CAP CHAIR

Importance of translational research:

Why are some treatments more beneficial than others?

What is Translational Research?

Translational research is sometimes referred to as 'bench-to-bedside' research. It is a type of medical research that focusses on converting basic science discoveries from the laboratory into answers that can be used in the clinic. The aim is to improve how we detect, diagnose and treat health conditions, and improve health outcomes for patients.

As well as taking findings from the laboratory and applying them in the clinic, translational research can also involve bedside-to-bench research. Here samples are taken from patients and profiled in the laboratory to better understand why patients do or do not benefit from treatment, and why treatment stops working.

The more knowledge gathered from basic sciences means we can develop more targeted new drugs, devices, and treatment options for patients. The end point of translational research is the production of a promising new treatments that can be used with practical applications.

THE CRYOBANK AT CHRIS O'BRIEN LIFEHOUSE WITH BIOSPECIMENS FROM ANZUP'S ENZAMET AND ENZARAD TRIALS.

ANZUP and Translational Research

At ANZUP, we have a strong translational focus. Patients who participate in ANZUP trials are asked to consent to the collection of blood and tissue samples which might be used to conduct translational research studies in Australia and/or overseas.

Our goal is to bring together all the different professional disciplines and groups involved in researching and treating urogenital cancers. We do this through our Translational Research Subcommittee, which is made up of a group of multi-disciplinary ANZUP members from across the globe.

With this approach, ANZUP helps find new ways to treat below the belt cancers, taking research from the laboratory bench to the patient.

ANZUP has been extremely successful in a relatively short space of time with leading pivotal studies in below the belt cancers. The data from these studies has had a major impact on clinical practice, as best evidenced by a study such as ENZAMET. This study was a key factor in enzalutamide being approved by the Food and Drug Administration (FDA) in America, for metastatic hormone-sensitive prostate cancer. This was a major milestone.

The integration of translational research sample collection is now taking place in all ANZUP-sponsored trials. This research provides an important opportunity to leverage the pivotal clinical trials we are doing to help deliver better outcomes for patients and their families.

Biospecimen collection for ANZUP's ENZAMET and ENZARAD trials

People who participated in the ENZAMET and ENZARAD trials were asked to consent to the collection of blood and tissue samples for the purpose of laboratory research. This will help ANZUP to greater understand why some types of prostate cancer behave differently, why some people respond better than others to treatment, and to help us work out ways to do better in the future.

Over 100,000 samples have been collected around the world through the ENZAMET and ENZARAD trials and are in the process of being transported to the biobank at Chris O'Brien Lifehouse in Sydney. A comprehensive plan of research for these samples has been developed and will be rolled out soon.

Biospecimen collection for ANZUP's TheraP trial

Lutetium-PSMA (Lu-PSMA) is a brand new radioactive molecule that is very effective in treating prostate cancer. Given intravenously every 6 weeks for up to 6 cycles (or doses), Lu-PSMA is well tolerated and is like a form of intravenous radiation. ANZUP recently conducted a trial called TheraP, which showed that Lu-PSMA is more effective than chemotherapy in advanced prostate cancer. Although this is very promising and exciting, we know that not all men benefit from Lu-PSMA and after a period of time, the treatment stops working in all men. We have developed technology to pick up tiny amounts of DNA (the genetic blueprint) released by cancer cells into the bloodstream. This is also referred to as circulating tumour DNA (ctDNA). By testing ctDNA in the laboratory from blood samples collected on the TheraP trial, we will try to understand which men get excellent responses to treatment, which men never respond to treatment, and what causes Lu-PSMA to stop working.

Translational research program moving forward

ANZUP's work aims to improve the ways a patient with below the belt cancer can be treated. ANZUP is building a very strong translational focus across all of their trials. The use of the biospecimens provides researchers with a valuable resource to help understand and identify clinical and molecular markers of disease, investigate drivers that underpin responses to treatment, and explore emerging concepts that would otherwise not be possible to do so.

"As always, we are grateful for the patients and families who enrol on our trials and donate bio-specimens that support our translational research. We could not conduct our activities without these high-quality samples. We would also like to acknowledge the participating sites thoroughness in obtaining correlative samples from our ANZUP trials. Bio-specimen collection continues as part of existing trials, including ENZA-p and DASL-HiCaP, BCGMM, P3BEP, KEYPAD, UNISoN and PCR-MIB."

A/Prof Arun Azad

ARUN AZAD, CHAIR OF ANZUP'S TRANSLATIONAL RESEARCH SUBCOMMITTEE

FREE to Join!

FRIENDS OF ANZUP®
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Connect with a community impacted by below the belt cancers and learn from clinical experts

Friends of ANZUP was established to connect people whose lives have been affected by prostate, kidney, bladder, penile and testicular cancer, ie below the belt cancers. If you are seeking more information about any of these cancers, would like to hear from people who have been faced with the same challenges, and if you have questions about clinical trials, what they are and if there is a clinical trial suitable for you – then this program could provide some answers.

Friends of ANZUP aims to provide:

- Information about the benefits of clinical trials and how to access them;
- Information about the clinical trials research conducted by ANZUP;
- Biannual community magazine 'A little below the belt' featuring regular updates and stories from health professionals, researchers, cancer survivors and cancer trial participants;
- Invitation to Community Engagement Forum/s;
- Practical information and e-news to help those living with below the belt cancers;
- Updates from the ANZUP clinical community

And remember, if you are wondering if a clinical trial is the correct treatment pathway then consider each point below:

- Participation in a clinical trial may increase the total number of treatment options available to you – even if you have not yet had all the standard (current) treatment options.
- You could have access to treatment not yet commercially available, which might work better or be safer than current treatment options.
- Making the decision to take part in a clinical trial may make you feel you have more control over your situation and that you are taking a more active role in your treatment.
- Your cancer care team will probably provide more attention and more careful monitoring of your condition and possible side effects of treatment if you take part in a clinical trial.
- And importantly, you might help others who have the same cancer type in the future by helping advance cancer research.

It's only through clinical trials we can improve treatment options and outcomes for over 27,000 Australians diagnosed with "below the belt" cancers each year. By joining our community, you can take control of your treatment, be better informed, hopefully become an advocate for clinical trials and assist us in raising awareness of the benefits of clinical trials research and ultimately help us continue to fight cancer below the belt.

To find out more visit **https://anzup.org.au/join-us-friends-of-anzup/**

Patient-led concept development

When confronted with the daunting prospect of a cancer recurrence, patients are faced with the overwhelming decision about what course of treatment is best for them. This was the reality for Colin O'Brien, a member of ANZUP's Consumer Advisory Panel (CAP) who, five years ago, discovered his prostate cancer had returned. This time around, the way forward and the treatment pathway was unclear. There was additional factors Colin had to consider that added complexity to the decisions he needed to make.

COLIN O'BRIEN

Men face many issues when their prostate cancer returns. Once Colin recovered from the initial shock of finding out the cancer had come back, he adjusted to the reality it was not likely to go away. He started to consider what was important to his life and what impact treatment would have on his ability to do the things he loved, like travel. Colin also had to take into account other preexisting health conditions and understand what effect treatment would have on his overall health and wellbeing.

Colin spoke to his oncologist, Professor Scott Williams, about his treatment options and his uncertainty. Prof. Williams admitted he sees at least one man a day, diagnosed with prostate cancer, who faces similar confusion about the way forward.

Thousands of men in Australia are diagnosed with prostate cancer each year and 30% to 40% undergo a radical prostatectomy (4,200 in 2020 across Australia), the 'gold standard treatment' for providing the best possible outcome. Of these, 30-40% of men will see their cancer return, i.e., biochemical recurrence when PSA blood levels are 0.2 or higher. This means thousands of men are in the same predicament as Colin.

It was this revelation that motivated Colin to bring this problem to the ANZUP Concept Development Workshop.

ANZUP encourages members to bring new concepts forward for development through a series of Concept Development Workshops (CDWs). The CDWs are designed to facilitate and support members who have an idea or concept they would like to present for discussion and, if supported, to develop further.

The ANZUP concept development process:

IDEA
- New idea or concept
- Complete concept outline

CDW
- Reviewed by MDT
- Written feedback

SAC
- SAC Endorsement based on subcommittee recommendations

WORKING GROUP
- Working group for development, mentoring and support

CDW – Concept Development Workshops
SAC – Scientific Advisory Committee
MDT – Multi-Disciplinary Team

Radical prostatectomy is surgery to remove the entire prostate gland and surrounding lymph nodes to treat men with localised prostate cancer.

The concept Colin brought to the prostate cancer workshop was titled: 'The decision-making process for men with rising PSA post radical prostatectomy after ten years who have metastasis identified after PSMA PET-CT scans'. And what is most exciting about this concept is that it has been put forward by a patient and member of the CAP. The benefit of having someone experiencing the problem is invaluable in discovering all the elements that need to be considered.

PSMA-PET scan: PET scans use a radioactive label to light up specific regions in the body. PSMA-PET scans look for areas of the body where the PSMA protein is found, showing the presence of prostate cancer cells.

Recent trials of PSMA PET-CT in Australia that provide detailed body scans, have enabled earlier detection and more accurate images of any metastasis for men with biochemical recurrence of prostate cancer. In theory, this is a positive outcome as it better informs the treating physician and patient about how to target treatment earlier and more precisely.

However, the early metastasis diagnosis from a rising PSA presents a different dilemma than the initial cancer diagnosis. Men understand this is not a problem likely to go away and leads to greater uncertainty regarding what, and if any, treatment should now be commenced, that is, men know they are no longer cancer free. After the initial diagnosis, patients believed their treatment would be successful. This earlier detection is welcomed but leads to the emotional and psychological dilemma of how, when, or if to treat a chronic disease that is likely to grow and spread.

So, after presenting some of his own ideas, Colin and the group then decided the concept should focus on further research to better understand men's decision-making process prior to determining their treatment options and, given the shock and stress of cancer return, whether this process can be improved.

Research objectives:

1. Determine the best decision-making process of choosing treatment (or no treatment) for men who have had a radical prostatectomy, biochemical recurrence after ten years, and PSMA PET-CT that has identified metastasis.
2. Understand if the decision-making process can be improved by providing guidelines for the patient during the decision-making process.

The multidisciplinary approach taken at Concept Development Workshops facilitates a process whereby clinicians, researchers, and patients can come together to problem-solve. Through the support of ANZUP members and executives, Colin has been able to take a problem he is experiencing and progress it from a concept to a research project and ultimately a solution. Through this important work, soon men like Colin will have access to tools and decision aids to help them better understand and make choices on treatment best suited for their individual lifestyle and needs.

Noel Castan Fellowship Update

The Noel Castan Fellowship was established by Anita Castan, in memory of her husband, who passed away from cancer two decades ago. Below you can read the latest updates from our Noel Castan Fellows.

"I understand the value of supporting clinical trials and take this opportunity to congratulate ANZUP on its many successes to date and its collaborative approach." - Anita Castan

The aim of the Noel Castan Fellowship is to build ANZUP's research capacity and increase the translation of information collected from our trials, which will contribute to a better understanding of how to optimise patient care.

The Noel Castan Fellowship was awarded to ANZUP members, Dr Hui-Ming Lin, Senior Research Officer at The Garvan Institute of Medical Research and Kathyrn Schubach, a nurse practitioner with clinical expertise working with uro-oncology patients.

Hui-Ming Lin's 'Bioinformatics' project is an analysis of the lipidomic and cytokine profiles from ANZUP's ENZAMET study, which may identify novel biomarkers from the enzalutamide response, and provide new therapeutic targets to overcome enzalutamide resistance to improve the outcome of prostate cancer patients.

Kathryn Schubach's 'Quality of Life' project will develop new questions in trials, using existing data innovatively enhancing and facilitating collaboration and thereby drawing attention and meaning to 'the patient experience' and aligning with the mission of ANZUP's clinical research to improve outcomes.

Dr Hui Ming Lin

Project Title:

Identification of circulating immuno-lipid biomarkers of enzalutamide response

Grant Purpose:

The Noel Castan Fellowship is enabling Dr Lin to carry out research on blood specimens and clinical data from the ENZAMET trial. The ENZAMET trial, led by ANZUP, is an international Phase 3 trial of 1,125 men with metastatic hormone-sensitive prostate cancer (mHSPC).

Update:

The ENZAMET trial, which was led by ANZUP, is an international Phase 3 trial consisting of 1,125 men with metastatic hormone-sensitive prostate cancer (mHSPC). The trial found that addition of enzalutamide to standard testosterone suppression improved survival and delayed PSA/clinical progression. However, not all men responded to enzalutamide, and in addition, responders eventually stop showing positive outcomes. The aim of this project is to look

for biological markers in blood that can predict who will respond to enzalutamide, as this will help decide the best course of treatment. Additionally, these biological markers will help uncover mechanisms of enzalutamide resistance, which will lead to new treatments that can improve the outcome of men with metatstatice hormone sensitive prostate cancer. The type of biological markers that will be investigated are lipids and cytokines, which are respectively linked to fat metabolism and the immune response.

Research on the blood specimens from the ENZAMET trial was meant to commence at the start of 2021. Unfortunately, the COVID-19 pandemic has delayed the retrieval of blood specimens from the multiple study sites which are located overseas. All the blood specimens have only recently arrived at the Chris O'Brien Lifehouse. Given the large number of specimens (>1000), it will take a while to lodge all of them into the cryostorage system and divide them into the amounts required for their designated research projects. Thus, these blood specimens are expected to be available for this research project early 2022.

Nevertheless, the past year has not been wasted. Hui-Ming has been working on blood specimens and clinical data on another group of 168 men with metastatic castration-resistant prostate cancer (mCRPC). The project aims are similar except that the disease is the castration-resistant stage. Researching this group helps to lay the groundwork and develop the analytical strategies for the ENZAMET blood specimens. From this mCRPC group of men, Hui-Ming has managed to identify lipid markers that are associated with poor response to enzalutamide and abiraterone. Lipids and cytokines that may be connected have also been identified. Two manuscripts of these findings have been written and are currently being reviewed by the scientific journals.

While Hui-Ming awaits the availability of the ENZAMET blood specimens, she will continue analysing the data from the mCRPC group, and plans to test different statistical algorithms to develop the best model to predict response to therapy. We look forward to future updates once work begins on the blood samples.

Kathryn Schubach

Project Title:

The unmet informational and supportive care needs among patients diagnosed and living with non-muscle invasive bladder cancer (NMIBC).

Grant Purpose:

Conducting a series of sub-studies and secondary analyses provides us with an opportunity to build ANZUP's capacity to strategically conduct research to understand which 'quality of life' instruments best capture the impact of below the belt cancers and their treatment on the lives of patients and their families and to research how to improve supportive care in this population.

Update:

Kath has commenced her first year of her PhD at the University of Canberra. Her primary Supervisor is Dr Catherine Paterson. Throughout this year she has managed to complete two compulsory subjects: 'The Practice of Research', completed in semester one and currently the 'Principles of Research' to be completed in semester two. She has also attended intensive workshops gaining knowledge and skills to be utilised throughout her doctorate.

Kath has completed her PhD by publications, and has now submitted her manuscript in the Journal of Cancer Survivorship. This will provide the first paper of her doctorate. The title of the paper is; 'What are the experiences of sexual wellbeing interventions in males affected by genitourinary cancers and their partners: A systematic integrative review.'

Kath is also working fulltime as a Urology Nurse Practitioner providing clinical support to men and women with urological issues. The generosity of the Noel Castan Fellowship will provide her with financial support to back fill her clinical role so that she can fully commit to her studies. It will also provide her with the financial resources to attend classes /courses that will assist the completion of her thesis. This year she has been able to attend online all-day classes and attend valuable courses to enhance her research skills.

Kath presented the first year of her PhD at the ANZUP ASM Nurses Session on October 17th 2021. It provided information and a pathway for other nurses and allied health professionals caring for patients with below the belt cancers.

Grant Application Success

Australian Government
Cancer Australia

Cancer Australia was established by the Australian Government in 2006 to benefit all Australians who are diagnosed with cancer, including their families and carers. Cancer Australia aims to decrease the effect of cancer, address inequalities and improve outcomes for people affected by cancer. This is done by leading and coordinating national, evidence-based interventions to maintain a continuity of medical care delivered to the patient.

Cancer research and clinical trials are vital to increase our understanding of how to prevent cancer, develop new approaches to detecting, diagnosing and treating cancers, and improve support and care for people affected by cancer.

Australia is a world leader in cancer research and the Australian Government is committed to ensuring Australia remains at the forefront of research, treatment and the care of people affected by cancer at a local and international level.

Cancer Australia continues to fund priority cancer research through a number of initiatives, including: the awarding of research grants through Cancer Australia's Priority-driven Collaborative Cancer Research Scheme (PdCCRS) and providing funding support to four National Technical Services as well as Australia's 14 Collaborative Cancer Clinical Trials Groups, of which ANZUP is one.

ANZUP is extremely grateful for the continued support received from Cancer Australia. The awarded grant will provide valuable infrastructure funding allowing ANZUP to continue to develop clinical trials. One mechanism adopted by ANZUP to build the clinical trials portfolio is through our Concept Development Workshops. At these workshops clinical trial ideas, conceived by ANZUP members, are discussed initially as concepts. These ideas are then fleshed out with the assistance of experienced members, as well as with broad multidisciplinary input and consumer engagement, with the hope of future trial development and execution.

Looking to the future, it is essential that Australia has a sufficient cancer research workforce and appropriate infrastructure to take advantage of rapid advances in our understanding of cancer to achieve improved outcomes for all Australians affected by this disease.

Addressing Disparities in Cancer Care

It is said "cancer is the great equaliser". But is that really the case?

This saying suggests cancer doesn't know your race, sex, education level, socioeconomic status or whether you're a celebrity or not. It can affect anyone at anytime, anywhere.

However, here at ANZUP, we unfortunately know that this isn't the case. Just like many other areas in our society, our First Nations people, that is Aboriginal and Torres Strait Islanders, are at a disadvantage.

Aboriginal and Torres Strait Islander peoples experience inequities in their cancer care, compared to non-indigenous Australians, and the disparity in care is continuing to increase.

We invited **Professor Gail Garvey**, and **Dr Daniel Lindsay** from the University of Queensland, to our ANZUP Annual Scientific Meeting (ASM) on 18 October 2021 to discuss this issue.

An overview of research strategies to improve outcomes for Aboriginal and Torres Strait Islander with cancer, Gail Garvey

PROF GAIL HARVEY

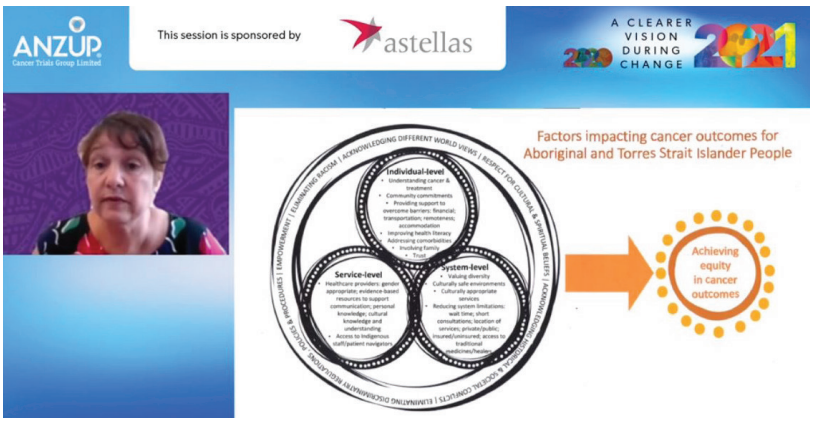
Prof Garvey is a Professor of Indigenous Health Research, a proud Kamilaroi woman and a standout leader in cancer care for Aboriginal and Torres Strait Islander populations. She leads an extensive and targeted research program on well-being and cancer care for indigenous peoples.

"Cancer is one of the leading causes of death for Aboriginal and Torres Strait Islander people, and the cancer mortality gap between Indigenous and non-indigenous Australians continues to widen over time", says Prof Garvey.

Indigenous peoples are experiencing inequities at every point in their cancer care, including higher risk factors, lower prevention and early detection, high incidence levels and untimely diagnosis and treatment. The result of this is lower survival rates and increased mortality.

Prof Garvey leads several targeted research projects focussing on supporting caregivers, building communication programs, understanding fear of recurrence, and improving cardiovascular health.

"It's important that we understand the broader context in which health care is experienced and aspects of the broader social, cultural, and political environment…can influence either negatively or positively the way individuals, families, communities engage with health care and manage their own health," explains Prof Garvey of her research focus areas.



"The five-year survival rate for First Nations men is lower than it is for other Australians, it's about 75% for First Nations and 83% for other Australian males" Dr Garvey explains.

Health service usage and costs in prostate cancer for Aboriginal and Torres Strait Islander people, Daniel Lindsay

DR DANIEL LINDSAY

Dr Lindsay is a Research Fellow working with Prof Garvey in the First Nations Cancer and Wellbeing Research Team. He focuses his research on health service usage and costs in diagnosing and treating prostate cancer.

Prostate cancer is the most common cancer in Australia. However, as Dr Lindsay advises, there is a large disparity in survival rates for this disease.

Dr Lindsay shared with the ANZUP ASM attendees his research into the financial costs associated with treatments provided to First Nations men with prostate cancer. The data showed some promising indications.

The dataset, which included all cancer diagnoses, hospital and emergency department admissions, as well as Medicare Benefits Schedule and Pharmaceutical Benefits Scheme records, showed that Indigenous men were more likely to access the publicly funded service, and they experienced lower out of pocket expenses for their cancer care, as compared to non-Indigenous Australians.

"This suggests that something like the Australian universal health care policies, such as the Closing the Gap payment, PBS programmes, may be supporting equity and cancer patients by keeping those out-of-pocket costs fairly low for these individuals," Dr Lindsay explained.

"This was really just an exploration of this, what we can do with the data set, and it requires further investigations."

This research conducted by Prof Garvey and Dr Lindsay is helping Australia move in the right direction to address disparities in cancer care.

However, as Associate Professor Haryana Dhillon, who hosted the ASM session asserts, "this is a conversation that is clearly going to be ongoing and there's a lot of work to be done".

Associate Professor Dhillon is the Chair of the Quality of Life and Supportive Care Subcommittee (QoL Subcommittee), an ANZUP committee that addresses important areas of unmet supportive care needs to optimise quality of life in below the belt patient groups. This is fundamental to co-designing new innovative models and care pathways.

"There is a huge amount of variability and populations that we can be talking about and it's really important to focus on what it is that we want to be addressing in the specific groups and their specific needs," says A/Prof Dhillon.

Increasing the awareness and understanding of some of the social and cultural issues, as well as acknowledging the challenges faced by Aboriginal and Torres Strait Islander communities, is one of the first steps in addressing equitable access to cancer care.

A further important factor in making positive change includes raising awareness in the clinical community. Clinicians should be challenged in the way they deliver care and the manner in which they communicate with their patients. Ask your patient if they identify as Aboriginal or Torres Strait Islander. You can then have conversations tailored to their cultural and communication needs that will then aid their cancer care journey.

Another step towards addressing inequities is the development and implementation of policies and useful documents. Cancer Australia is at the forefront of making such policies available – but unless they are implemented in practice and become part of clinical education, the gaps in cancer care will continue.

"We've really just scratched the surface of talking about this and actually formulating a way forward for both ends as a trials group and for our partners in the Indigenous community. I'm glad that I'm part of an organisation that has the vision and the foresight to make a commitment towards that over time." A/Prof Dhillon.

Below the Belt YOUR WAY

SUPPORTING ANZUP Cancer Trials Group Limited

Registrations are now open
1-31 May 2022

THIS MAY, RAISE AWARENESS AND FUNDS FOR BELOW THE BELT CANCER RESEARCH

31 days to get active, have fun and improve your fitness.

At ANZUP, we conduct clinical trials and research for below the belt cancers to improve lives. But without extraordinary people like you, it wouldn't be possible.

Improve your fitness, raise awareness and help us fund future clinical trials.

To find out more or to register go to www.belowthebelt.org.au/yourway

Fight Cancer Below the Belt, #YourWay

Trials coming soon

EVOLUTION PRINCIPAL INVESTIGATOR, ASSOCIATE PROFESSOR SHAHNEEN SANDHU

Prostate Cancer: EVOLUTION (ANZUP 2001)

A Phase II Trial of dual Immunotherapy and Lu-PSMA in metastatic castration resistant prostate cancer (mCRPC)

Although men with metastatic prostate cancer initially respond to hormone treatments, many will develop castration-resistant prostate cancer, i.e., their cancer continues to grow despite hormone treatment. This condition is called mCRPC. Immunotherapy and Lutetium-177 PSMA (Lu-PSMA for short) are two treatments that we hope might help men in this situation.

Ipilimumab and nivolumab are immunotherapy drugs that activate the body's own immune response to kill cancer cells. Both ipilimumab and nivolumab allow the immune system to "see" the cancer, seek it out and destroy it. These treatments are given intraveneously (IV) and have been effective in treating other cancers like melanoma, kidney and lung cancers, but studies of ipilimumab and nivolumab in men with prostate cancer remain experimental at present.

Lu-PSMA is a type of treatment called radionuclide therapy that can be used to treat prostate cancer by bringing radioactive atoms into the cancer cells. Many prostate cancers, in particular those that have spread or become resistant to hormonal therapies, have a substance on their cell surface called prostate specific membrane antigen (PSMA). Lu-PSMA attaches to PSMA on the surface of prostate cancer cells and delivers radiation to the cancer cell, without much radiation exposure to other parts of the body. Recent studies have shown that Lu-PSMA is a promising treatment for men with metastatic prostate cancer that is no longer under control after several standard treatments.

The aim of this study is to see if combining ipilimumab and nivolumab with Lu-PSMA can further improve the anti-cancer effects of Lu-PSMA. It is thought that ipilimumab and nivolumab and Lu-PSMA may work together to treat the cancer. Lu-PSMA can potentially kill cancer cells and break up the tumour into small pieces that may be recognised by your immune system while ipilimumab and nivolumab helps your immune system to be activated to find and attack your cancer. This new treatment combination may lead to shrinkage or stabilisation of previously progressing tumours and therefore hopefully stop or reverse the growth of your cancer. We plan to enrol 100 Australian men in this trial.

DIPPER PRINCIPAL INVESTIGATOR, DR MATT ROBERTS

Prostate Cancer: DIPPER (ANZUP 2002)

A multi-centre, randomised phase 2 clinical trial of early salvage radiotherapy versus surveillance for biochemical recurrence after radical prostatectomy incorporating clinical and imaging-based risk stratification.

Current best standard treatment for prostate cancer following radical prostatectomy is uncertain. Previous studies using traditional imaging methods, including computed tomography (CT) and bone scan, showed that radiation therapy was the best way to control PSA levels and return of cancer where the prostate was previously located (local recurrence). Whether radiation therapy reduced the spread of cancer around the body (metastases) or prolonged life (overall survival) was not conclusively proven. Use of radiation therapy also can result in significantly unpleasant side effects, which can affect quality of life. Conversely, personalised selection of men for surveillance using pathology, blood and imaging tests may identify a group of men who can forego additional treatments for the same cancer outcome and avoid side effects. Currently in Australia, with widespread adoption of PSMA PET scanning, unfortunately clinicians cannot agree on the best approach.

The main aim of the study is to see if using radiation therapy to the prostate bed and/or close lymph glands is better than active surveillance for cancer control in a carefully selected group of men with low-risk features and negative PSMA PET imaging. The study also aims to determine:

i. the effect of study treatment on other measures of how well the prostate cancer is controlled,
ii. the effects of treatment on quality of life,
iii. differences in the costs of care for people on treatment,
iv. tests that might identify people who are more or less likely to benefit from treatment, and
v. practice patterns among clinicians in participating hospitals.

Recent studies show that radiation therapy leads to good cancer control rates, but almost half of men will have acceptable control with no treatment. This phenomenon was shown in Australian and international clinical trials comparing this approach immediately after surgery (adjuvant versus early salvage radiation therapy), where similar cancer control was observed overall but >60% of men avoided radiation therapy. This is the first randomised clinical trial evaluating the potential benefit of personalised patient selection and different treatments for your type of prostate cancer. We plan to enrol almost 200 participants in the study in Australia.

Spotlight on prostate cancer

The prostate is a walnut-sized gland located in front of the rectum, behind the base of the penis, and below the bladder. It surrounds the urethra, the tube-like channel that carries semen and urine through the penis. The main function of the prostate is to make seminal fluid, the liquid in semen that protects, supports, and helps transport sperm.

In 2021:

18,110+

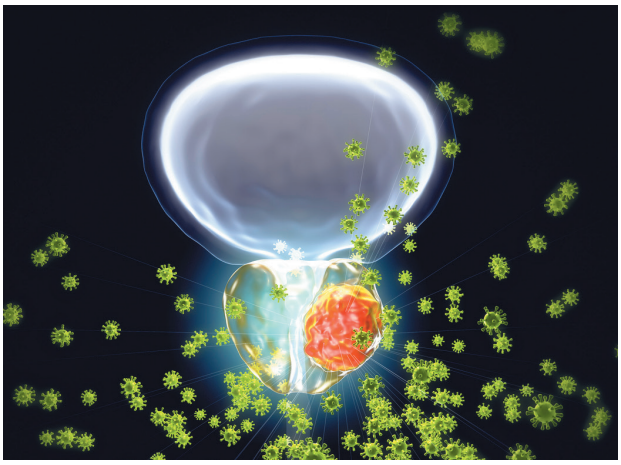
estimated **new diagnoses** in **Australia**

95%

five year survival rate after diagnosis

3,150+

deaths in **Australia** each year



What is prostate cancer?

Prostate cancer begins when healthy cells in the prostate change and grow uncontrollably, forming a tumour. A tumour can be benign or cancerous. A cancerous tumour is malignant, meaning it can grow and spread to other parts of the body. A benign tumour means the tumour can grow but will not spread.

Prostate cancer is slightly unusual when compared with other cancer types. This is because many prostate tumours do not spread rapidly to other parts of the body. Some prostate cancers grow at a very slow rate and may not cause problems or symptoms for years, or sometimes ever. Even when prostate cancer has spread to other parts of the body often it can be managed for a long time. So people with prostate cancer, and even those with advanced prostate cancer, may live with good health and quality of life for many years. However, if the cancer cannot be well controlled with existing treatments, it can cause symptoms like fatigue and pain and sometimes can lead to death. An important part of managing prostate cancer is monitoring it for growth over time, in order to find out if it is growing slowly or rapidly. Based on the pattern of growth, your doctor can then decide the best available treatment options and when to give them.

Prostate cancer is the second most common cancer diagnosed in men in Australia and the third most common cause of cancer death. By the age of 85, it is estimated one in six men will be diagnosed with prostate cancer. It is more common in older men, with 63 per cent of cases diagnosed in men over 65 years of age.

In 2021, it was estimated that 18,110 new cases of prostate cancer will be diagnosed in Australia.

The five-year survival rate for men diagnosed with prostate cancer has increased over the years from 60 per cent to 95 per cent. Nearly all patients who present with localised disease will live beyond five years.

In 2021, deaths from prostate cancer were estimated to be 3,323.

Prostate cancer symptoms

Symptoms are not usually seen with early prostate cancer. Advanced prostate cancer symptoms can include:

- Frequent urination, particularly at night;
- Pain on urination;
- Blood in the urine;
- A weak urine stream;
- Pain in the pelvis or back
- Weak legs or feet

If the disease becomes more widespread and found in the bones, it can cause unexplained pain, fatigue and weight loss.

Spotlight on prostate cancer

Causes of prostate cancer

Some of the risk factors for prostate cancer:

- Age, increasing greatly if you are aged over 50 years;
- Family history of prostate, breast or ovarian cancer, especially BRCA1 and BRCA2 gene mutations;
- A brother or father diagnosed with prostate cancer before the age of 60 years
- There is also an association with high testosterone levels.

Treatment Options

If you do not have a family history of prostate cancer, you may want to consider tests for early detection after discussing the risks and benefits with your general practitioner (GP).

If you have a family history of prostate cancer, your GP should discuss the option for annual PSA testing.

Your general practitioner (GP) will assess your symptoms, conduct a physical examination and arrange blood tests if needed. Your GP should also discuss your needs (including psychological, physical, social and information needs) and suggest sources of reliable information and support.

Treatment and care of people with cancer is usually provided by a multidisciplinary team, i.e a team of health professionals, both medical and allied health. Your health care team will help decide the optimal course of treatment and take into consideration:

- the stage of the disease
- the location of the cancer
- the severity of symptoms
- your general health and wishes.

Treatment may take various forms and may not be recommended straight away. Options include:

1. **Watchful waiting** where you might be monitored in case symptoms develop or change.
2. **Active surveillance** when you will likely have regular blood tests to check your PSA level, regular digital rectal examinations, and maybe ultrasounds or biopsies. If the cancer starts to grow or there are signs it is worsening, you might begin treatment.
3. **Surgery** will become an option if the tumour has not spread outside the prostate. The prostate and some of the surrounding tissue will be removed, including the seminal vesicles. This is called a radical prostatectomy.
4. **Radiotherapy can take two forms:**
    a. external beam radiation therapy – where a machine outside the body directs radiation towards the prostate gland
    b. internal radiation therapy (brachytherapy) – where small radioactive 'seeds' are placed inside the prostate.
5. **Cryosurgery** involves inserting long needles through the perineum into the prostate. Very cold gases are then passed through the needles, which freezes the prostate and destroys cancer cells.
6. **Hormone therapy** involves reducing the levels of certain hormones in the body, so the cancer can slow its growth or even shrink. Hormone therapy for prostate cancer is also called androgen deprivation therapy (ADT).
7. **Chemotherapy** can also be used to treat prostate cancer.

Clinical Trials

New drugs and treatment approaches are constantly being developed and researched. New combinations of different strategies and therapies, as well as the development of new drugs, are constantly being trialled and tested to see if they can further improve treatment options and quality of life for men with advanced prostate cancer. Please talk with your doctor to see if there is a clinical trial suitable for you.

ANZUP is currently running a number of prostate cancer trials. You can read about ANZUP prostate cancer trials from page 29 or for more information, go to the ANZUP prostate cancer trials web page: **https://anzup.org.au/clinical-trials/prostate-cancer-trials/**

References:

https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/cancer-rankings-data-visualisation
https://www.cancer.org.au/about-cancer/types-of-cancer/prostate-cancer/
https://www.prostate.org.au/awareness/for-recently-diagnosed-men-and-their-families/advanced-prostate-cancer/treatment/are-there-new-treatments/

ANZUP and TrialHub bring prostate study to regional Victoria

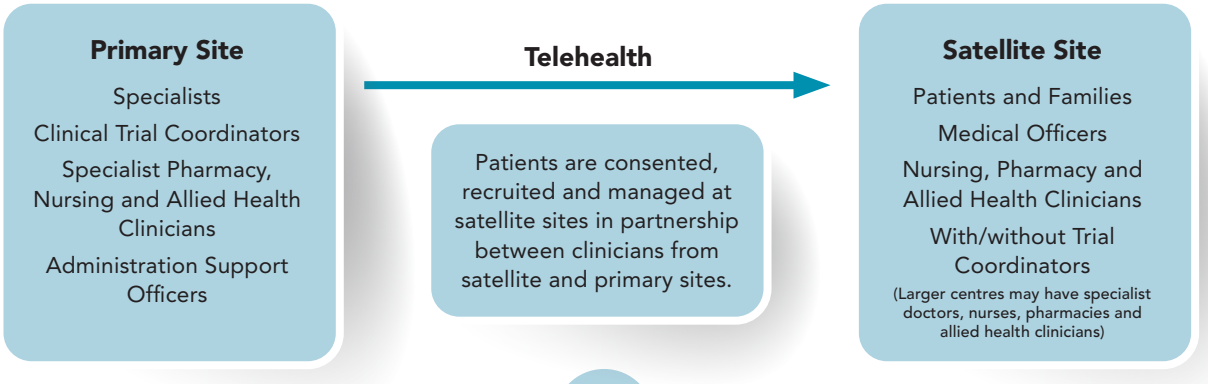
In April 2020, the ANZUP-led prostate cancer trial, DASL-HiCaP (ANZUP 1801), recruited the first patient and started the journey to further recruit and follow up 1,100 eligible patients from over 100 cancer centres across Australia, New Zealand, US, Canada, UK and Ireland. The purpose of this study is to see if a new tablet drug, darolutamide, combined with the current best treatments, can improve outcomes for men with high-risk prostate cancer that has not spread beyond the prostate area.

As well as recruiting amazingly well and opening in various regions worldwide, this trial has now reached another milestone – DASL-HiCAP is now a teletrial.

But what is a teletrial?

A teletrial allows a clinician at a larger centre (primary site) to enrol, consent and treat patients on clinical trials in collaboration with smaller regional and rural centres (satellite sites), allowing patients to participate closer to home and thereby reducing disparities in cancer care and treatment.

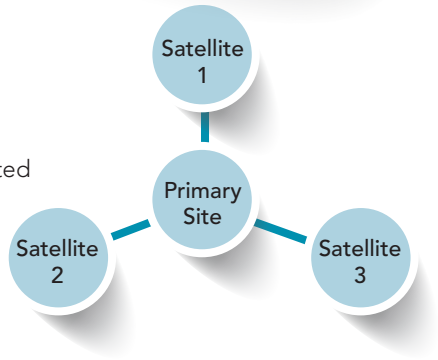
Australasian Teletrial Model



Trial Cluster

Primary and satellite sites are connected through tele-health models of care.

(Satellite sites can be regional, rural or larger metropolitan centres.)



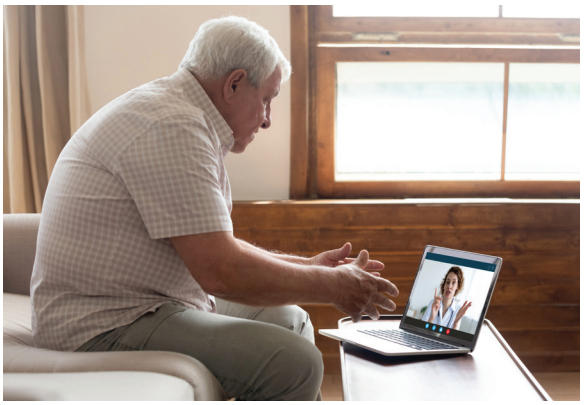
(Source: COSA implementation guide. Colour figure can be viewed at wileyonlinelibrary.com)

Benefits of a teletrial for patients

Through teletrials, patients can be looked after closer to home leading to:

- participation in a clinical trial with family, community and local healthcare support;
- a reduction in travel and accommodation costs;
- equity of access for all Australians to clinical trials and improved access to potential new therapies.

Participation in clinical trials is recommended as the best option for many cancer patients. The teletrial model means access to novel, ground-breaking treatments for everyone no matter where they are based – regional, rural and remote areas. This model has the potential to connect larger centres, even within the same city, and improve the rate of recruitment to highly specialised clinical trials, such as the DASL-HiCaP trial.



ANZUP and teletrials

ANZUP is progressing innovative clinical trial delivery and breaking down participation barriers for prostate cancer patients in Victoria through a collaboration with an Australian-first pilot model called TrialHub.

TrialHub is based at The Alfred Hospital in Melbourne. It is a federally funded program that has been tasked to increase the availability and participation in cancer clinical trials in regional and remote Victoria and outer metropolitan Melbourne.

TrialHub is an Australian-first clinical trial partnership model.

This partnership model involves:

- **Metropolitan hospital** - with an extensive clinical trial portfolio
- **Regional and remote hospitals** - with many patients who want to take part in clinical trials, but don't get the opportunity given their location

ANZUP and TrialHub have worked with Latrobe Regional Hospital to establish and initiate the conduct of the DASL-HiCaP prostate study. This will allow regional and rural patients in Gippsland, and surrounding areas, to participate in the study using Latrobe Regional Hospital as their local clinical trial site.

Participants in DASL-HiCaP are trialling a new drug, darolutamide, with the current best treatment for men with high-risk prostate cancer that has not spread to different areas of the body.

This trial is using the teletrial model, which allows a clinician at a large and experienced clinical trial centre, The Alfred, to support the conduct of a clinical trial at a smaller health service, ie the Latrobe Regional Hospital.

Alfred Health will oversee the key responsibilities of the trial, allowing Latrobe Regional Hospital patients to receive their trial medications locally.

This benefits patients by reducing travel distances, whilst increasing convenience. This model also helps the smaller health service by providing the administrative and clinical support for that institution to conduct clinical trials which they would otherwise be unable, or experience difficulty, in resourcing.

TrialHub director, Anne Woollett, said the study is a great fit for the teletrial model.

"It lends itself well for a number of reasons; great protocol design, an enthusiastic partner, a lot of scientific merit, and a cohort/regional need for this type of study."

Anne Woollett

Prostate cancer is one of three cancers identified as needing more clinical trial accessibility in remote and regional areas.

"We know that regional and rural patients don't have the same access to clinical trials as their metro counterparts, which is why this collaboration is vital in closing the gaps."

"I've spoken to participants who have made 1000km round trips, and lost income, to be on a trial. The aim is that these participants won't have these types of barriers in the long-term," she said.

The teletrial model is at the core of delivering more clinical trials to more Victorians.

"Teletrials means greater access to potentially life-saving treatments," Anne said.

It is anticipated that the teletrial model will be at the centre of more innovative trial delivery models across not only Victoria but all our geographically disparate Australian states.

Learn more about TrialHub;
https://www.alfredhealth.org.au/trialhub

A clinical trial and a lucky life

Speaking with Rob Lewis you would never guess he has prostate cancer and is currently on an innovative ANZUP trial that is harnessing the power of theranostic medicine - the ENZA-p trial.

LEFT:
ROB LEWIS
'LUCKY LIFE'

BELOW:
ROB LEWIS
(SECOND FROM
LEFT) AND HIS
FAMILY.

Rob Lewis is 68 years old, married with two adult sons and his first grandchild soon to arrive. He strongly believes he has had an idyllic life. As a child he was what is called a 'navy brat' – constantly moving when his father was relocated with the navy. Rob then spent time in southern California during a great period of change in the 1960s-70s, before returning to boarding school in Sydney.

Life then led him to his wife whilst working in a wine bar and studying law. Rob then settled in Cronulla where he has lived most of his adult life. He spends his downtime sailing or at the local bowling club and still works as a lawyer.

When Rob developed a sore hip, he believed it was a pulled muscle from sailing, and also possibly due to the fact he had not adequately looked after his health over the years.

When physiotherapy treatment did not lead to any significant improvement in Rob's movement, medical tests were undertaken. The diagnosis was prostate cancer. Rob started chemotherapy, his PSA (prostate specific antigen) levels dropped drastically and his mobility – and ability to sail – returned. However, this did not last, and his PSA levels again started to rise, indicating his prostate cancer was worsening.

ENZA-p is a clinical trial that aims to use new theranostic agents to allow more accurate prognostic decision making, and subsequently more effective personalised treatment with less side effects, for men confronting metastatic castrate resistant prostate cancer. When prostate cancer spreads (becomes metastatic), it often causes health problems and frequently shortens the lifespan of those affected.

So, what was Rob's next course of action? His medical oncologist at the Chris O'Brien Lifehouse in Sydney suggested Rob join the ENZA-p trial – a decision that has seen remarkable results.

Rob considered his oncologists' recommendation to join a trial and decided it was the right approach for him. Rob's treatment was moved to the Kinghorn Cancer Centre under the care of Dr Megan Crumbaker.

Treatment began with enzalutamide, a potent hormone therapy that prevents testosterone from reaching prostate cancer cells. Following this, Rob was to have 4 doses of lutetium, a radioactive molecule that attaches to the surface of prostate cancer cells throughout the body. This drug is given as an injection through the vein and allows targeted radiation to be delivered directly to prostate cancer cells.

After only 2 doses of lutetium Rob's scans indicated his prostate cancer had all but vanished. He responded extremely well to the treatment and the additional 2 doses of lutetium are currently being kept in reserve – for if and when they are needed.

Rob cannot believe how lucky his life has been. He has embraced this remarkable opportunity to put his prostate cancer at arm's length. He decided that to tackle this disease he needs to listen to all his medical team, accept all treatment offered, but also be in the best shape possible both physically and mentally. Rob lost weight and now enjoys a healthy diet with less excesses and more moderation. When exercise is proposed he incorporates it into his daily activities. If counselling is made available, then Rob utilises that service too. Rob is using all the tools offered and tackling his cancer like any other disease.

Rob realises his response on the ENZA-p trial has added to his 'lucky life'. He is sailing as much as he can, continuing to work and being involved in his local area whilst catching up with friends at the bowling club. Rob believes clinical trials are extremely important. And if the ENZA-p trial stops showing such positive results, he is more than happy to try another trial. His motto is definitely 'take every opportunity offered'.

Dr. Megan Crumbaker is a medical oncologist specialising in below the belt cancers (prostate, kidney, bladder and testicular cancers). She is an investigator on multiple international clinical trials and has developed therapeutic studies that are currently underway at the Kinghorn Cancer Centre. She completed a PhD in prostate cancer genomics at the Garvan Institute with the goal of translating this knowledge into clinical practice to improve the lives of patients with below the belt cancers.

Dr Crumbaker took the time to answer some questions about her patient Rob Lewis, prostate cancer treatment pathways, gathering information and clinical trials.

Q: When Rob was referred to you, what steps did you take to assist with his decision- making process?

We walked through the standard (non-trial options) as well as the logistics of enrolling in a trial and its benefits and drawbacks. Then we gave Rob time to read through the patient information sheet to be certain he knew to what he was committing.

Q: Was this trial a good option for Rob? If so, why?

Yes. He was keen to engage in the trial, not only the aspects that might benefit him, but also the research components that aim to benefit future patients.

Q: Can you give a brief outline of Rob's previous treatment history?

- Diagnosed in 2019 following investigations for hip pain. Biopsy confirmed prostate cancer and imaging revealed metastatic disease.
- Commenced androgen deprivation therapy (ADT) + docetaxel chemotherapy with good response.
- PSA starting to rise mid 2020, enrolled onto the ENZA-p trial with Lutetium PSMA in combination with enzalutamide.
- His PSA remains undetectable.

Theranostics is a combination of the terms therapeutics and diagnostics. Theranostics is the term used to describe the combination of using one radioactive drug to identify (diagnose) and a second radioactive drug to deliver therapy to treat the main tumour and any metastatic tumours (cancer that has spread from the original sire to other organs or tissues in the body) tumours.

Q: In your role as a doctor, how do you explain the patient's cancer, their options, what each treatment means for them, and what outcomes they will have?

It's important the patient understands the extent of their cancer and their estimated prognosis (we can only provide rough guides though unfortunately).

From there I explain the aims of treatment (curative, vs. longevity and quality of life) and their treatment options.

After that I am generally guided by the patient's level of understanding and preferences to make my recommendation on a treatment pathway while also highlighting the areas that are less clear cut.

I always ensure I provide written information to the patient as well, because it's always a lot to absorb in a single consultation, then I bring them back to discuss further.

Q: How do you explain a clinical trial?

I explain the overall trial treatments and the chance the patient would be allocated to each, ie. the best standard treatment or the drugs being used in the trial.

I then explain the question the trial is trying to answer and what we know is true already.

I outline the points of difference between the trial and what the patient would do if they weren't on the trial (differences in treatments, possibility of extra visits/ bloods tests/scans, benefits of being on the trial).

I run through the most important side effects of the treatments and then provide the written information for them to consider prior to proceeding.

Q: Has Rob benefited from being on the ENZA-p trial? Is this the result you are seeing with the majority on the trial?

The ENZA-p trial selects men less likely to respond well to enzalutamide alone and this has been the case for most of my patients on the standard (enzalutamide only arm), whereas Rob, and most of my other patients on the combination arm, have done very well.

Q: What do you recommend if someone is considering taking part in a clinical trial?

I would encourage them to ensure they have an appointment with a doctor administering the trial whether that's a discussion with their usual oncologist, or a referral to a centre enrolling that trial. The discussion doesn't commit them to anything but can often give them a better understanding as to what the pros and cons of the trial would be for them as an individual.

I also encourage all cancer patients to ask their clinician if there is a trial option for them at each stage of their disease (i.e. every time a treatment seems to be starting to fail). There isn't always something suitable, but it should be considered at each line of treatment.

PROF LOUISE EMMETT, PRINCIPAL INVESTIGATOR OF THE ENZA-P TRIAL

How did the ENZA-p trial come about?

The birth of ENZA-p was really all about failure and how to prevent it. In our first pilot trial of Lu-PSMA therapy in men with end-stage prostate cancer at St Vincent's, the first few men we treated did not respond at all. We discovered it was because their PSMA PET screening scans did not have bright enough disease (not enough lutetium entering the cell). This really got us thinking about how to increase the PSMA receptor on the cell and how to improve treatment responses in all men. As it turns out - enzalutamide does exactly that. It dramatically increases PSMA receptor expression in the prostate cancer cell. It is also a radiation sensitiser, and in cell models it increases prostate cancer cell kill if teamed up with Lu-PSMA. It seemed like a match made in heaven. Guaranteed not to fail these men.

ENZA-p is all about seeing whether that is correct. It is also about identifying predictors for treatment response - so we can tailor treatments more carefully to the needs of the individual.

ENZA-p

ANZUP 1901

Status: Open and recruiting

Location: Australia wide

Planned sites: 15

Patients recruited: 115 • **Patients required:** 160

Enzalutamide is a potent hormone therapy that prevents testosterone from reaching prostate cancer cells, thereby stopping cancer growth. It is already widely used in men with prostate cancer that has stopped responding to standard hormone treatments (castration-resistant prostate cancer). However, most cancers become resistant to enzalutamide over time, with almost 1 in 4 being resistant from the start of treatment.

Many prostate cancers, in particular those that have spread or become resistant to hormonal therapies, have a substance on their cell surface called prostate specific membrane antigen (PSMA). Lutetium-177 PSMA (Lu-PSMA for short) is a new treatment in advanced prostate cancer. Lu-PSMA is a radioactive molecule that attaches to the surface of prostate cancer cells throughout the body. This drug is given as an injection through the vein and allows targeted radiation to be delivered directly to prostate cancer cells.

Smaller pre-clinical studies have demonstrated synergistic effects by combining Lu-PSMA with enzalutamide. It is possible that Lu-PSMA can prevent early resistance to enzalutamide, extending the time that men benefit from treatment.

The ENZA-p clinical trial aims to compare the effectiveness of enzalutamide in combination with Lu-PSMA, versus enzalutamide alone for the treatment of prostate cancer. This is a randomised study, so half the men in this trial will be randomly allocated to receive Lu-PSMA and enzalutamide, and the other half will be randomly allocated to receive enzalutamide alone. We plan to enrol 160 participants across Australia.

For more information please refer to **https://anzup.org.au/clinical-trial/enza-p/**

Current locations for the ENZA-p trial:

NSW
- Calvary Mater Newcastle
- Chris O'Brien Lifehouse
- GenesisCare Northern Cancer Institute St Leonard's
- Liverpool Hospital
- Macquarie Hospital
- St George Hospital
- St Vincent's Hospital

VIC
- Austin Health
- Peter MacCallum Cancer Centre
- The Alfred Hospital
- Monash Moorabbin Hospital

QLD
- Royal Brisbane and Women's Hospital

SA
- Royal Adelaide Hospital

WA
- Fiona Stanley Hospital
- Sir Charles Gairdner

ENZA-p is funded through the Prostate Cancer Research Alliance (PCRA) – a program jointly funded by the Australian Government and the Movember Foundation (Movember).

GUIDE

ANZUP 1903

Status: Open and recruiting

Location: Australia wide

Planner sites: 6

Patients recruited: 0 (just opened) • **Patients required:** 120

The purpose of this study is to see if a prostate cancer marker in the blood (mGSTP1) can be used to guide chemotherapy treatment. Based on the level of this blood marker, some men may be able to have breaks in treatment rather than having chemotherapy continuously which is the current standard of care. This study will tell us if having these treatment breaks guided by mGSTP1 can improve how men feel during treatment while still treating the prostate cancer effectively.

GUIDE is an investigator-initiated study sponsored and led by ANZUP. The study is funded by ANZUP Discretionary Funding Initiative, ANZUP Below the Belt Research Fund and Chris O'Brien Lifehouse Philanthropic Fund.

For more information please refer to **https://anzup.org.au/clinical-trial/guide/**

Current locations for the GUIDE trial:

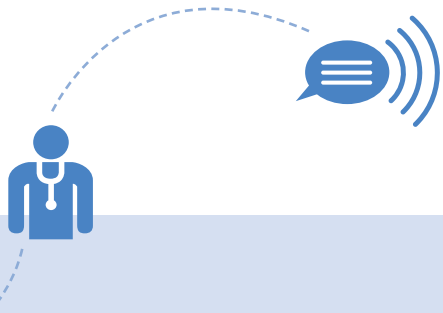
AUSTRALIA

NSW
- Chris O'Brien Lifehouse
- Concord Repatriation General Hospital
- Dubbo Base Hospital
- Border Medical Oncology

VIC
- Goulburn Valley Health
- St Vincent's Hospital - Melbourne

Dr Kate Mahon GUIDE Principal Investigator,

"The GUIDE study is investigating how we can use a blood marker to optimise chemotherapy treatment in metastatic prostate cancer. Using this marker, we aim to personalise chemotherapy to minimise side effects and improve quality of life while ensuring that treatment is still effective."



DASL-HiCaP

ANZUP 1801

Status: Open and recruiting

Location: Australia & Internationally

Activated sites: 39

Patients recruited: 414 • **Patients required:** 1100

The purpose of this study is to see if a new tablet drug, darolutamide, combined with the current best treatments, can improve outcomes for men with high risk prostate cancer that has not spread beyond the prostate area.

Previous studies have shown promising results for darolutamide preventing disease progression and improving survival for men with advanced prostate cancer.

DASL-HiCaP is being led internationally by ANZUP with another exciting opportunity to collaborate with our partners at the NHMRC Clinical Trials Centre, the Canadian Cancer Trials Group, Cancer Trials Ireland (Ireland and UK), and the Memorial Sloan Kettering Cancer Center and Prostate Cancer Clinical Trials Consortium in the US. The University of Sydney is the Sponsor and and the NHMRC Clinical Trials Centre is the global coordinating centre. We plan to enrol 1,100 men from Australia, New Zealand, Canada, US, Ireland, and the UK.

We thank and acknowledge Bayer for providing funding and product fo the DASL-HiCaP Trial.

For more information please refer to
https://anzup.org.au/clinical-trial/dasl-hicap-trial/

Current locations for the DASL-HiCAP trial:

AUSTRALIA

NSW
- Border Medical Oncology Research Unit
- Calvary Mater Newcastle
- Campbelltown Hospital
- Chris O'Brien Lifehouse
- GenesisCare Newcastle
- Gosford Hospital
- Liverpool Hospital
- Northern Cancer Institute-St Leonards
- Prince of Wales Hospital
- St George Hospital
- St Vincent's Public Hospital, Sydney
- Sydney Adventist Hospital
- Wollongong Hospital

VIC
- The Alfred Hospital
- Box Hill Hospital
- GenesisCare Cabrini
- Peter MacCallum Cancer Centre
- Peter MacCallum Cancer Centre - Bendigo Campus
- Peter MacCallum Cancer Centre - Moorabbin Campus
- Sunshine Hospital

QLD
- Icon Cancer Centre-Gold Coast University Hospital
- Princess Alexandra Hospital
- Radiation Oncology Princess Alexandra Hospital Raymond Terrace
- Royal Brisbane and Women's Hospital
- Townsville Hospital

SA
- Ashford Cancer Centre Research

WA
- Fiona Stanley Hospital
- Sir Charles Gairdner

TAS
- Royal Hobart Hospital

NEW ZEALAND
- Auckland City Hospital
- Christchurch Hospital
- Palmerston Hospital

IRELAND
- Bon Secours Hospital Cork in association with UPMC Hillman Centre
- Mater Misericordiae University Hospital
- Mater Private Hospital - Dublin
- St. Luke's Hospital

CANADA
- Centre Hospitalier Universitaire de Sherbrooke
- Jewish General Hospital
- Odette Cancer Centre - Sunnybrook Hospital
- Ottawa Health Research Institute
- Queen Elizabeth II Health Sciences Centre

USA
- Memorial Sloan-Kettering Cancer Center (MSKCC)
- MSKCC - Commack
- MSKCC - Westchester
- MSKCC - Monmouth
- MSKCC - Bergen
- Dana Farber Cancer Institute
- Urology Cancer Center

#UpFrontPSMA

Status: Open & recruiting

Location: Australia wide

Activated sites: 10

Patients recruited: 82 • **Patients required:** 140

Most prostate cancer cells have a molecule on their surface called prostate cancer specific membrane antigen (PSMA). PSMA can be targeted with Lutetium-177 PSMA (Lu-PSMA), a radioactive drug that kills prostate cancer cells anywhere in the body. This investigational drug is not approved for use in Australia by the Federal Government's Therapeutic Goods Administration (TGA). It is a new form of treatment that is effective in some patients with metastatic prostate cancer. It is a radioactive substance that, after injection into a vein, attaches to prostate specific membrane antigen (PSMA). The treatment enables delivery of highly targeted radiation to cancer cells. The emitted radiation only travels about 1mm, which means it mainly causes the death of cancer cells, while avoiding healthy cells, and seems to be well tolerated with few side effects. This is called radionuclide therapy or theranostic therapy. The purpose of this randomised controlled clinical trial is to compare the effectiveness of Lu-PSMA therapy followed by docetaxel chemotherapy versus docetaxel chemotherapy on its own. Previous clinical trials have shown promising activity of Lu-PSMA in treatment of patients with metastatic prostate cancer. Docetaxel is a chemotherapy drug that is approved by the TGA to treat prostate cancer and has been used for many years in the treatment of metastatic prostate cancer. Since Lu-PSMA radiotherapy and docetaxel chemotherapy are both effective in treating metastatic prostate cancer, it is possible that using Lu-PSMA in addition to standard docetaxel chemotherapy at the beginning of the treatment course may improve patient outcomes when compared to treatment with docetaxel alone.

A recent phase 2 clinical trial, showed the effectiveness of Lu-PSMA when used as a last treatment option and helped control disease progression.This study brings the use of Lu-PSMA forward as a first option to patients, with the hope of disease eradication and potential cure.

The trial is open and recruiting.

For more information please refer to **https://anzup.org.au/clinical-trial/upfrontpsma-trial/**

Current locations for the #UpfrontPSMA trial:

NSW
- Liverpool Hospital
- Royal North Shore Hospital
- St Vincent's Hospital Sydney

VIC
- Alfred Health
- Peter MacCallum Cancer Centre
- Austin Hospital

QLD
- Royal Brisbane and Women's Hospital

SA
- Royal Adelaide Hospital

WA
- Sir Charles Gardiner Hospital
- Fiona Stanley Hospital

#UpFrontPSMA is funded through the Prostate Cancer Research Alliance (PCRA) – a program jointly funded by the Australian Government and the Movember Foundation (Movember).

NINJA

Status: Open & recruiting

Location: NSW and VIC

Activated sites: 16

Patients recruited: 164 • **Patients required:** 474

The NINJA clinical trial aims to compare two emerging schedules of radiotherapy in the treatment of intermediate or high risk prostate cancer. Participants will be randomly assigned to one of two radiotherapy schedules as part of this study. In schedule 1 (called Stereotactic Body Radiotherapy) participants will receive 5 radiotherapy treatments over 2 weeks, and in schedule 2, (called Virtual High Dose Rate Boost), participants will receive Stereotactic Body Radiotherapy delivered in 2 treatments over 1 week followed by 12 treatments of conventional external beam radiotherapy over 2 and a half weeks. It is hoped this research will potentially improve the accuracy and quality of radiotherapy treatment in prostate cancer.

This study will include 474 men. Currently we have active sites across Australia and New Zealand with 120 patients currently enrolled.

This trial is open and recruiting. If you are interested in participating in the trial, please refer to **https://anzup.org.au/clinical-trial/ninja/**

This study is being led by the TransTasman Radiation Oncology Group and co-badged with ANZUP. The study is being funded by Cancer Australia, and we acknowledge MDI for providing the study drug.

Current locations for the NINJA trial:

NSW
- Blacktown Hospital
- Calvary Mater Newcastle
- Campbelltown Hospital
- GenesisCare Hurtsville
- GenesisCare Newcastle
- Liverpool Hospitals
- Illawarra Cancer Centre
- St George Hospital
- Westmead Hospital

VIC
- Peter MacCallum Cancer Centre (Parkville)

QLD
- Princess Alexandra Hospital

SA
- Genesis Care South Australia

WA
- 5D Clinics
- Genesis Care Fiona Stanley Hospital
- Sir Charles Gairdner Hospital

NEW ZEALAND
- Waikato Hospital NZ

Make a difference with ANZUP

We need your help to improve outcomes for people affected by these below the belt (prostate, testicular, penile, bladder and kidney) cancers and for future generations.

Any donation, large or small, goes straight into the hands of experts to find the answers we need.

ANZUP®
Cancer Trials Group Limited

To find out more or to donate please go to https://anzup.org.au/donate/

Spotlight on bladder and urothelial cancer

What is bladder cancer?

The bladder is a hollow organ in the pelvis that holds urine before it is eliminated by the body during urination. This function makes the bladder a crucial part of the urinary tract. The urinary tract is also made up of the kidneys, ureters, and urethra. The renal pelvis is a funnel-like part of the kidney that collects urine and sends it into the ureter. The ureter is a tube that runs from each kidney into the bladder. The urethra is the tube that carries urine out of the body. The prostate gland is also part of the urinary tract.

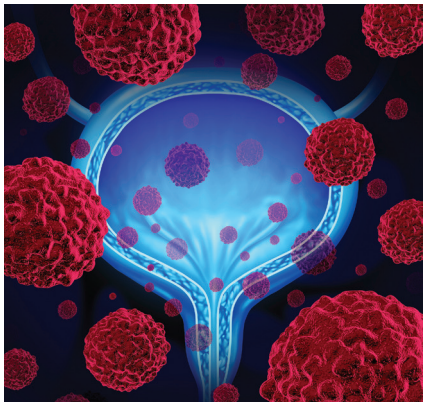
The bladder, like other parts of the urinary tract, is lined with a layer of cells called the urothelium. This layer of cells is separated from the bladder wall muscles, called the muscularis propria, by a thin, fibrous band called the lamina propria.

Bladder cancer starts when healthy cells in the bladder lining – most commonly urothelial cells – change and grow uncontrollably, forming a mass called a tumour. Urothelial cells also line the renal pelvis and ureters. Cancer that develops in the renal pelvis and ureters is also considered a type of urothelial cancer and is often called upper tract urothelial cancer. In a lot of cases, it is treated similarly to bladder cancer. A tumour can be cancerous or benign. A cancerous tumour is malignant, meaning it can spread and grow to other parts of the body. A benign tumour means the tumour can increase in size but will not spread. Benign bladder tumours are quite rare.

Types of bladder cancer

Bladder cancer takes different forms:

- urothelial carcinoma, formally known as transitional cell carcinoma, is the most common form of bladder cancer (80-90%) and starts in the urothelial cells in the bladder wall's innermost layer
- squamous cell carcinoma begins in the thin, flat cells that line the bladder
- adenocarcinoma is a rare form which starts in mucus-producing cells in the bladder.



Bladder cancer may be limited to the lining of the bladder (non-muscle invasive bladder cancer NMIBC), invade the bladder wall (muscle invasive bladder cancer MINC) or spread further to lymph nodes or other organs (advanced or metastatic bladder cancer).

Among Australia's 15 most common malignancies, bladder cancer remains the only one with survival rates that have worsened over the past 30 years.

Bladder cancer was the 11th most commonly diagnosed cancer in Australia in 2021. In 2021, it was estimated 3066 cases of bladder cancer would be diagnosed in Australia (2369 males and 697 females). This is equivalent to an estimated incidence rate of 9.3 cases per 100,000 persons. Bladder cancer is more common in men than women and in people aged over 60 years. In addition, it was estimated there would be 1020 deaths in Australia from bladder cancer but from 2013 - 2017 on average, 55.3% of people diagnosed with bladder cancer survived 5 years after diagnosis.*

Bladder cancer can be treated effectively if found early and before it spreads outside the bladder.

Spotlight on bladder and urothelial cancer

Bladder cancer symptoms

The most common symptom of bladder cancer is blood in the urine (haematuria), which usually occurs suddenly and is generally not painful.

Other less common symptoms include:

- Problems emptying the bladder;
- A burning sensation when passing urine;
- Pain when urinating;
- Need to pass urine often;
- Back pain or lower abdominal pain.

Causes of bladder and urothelial cancer

Environmental risk factors are thought to be more important than genetic or inherited susceptibility when it comes to bladder cancer. Some factors that can increase the rise of bladder and urothelial cancer include:

- smoking;
- older age;
- family history;
- diabetes treatment using the drug pioglitazone;
- workplace exposure to certain chemicals used in dyeing in the textile, rubber and petrochemical industries;
- use of the chemotherapy drug cyclophosphamide;
- chronic urinary tract infections.

Common treatment approaches

Many times, the best option might include more than one of type of treatment. Surgery, alone or with other treatments, is used to treat most bladder cancers. Early-stage bladder cancers can often be removed. But a major concern in people with early-stage bladder cancer is that new cancers often form in other parts of the bladder over time. Taking out the entire bladder (called *radical cystectomy*) is one way to avoid this, but it causes major side effects. If the entire bladder is not removed, other treatments may be used to try to reduce the risk of new cancers. Whether or not other treatments are given, close follow-up is needed to watch for signs of new cancers in the bladder.

Depending on the stage of the cancer and other factors, treatment options can include:

Bladder cancer surgery - type of surgery done depends on the stage of the cancer.

Intravesical therapy - the doctor puts a liquid drug right into your bladder rather than giving it by mouth or injecting it into your blood.

Chemotherapy - it can be given in 2 different ways, either straight into the bladder or given in pill form or injected into a vein or muscle. The drugs then go into the bloodstream and travel throughout the body.

Radiation therapy - uses high-energy radiation to kill cancer cells.

Immunotherapy - is the use of medicines to help a persons own immune system recognise and destroy cancer cells.

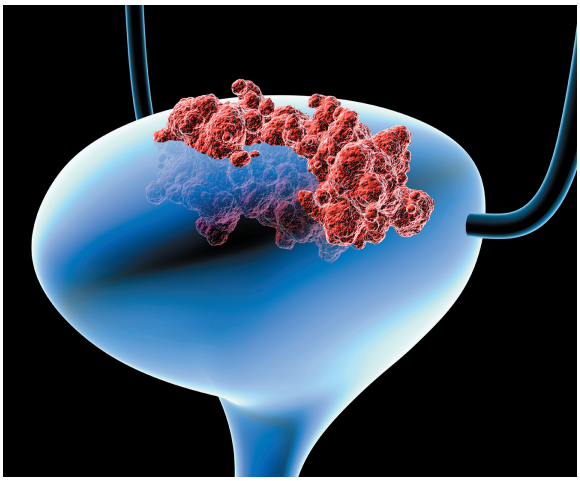
Targeted therapy - as researchers have learned more about the changes inside cells that cause cancer, they have developed newer drugs that target some of these changes. These targeted drugs work differently from other types of treatment, such as chemotherapy, and they may work in some cases when other treatments don't.

Clinical trials - several ground-breaking bladder cancer trials using some of the therapies listed above, are currently underway in Australia. *You can read more about ANZUP's bladder cancer trials on pg 39.*

The worsening bladder cancer survival rates over the past 30 years can mainly be attributed to Australia's ageing population as the percentage of patients diagnosed with bladder cancer over the age of 80 years has gradually increased. Early identification and referral can lead to timely diagnosis. In addition, the hope is that novel approaches are identified through clinical trials and help reverse the trend of deteriorating survival rates in bladder cancer.

* https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/summary

A translational sub-study for bladder cancer



DR STEVE MCCOMBIE, UROLOGY SPECIALIST,
FIONA STANLEY HOSPITAL, WA

The Below the Belt Research Fund has supported many members in the development of investigator-initiated studies. The fund has provided much needed seed funding to support four ANZUP members to progress new trial ideas to the point of becoming full scale studies. We congratulate Steve McCombie on his pilot study.

Identifying tumour and immune stromal features that correlate with optimal benefit from BCG and mitomycin: a translational sub-study of patients in the BCGMM Trial

Optimal treatment of aggressive bladder cancer that has not yet invaded the muscle of the bladder wall involves removing all visible tumour using a fibreoptic telescope, followed by regular instillation of a bacterial protein called Bacillus Calmette–Guérin (BCG) into the bladder. BCG activates the body's immune system to help kill cancer cells. Instillation of a chemotherapy agent called mitomycin into the bladder also has proven effective in the treatment of these tumours. Mitomycin works both by directly destroying cancer cells and may also cause release of cancer cell components that assist activation of the body's immune system to help kill cancer cells.

The BCGMM Trial is a currently recruiting ANZUP trial aiming to determine if the combination of BCG and mitomycin is more effective than BCG alone in the treatment of patients with aggressive bladder cancer that has not yet invaded the muscle of the bladder wall.

As part of this trial, tumour and biopsy tissue samples are telescopically removed from patient's bladders at several timepoints during their treatment. We plan to perform extensive analyses on these samples to try and determine if it can be predicted which patients may do better with BCG treatment alone, combined BCG and mitomycin treatment, or those that may not be likely to respond to either BCG or the combination. These analyses include looking at how BCG sticks to cancer cells, studying ways in which cancer cells can defend themselves against mitomycin, testing whether the immune cells visible in the cancer tell us who will do best with which treatment, and identifying if different tumour sub-types do better with different treatments.

'The core goal is to be able to predict the best treatment for patients with these bladder cancers through studying the cancer cells themselves, in order to better deliver personalised treatment that is most likely to improve outcomes without exposing the patient to unpleasant or dangerous side-effects from therapy that is unlikely to be effective.' Dr Steve McCombie

ANZUP trials - bladder

This bladder cancer trial is currently being run by ANZUP.
For more information about this trial, go to the ANZUP bladder cancer trials web page: ***https://anzup.org.au/clinical-trials/bladder-cancer-trials/***

BCGMM

ANZUP 1301

Status: Open & recruiting

Location: Australia

Activated sites: 15

Patients recruited: 400

Patients required: Stage one: 130 / Stage two: 370

Non-muscle invasive bladder cancer is common and causes substantial suffering. It requires removal or irradiation of the bladder within five years in more than 30% of people with high-risk tumours, despite best current treatment.

Recent preliminary studies show promising results from adding mitomycin (MM), a chemotherapy drug, to current treatment with BCG (Bacillus Calmette-Guérin, a strain of modified bacteria which stimulates an immune response to early cancer cells).

This randomised trial will determine the effects of adding mitomycin on cure rates, survival, side effects and quality of life. This could potentially provide a simple and cost-effective treatment for patients who suffer from this cancer.

This study is currently active and recruiting. Please speak with your doctor if this is of interest to you or someone you know.

ANZUP collaborates with the University of Sydney through the National Health and Medical Research Council Clinical Trials Centre (NHMRC CTC).

This ANZUP investigator-initiated study is being funded by Cancer Australia and the National Health and Medical Research Council. We acknowledge Omegapharm and Merck Sharp & Dohme for providing the study drugs.

Current site locations for the BCGMM trial are:

NSW
- Concord Repatriation General Hospital
- John Hunter Hospital
- Nepean Hospital
- Northern Cancer Institute (GenesisCare)
- SAN Clinical Trials Unit
- Southside Cancer Care Centre
- The Tweed Hospital
- Westmead Hospital

VIC
- Austin Health
- Epworth HealthCare (Richmond)
- Footscray Hospital
- Frankston Hospital
- Royal Melbourne Hospital
- The Alfred Hospital

WA
- Fiona Stanley Hospital

QLD
- Redcliffe Hospital

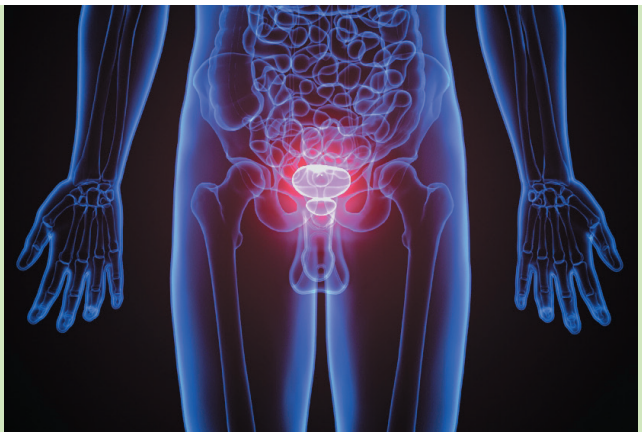
UK
- Nottingham University Hospital

Spotlight on testicular cancer

The testicles are part of the male reproductive system. There are normally 2 testicles, and they are located under the penis in a sac-like pouch called the scrotum. They can also be called gonads or testes. The testicles produce sperm and testosterone. Testosterone is a hormone that plays a role in the development of masculine characteristics and the male reproductive organs.

980
estimated diagnoses

in **Australia** in **2021**



33
estimated deaths

from testicular cancer in **2021**

What is testicular cancer?

Cancer that develops in a testicle is called testicular cancer or cancer of the testis. Usually only one testicle is affected, but in some cases both. About 90 to 95 per cent of testicular cancers start in the cells that develop into sperm - these are known as germ cells.

Compared with other types of cancer, testicular cancer is rare. But testicular cancer is the second most common cancer in young men (aged 18 to 39) excluding non-melanoma skin cancer. However, this form of cancer is highly treatable, even when cancer has spread beyond the testicle.

It was estimated only 980 men would be diagnosed with testicular cancer in Australia in 2021. This equates to 1% of all cancers in men. For Australian men, the risk of being diagnosed with testicular cancer by the age of 85 is 1 in 202. The rate of men diagnosed with testicular cancer has grown by more than 50% over the past 30 years, however the reason for this is not known.

Germ cell tumours are the most common testicular cancers. Under a microscope there are two main types that are quite different when observed – seminoma and non-seminoma cells. Seminoma cells usually occur in men aged 25-45 but can also occur in men over the age of 60 or at any age. This form of testicular cancer develops more slowly than non-seminoma cancers. The faster developing, rarer form of testicular cancer occurs in younger men in their late teens and early 20s.

In 2021 a total of 33 deaths from testicular cancer were estimated. In 2013 - 2017, on average 97.4% of males diagnosed with testicular cancer survived 5 years after diagnosis.

Testicular cancer symptoms

Testicular cancer may cause no symptoms. The most common symptom is a painless swelling or a lump in a testicle.

Less common symptoms include:

- Feeling of heaviness in the scrotum;
- Change in the size or shape of the testicle;
- Pain or ache in the lower abdomen, the testicle or scrotum;
- Back pain;
- Feeling of unevenness;
- Tenderness or tenderness of the breast tissue (due to hormones created by cancer cells).

Self-checking is so important – because if found early, testicular cancer is one of the most curable cancers.

Spotlight on testicular cancer

Causes of testicular cancer

A couple of factors that may increase a man's risk of testicular cancer include an undescended testicle as an infant, or family history, mainly having a father or brother who has had testicular cancer.

In addition, personal history may contribute to testicular cancer. If you have had cancer in one testicle you are more likely to develop cancer in the other testicle. It is also found that infertility may be another possible cause.

There is no known link between testicular cancer and injury to the testicles, hot baths, wearing tight clothes or sporting strains.

Testicular cancer treatment

Treatment for testicular cancer depends on the type of cancer you have and how far it has spread. Your medical team will advise the best treatment for you. They will consider various points:

- your general health
- the type of testicular cancer
- the size of the tumour
- the number and size of any lymph nodes involved
- if the cancer has spread to other parts of your body. If testicular cancer does spread, it most commonly spreads to the lymph nodes in the pelvic and lower abdominal regions.

Understanding testicular cancer, the treatments available and possible side effects can help you decide your treatment pathway. You may also want to talk to your doctor about how treatment for testicular cancer may affect your fertility.

In almost all cases if testicular cancer is suspected, the affected testicle is surgically removed in an operation called an orchiectomy. A laboratory will then examine the tissue to confirm the type of cancer and the stage it is at.

After the surgery, you may not need any further treatment but will be closely monitored. This is called surveillance. If other treatments are required they may include chemotherapy or radiotherapy to stop the spread of cancer cells to other parts of the body. Some people may require further surgery.

Testicular cancer clinical trials

Several decades ago testicular cancer was a disease with a very poor prognosis. But now, because of new treatments, tested carefully in clinical trials, it is almost always curable even when it has spread. However, even though there are excellent treatments available, we still need to do more. This can only happen through understanding the science and by performing clinical trials to see which treatments are most likely to help further improve outcomes. ANZUP is involved in clinical trials in testicular cancer through its clinical trials program.

Speak with your doctor if you would like to know more about testicular cancer clinical trials. You can also read about ANZUP's trials on the following pages.

For more detailed information about these trials, go to the ANZUP testicular cancer trials web page: **https://anzup.org.au/clinical-trials/testicular-cancer-trial**

References

https://www.cancer.org.au/about-cancer/types-of-cancer/testicular-cancer.html
https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/cancer-summary-data-visualisation

Just opened!

CLIMATE

ANZUP 1906

Status: Open & recruiting

Location: Australia wide

Planned sites: 11

Patients recruited: 0 • **Patients required:** 200

Testicular cancer is the most common cancer diagnosed in men aged between 15 and 39 in Western countries, however it can occur at any age. Most men diagnosed with testicular cancer will have cancer confined to the testicle, without evidence of spread to other areas of the body. These men are highly likely to be cured following surgical removal of the testicle (orchidectomy) alone, and most will not require additional chemotherapy or radiotherapy. Sometimes, a man may choose to undergo preventive chemotherapy or radiotherapy, which reduces the risk of their cancer coming back; however, this may result in long-term side effects for some men.

For this reason, most men in Australia are recommended "active surveillance," which involves regular reviews with their doctor, computerised tomography (CT) scans and blood tests, but no chemotherapy or radiotherapy.

With this approach, most men will be spared from unnecessary treatment and side effects. However, a small number of these men will have recurrent cancer detected during active surveillance. Reassuringly, these men are also highly likely to have a positive outcome following additional treatment.

A new blood test, micro-ribonucleic acid (miRNA), which evaluates a protein commonly found in testicular cancer is under investigation. Early studies have found that miRNA is detectable in blood samples of men who have known testicular cancer.

CLIMATE is an investigator-initiated research project led by ANZUP in collaboration with the Walter and Eliza Hall Institute for Medical Research (WEHI). This study has been co-funded by the ANZUP Cancer Trials Group Discretionary Funding Initiative and WEHI.

For more information please go to the trials page on the ANZUP website:
https://anzup.org.au/clinical-trial/climate/

Active site:
NSW

- Calvary Mater Newcastle

Pending sites:
NSW

- Chris O'Brien Lifehouse
- Southside Cancer Care Centre
- St Vincent's Hospital - Sydney
- Sydney Adventist Hospital

VIC

- Austin Health
- Barwon Health
- Eastern Health
- Epworth Healthcare
- Peter MacCallum Cancer Centre

QLD

- Royal Brisbane & Women's Hospital

CLIMATE trial led by ANZUP now open

We're delighted to announce the CLIMATE trial is now open. This trial is a collaboration between ANZUP and the Walter and Eliza Hall Institute of medical research (WEHI).

This testicular cancer trial is called: Asessing the Clinical utility of miR-371a-3p as a marker of residual disease in Clinical Stage 1 Testicular Germ Cell Tumour, following orchidectomy. This all sounds highly technical so read on and learn more about this trial and what it will mean for testicular cancer patients.

Testicular cancer overview

Testicular cancer is the most common cancer diagnosed in males aged between 15 and 39 in Western countries, however it can occur at any age. Most individuals diagnosed with testicular cancer have cancer confined to the testicle, without evidence of spread to other areas of the body and are highly likely to be cured following surgical removal of the testicle (orchidectomy) alone. Sometimes, they may choose to undergo preventive chemotherapy or radiotherapy, which reduces the risk of the cancer coming back; however, this may result in long-term side effects.

Treatment options

Most individuals diagnosed with testicular cancer in Australia are therefore recommended "active surveillance," which involves regular reviews with their doctor, scans and blood tests, and no chemotherapy or radiotherapy. With this approach, they can be spared from unnecessary treatment and side effects; however, a small number will have recurrent cancer. Reassuringly even when this occurs, they are highly likely to have a positive outcome following additional treatment.

The CLIMATE trial

A new blood test, micro-ribonucleic acid (miRNA), which evaluates a protein commonly found in testicular cancer, is under investigation. Early studies have found that miRNA is detectable in blood samples of individuals who have known testicular cancer and appears to be more accurate than our existing blood tests. If miRNA can be reliably detected in individuals with active testicular cancer, it may guide recommendations around preventive chemotherapy and active surveillance in the future.

CLIMATE Principal Investigator Associate Professor Ben Tran:

"Testicular cancer is a highly curable cancer, however, in those who need treatment, side effects from treatment can result in long term impacts on quality of life. Sometimes, patients are given treatment when there is a high suspicion of recurrence of testicular cancer, but not all of these patients actually have a recurrence. Current blood tests and scans can only be so good at confirming recurrence of testicular cancer. A new blood test is being developed that looks very promising at being an extremely sensitive and specific blood test for testicular cancer. CLIMATE is an ANZUP study aimed at determining whether this blood test, miR-371, is sufficiently accurate in order to be used to guide treatment or non-treatment, thereby improving QOL in testicular cancer survivors."

TIGER

ANZUP 1604

Status: Open & recruiting

Location: Australia wide & Internationally

Activated sites: 4 (Australia)

Patients recruited: 11 • **Patients required:** 60 + 420 internationally

This randomised phase III trial will study how well standard-dose combination chemotherapy works compared to high-dose combination chemotherapy and stem cell transplant in treating patients with germ cell tumours that have returned after a period of improvement or did not respond to treatment.

Drugs used in chemotherapy, such as paclitaxel, ifosfamide, cisplatin, carboplatin, and etoposide, work in different ways to stop the growth of tumour cells. They either kill the cells by stopping them from dividing or stop them from spreading. Giving chemotherapy before a stem cell transplant halts the growth of cancer cells by stopping them from dividing or by killing them. Giving colony-stimulating factors, such as filgrastim or pegfilgrastim, and certain chemotherapy drugs, helps stem cells move from the bone marrow to the blood so they can be collected and stored. Chemotherapy is then given to prepare the bone marrow for stem cell transplant. The stem cells are then returned to the patient to replace the blood-forming cells that were destroyed by the chemotherapy.

It is not yet known whether high-dose combination chemotherapy and stem cell transplant are more effective than standard-dose combination chemotherapy in treating patients with refractory or relapsed germ cell tumours.

Up to 420 patients will be enrolled in Australia, New Zealand and other countries. Currently we have 11 patients enrolled and 4 sites open in Australia.

Please speak with your doctor if this is of interest to you or someone you know.

ANZUP is collaborating with the Alliance for Clinical Trials in Oncology (USA) and EORTC (Europe) and the NHMRC Clinical Trials Centre.

We thank and acknowledge the Movember Foundation for their funding support to conduct the TIGER trial.

For more information, please go to the trials page on the ANZUP website:
https://anzup.org.au/clinical-trial/tiger/

Current site locations for the TIGER trial are:

NSW
- Chris O'Brien Lifehouse

VIC
- Eastern Health
- Peter MacCallum Cancer Centre

QLD
- Princess Alexandra Hospital

P3BEP

ANZUP 1302

Status: Active & recruiting

Location: Australia wide & Internationally

Activated sites: 69

Patients recruited: 194 • **Patients required:** Stage 1 (150) Stage 2 (350)

The current standard practice for the treatment of germ cell tumours is the use of the chemotherapy combination called BEP, which consists of three chemotherapy agents – Bleomycin, Etoposide and Cisplatin – administered on a three-weekly cycle. BEP is given with a drug called pegylated G-CSF (or pegfilgrastim) that stimulates white blood cell production.

The purpose of this study is to determine whether giving the same dose of BEP on a two-weekly schedule will be more effective and better tolerated than a three-weekly schedule. The two-weekly schedule is called "accelerated BEP" and the three-weekly schedule is called "standard BEP".

For more information, please go to the trials page on the ANZUP website: **https://anzup.org.au/clinical-trial/p3bep/.**

ANZUP collaborates with the University of Sydney through the NHMRC CTC to conduct P3BEP Trial.

This ANZUP investigator initiated study is being funded by a Cancer Australia grant.

Current locations for the P3BEP trial:

NSW
- Calvary Mater Newcastle
- Chris O'Brien Lifehouse
- Concord Repatriation General Hospital
- Macquarie Cancer Clinical Trials
- Nepean Hospital
- Prince of Wales Hospitall

QLD
- Princess Alexandra
- Queensland Childrens Hospital
- Royal Brisbane & Womens Hospital

VIC
- Austin Health
- Border Medical Oncology
- Peter MacCallum Cancer Centre

SA
- Flinders Medical Centre
- Royal Adelaide Hospital

WA
- Fiona Stanley Hospital

TAS
- Royal Hobart Hospital

NEW ZEALAND
- Auckland Hospital
- Christchurch Hospital
- Starship Hospital –Paediatric
- Palmerston North Hospital
- Christchurch Children's Haematology Hospital

UK
- Royal Marsden Hospital
- University Hospital Southampton
- Cambridge Univerity Hospital
- Royal Preston Hospital, Lanchashire
- Beatson West of Scotland Cancer Centre
- St James University, Leeds
- Belfast City Hospital
- Nottingham University Hospital
- The Christie
- Northern General Hospital
- University College London Hospital
- St Barthalomews Hospital
- Bristol University Hospital
- Derriford Hospital, Plymouth
- Aberdeen Royal Infirmary
- Velindre Hospital

USA
- Lucile Packard Children's Hospital Stanford University
- Memorial Sloan Kettering Cancer Center
- Washington University School of Medicine
- Rady Childrens Hospital
- University of Texas Health Science Center at San Antonio
- Geisinger Medical Center
- Carolinas Medical Center/Levine Cancer Institute
- Advocate Children's Hospital - Oak Lawn
- NYU Winthrop Hospital
- Saint Mary's Hospital
- Dana Farber University of Minnesota/ Masonic Cancer Center
- Roswell Park Cancer Institute
- Children's Hospital of Alabama
- Augusta University Medical Centre
- University of Wisconsin Hospital
- University of Mississippi Medical Centre
- Vanderbilt University
- UT Southwestern Simmons Cancer Centre
- Hackensack University Medical Center
- Providence Sacred Heart Medical Center and Children's Hospital
- East Tennessee Children's Hospital
- Dell Children's Medical Center of Central Texas
- Memorial Health University Medical Center
- Miller Children's and Women's Hospital Long Beach
- Mayo Clinic
- Kaiser Permanente Downey Medical Center
- University of Iowa/Holden Comprehensive Cancer Center
- Palmetto Health Richland
- Children's Healthcare of Atlanta - Egleston
- Methodist Children's Hospital of South Texas
- Loma Linda University Cancer Centre
- University of Southern California
- Broward HealthCare
- LA Biomedical Research Institute at Harbor-UCLA
- Dayton Children's Hospital
- Presbyterian Hospital New Mexico
- Tufts Children's Hospital
- Dartmouth-Hitchcock Medical Center
- Children's Hospital of Alabama
- Ann & Robert H. Lurie Children's Hospital
- Driscoll Children's Hospital
- Children's Hospitals and Clinics of Minnesota

Spotlight on kidney cancer

People usually have two kidneys, located in the abdomen above the waist on either side. These bean-shaped organs are each about the size of a small fist and are located closer to the back of the body than to the front. Each kidney works independently so the body can function with less than one complete kidney.

The kidneys filter blood to remove excess minerals, salts and impurities, as well as extra water. Blood pressure, red blood cell production, and other bodily functions are controlled by hormones produced by the kidneys.

In 2021 it was estimated:

4,377+ diagnoses

of kidney cancer in **Australia**

2.9%

of all newly diagnosed **cancers** in Australia

men

are almost **twice as likely** to be diagnosed as women

What is kidney cancer?

Kidney cancer has become increasingly more commonly diagnosed and survival rates continue to improve. This cancer is the 7th most diagnosed cancer in Australia and in 2021 it was estimated there would be 4,377 new cases of kidney cancer diagnosed (2,936 males and 1,441 females).. Kidney cancer is rare in people under 40 but risk does increase with age. Also, men are almost twice as likely to be diagnosed with kidney cancer as women.

Kidney cancer generally refers to renal cell cancer, which develops in the lining of the small tubes in the kidney. There is usually just a single tumour in one kidney, but sometimes there may be more than one tumour, or tumours in both kidneys. Kidney cancer can be subdivided into several different types, based on the appearance of the cancer cells under a microscope as well as other genetic factors. About 90% of kidney cancers are renal cell cancer, and the most common subtype is clear cell renal cancer.

Other types of kidney cancers include:

- **Urothelial carcinoma.** This is also called transitional cell carcinoma. It constitutes 5% to 10% of the kidney cancers diagnosed in adults. Urothelial carcinoma begins in the area of the kidney where urine collects before moving to the bladder, called the renal pelvis. This type of kidney cancer is treated like bladder cancer because both types of cancer begin in the same cells that line the renal pelvis and bladder.
- **Wilms tumour** is most common in children and is treated differently from kidney cancer in adults. About 1% of kidney cancers are Wilms tumors. A different approach to treatment is used for this type of kidney cancer. This type of tumour is more likely to be successfully treated with radiation therapy and chemotherapy than the other types of kidney cancer when combined with surgery.
- **Sarcoma** of the kidney is rare. This type of cancer develops in the soft tissue of the kidney, i.e. the thin layer of connective tissue surrounding the kidney, called the capsule; or surrounding fat. This form of kidney cancer is usually treated with surgery. However, sarcoma commonly comes back in the kidney area or spreads to other parts of the body. After the first surgery additional surgery or chemotherapy may be recommended.

Spotlight on kidney cancer

In 2021, it was estimated there would be 935 deaths from kidney cancer (638 males, 297 females) and the five-year survival rate for Australians diagnosed with kidney cancer was 79%, although most people with kidney cancer localised only to the kidney can be cured.

Kidney cancer symptoms

In its early stages, kidney cancer often does not produce any symptoms. Many are diagnosed with the disease when they see a doctor for a different reason.

Symptoms may include:

- blood in the urine (haematuria);
- pain or a dull ache in the side or lower back that is not due to an injury;
- a lump in the abdomen;
- rapid, unexplained weight loss;
- constant tiredness;
- fever not caused by a cold or flu.

If you are experiencing some of these symptoms, please see your doctor.

Causes of kidney cancer

The causes of kidney cancer are not known, but factors that put some people at greater risk include:

- **Obesity** – Excess body fat may alter certain hormones that can lead to kidney cancer.
- **Smoking** – Up to one-third of all kidney cancers are thought to be related to smoking. People who smoke have almost twice the risk of developing kidney cancer as non-smokers.
- **High blood pressure** – Whether it is caused by another medical condition or due to being overweight, high blood pressure increases the risk of kidney cancer.
- **Kidney failure** – People with end-stage kidney disease have an increased risk of developing kidney cancer.
- **Family history** – People who have family members with kidney cancer, especially a sibling, are at a greater risk.
- **Inherited conditions** – About 3–5% of kidney cancers occur in people with particular inherited syndromes, such as von Hippel-Lindau disease, Birt-Hogg-Dubé syndrome, and hereditary papillary RCC.
- **Exposure to toxic substances at work** – After regular exposure to certain chemicals, such as arsenic, cadmium or some metal degreasers, the risk of kidney cancer may be higher.

Treatment options

Treatment will depend on the type of kidney cancer, the stage of the cancer and your general health. The main treatment for kidney cancer is surgery alone or with radiotherapy and will depend on the stage of the cancer. All treatment has benefits and side effects, which need to be discussed with your multidisciplinary cancer care team.

Treatment for kidney cancer is provided by a multidisciplinary team, comprising a urologist, urologic oncologist, medical oncologist and radiation oncologist. This team will regularly meet and discuss the patient's medical history, organise appropriate tests, assess the test results, and together determine the most appropriate treatment care plan.

Clinical trials

One treatment option is taking part in a clinical trial. A trial will help confirm whether novel medicines are safe and effective to introduce as new treatment for more kidney cancer patients. During a trial your health and progress is monitored extremely closely and as a participant in a trial you may also gain access to a treatment option that is not yet available to the wider public.

If you have already had one or more forms of cancer treatment and are looking for a new treatment option, you may be suitable for a clinical trial. Or, if you have just been diagnosed with cancer, the time to think about joining a trial is before you have any treatment.

Read more about kidney cancer trials:
https://anzup.org.au/clinical-trials/kidney-cancer-trials/

Reference:

https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/cancer-summary-data-visualisation

ANZUP is currently running a number of kidney cancer trials. For more details information about these trials, go to the ANZUP kidney cancer trials web page: https://anzup.org.au/clinical-trials/kidney-cancer-trials/

RAMPART

ANZUP 1606

Status: Open & recruiting

Location: Australia & Internationally

Activated sites: 12 (Australian) • **Patients recruited:** 3

Patients required: Australian recruitment target - 200pts (total international recruitment 1750pts)

Removing the kidney (or part of a kidney) by surgery is currently the best treatment if you have kidney cancer. The current standard treatment after surgery is 'active monitoring'. This means no further treatment, but having regular checks so that if the cancer does come back further treatment options can be considered as early as possible.

Surgery, together with ongoing regular follow-up and observation, is the standard approach for people diagnosed with kidney cancer that has required removal of the kidney (or part of a kidney) by surgery. For some people the cancer may return which is when other treatment is offered. We are aiming to find out whether taking one drug (durvalumab) or a combination of two drugs (durvalumab and tremelimumab) can prevent or delay kidney cancer coming back.

For more information, please refer to **https://anzup.org.au/clinical-trial/rampart/**

Current locations for the RAMPART trial:

NSW
- Calvary Mater Newcastle
- Campbelltown Hospital
- Concord Repatriation General Hospital

VIC
- Eastern Health (Box Hill Hospital)
- St Vincent's Hospital Melbourne

QLD
- Mater Cancer Care Centre, Mater Misericordiae Ltd
- Sunshine Coast University Hospital

SA
- Royal Adelaide Hospital

WA
- Fiona Stanley Hospital

Thoughts from a Trial Investigator

There are many health care professionals involved when conducting a clinical trial. A key clinical trials role is the Trial Investigator, the person responsible, individually or as a leader of the clinical trial team at a site, for the conduct of a clinical trial at that site. The Trial Investigator supports responsible clinical trial conduct in their health service organisation, in their field of practice, and is responsible for supervising the clinical trial team.

Dr Laurence Krieger

Over the past ten years, Laurence Krieger (Medical Oncologist and KEYPAD Site PI at GenesisCare) has been involved in just over 120 clinical trials. We asked Laurence a few questions about clinical trials:

My first involvement with clinical trials took place as a junior doctor (Resident) during an oncology term and two studies stick in my mind. The first being the introduction of the chemotherapeutic agent, Irinotecan, for the management of advanced colorectal carcinoma and the second, the assessment of Sunitinib as first line therapy in metastatic clear cell renal carcinoma.

The experience excited me and ignited my interest in clinical trials for many reasons. First, the implementation of putting the science of drug development into clinical practice. Second, the hope of expanding therapeutic options for patients, not only to hopefully improve the outlook, (including cure rates), but quality of life too. Third, being on the forefront of gaining clinical experience with new treatment options to learn and confidently manage potential side effects and how to assess benefit. And finally, the positive experience that comes from engaging with patients on a mutual learning pathway. Patients often participate not only for their own benefit, but for those that will be diagnosed in the future. There is often a grateful positivity (even if a trial does not demonstrate the intended gain), that comes with advancing our understanding in the field so that we can pose the next set of questions that inevitably arise from answering one.

One tip I have learned to make trials work better, is trusting and embracing your study coordinators/ nurses and team!

Dr Michelle Morris

Michelle Morris is a medical oncologist at the Sunshine Coast University Hospital.

Michelle worked as a medical oncologist for Cancer Research UK, Leeds, before returning to Australia in 2005 to take up a consultant position at Nambour General Hospital. Since then, she has consulted at Nambour General Hospital, Gympie Hospital and in private practice on the Sunshine Coast.

She has experience treating a broad range of solid tumour malignancies, with areas of interest including breast cancer, gastrointestinal and urological malignancies. Dr Morris has been active in improving cancer clinical trial access on the Sunshine Coast and promoting quality, multidisciplinary care for her patients.

Her first exposure to clinical trials was when training to become an oncologist in Brisbane. During her fellowship year in Leeds in the UK, her main role was to be responsible for the day to day running of their clinical trials in renal cancer and melanoma. This provided great experience. It was an exciting time with new oral therapies just starting to be trialed in this group of patients - and this definitely helped develop her interest in clinical trial work.

Michelle has now been the site principal investigator on almost 50 clinical trials since commencing work on the Sunshine Coast in 2005. She is proud to have been the lead in building the clinical trial capacity within the regional service and advocating over the years for the importance of clinical trials as part of the core service to their patients. They have expanded from having only conducted a few oncology trials with one trial coordinator, to now consistently having up to 10 trials recruiting at any one time and 5 trial coordinators.

Being a trial coordinator does have it challenges. One such challenge is having time within busy clinics for the additional assessments and documentation which are so important in clinical trials. But working towards consistent systems for all trials is crucial. Although trial systems and approvals are improving, the different processes and systems for each trial can be confusing and time consuming to navigate. However, making trials work better and more efficiently can happen. Michelle believes it is important to choose trials which make you feel excited to be part of.

Successful conduct of a clinical trial relies on the enthusiastic work our investigators all do.

The most common kind of advanced kidney cancer is called clear cell kidney cancer. This trial aims to improve survival rates for people with this cancer.

KEYPAD

ANZUP 1601

Status: Open & recruiting

Location: Australia wide

Activated sites: 15

Patients recruited: 54 • **Patients required:** 70

Renal cell carcinoma (RCC) is the 7th most diagnosed cancer in Australia and the 14th most common cancer in Western populations. Approximately 90% of kidney cancers are renal cell carcinomas (RCC). At the moment the five-year survival rate for Australians diagnosed with kidney cancer is 78.5%, although most people with kidney cancer localised only to the kidney can be cured.

Immune therapies have been shown to be effective in about a quarter of patients with clear cell renal cell carcinoma after the standard treatment (sunitinib or pazopanib) has failed.

This study will test if denosumab, a drug frequently used to treat osteoporosis, (thinning of the bones), can team up with immune therapy to improve survival and increase the chance of the cancer shrinking for people with clear cell kidney cancer.

In the trial, people with advanced clear cell kidney cancer will be offered treatment with two antibodies (a type of protein). This trial will investigate if these drugs taken together can increase the ability of the body's immune system to attack kidney cancer cells.

It is hoped that by combining pembrolizumab with denosumab, will stimulate the immune system, so that the immune therapy will work better in the tumours

ANZUP collaborates with the University of Sydney through the NHMRC CTC to conduct the KEYPAD Trial.

We thank and acknowledge Amgen and MSD for providing product and funding to support our KEYPAD Trial.

We are currently running the KEYPAD trial at the following locations:

NSW
- Calvary Mater Newcastle
- Northern Cancer Institute
- Concord Repatriation General Hospital
- St George Hospital
- Border Medical Oncology Research Unit
- St Vincent's Hospital Sydney

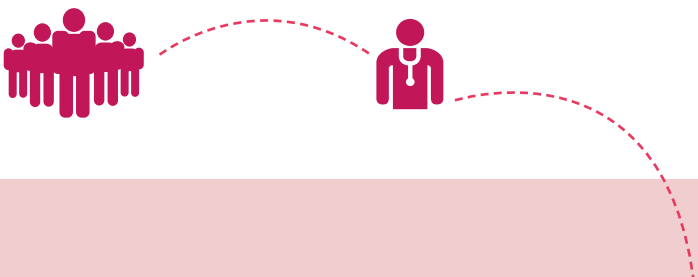
QLD
- Royal Brisbane & Women's Hospital
- Sunshine Coast University Hospital
- Icon Cancer Care
- The Townsville Hospital

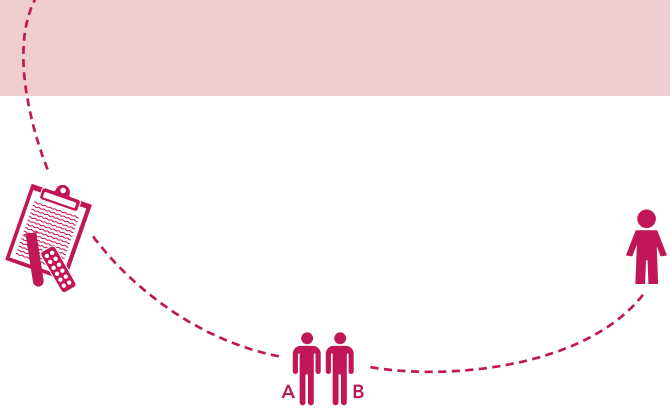
SA
- Flinders Medical Centre

VIC
- Eastern Health
- Monash Health Clayton
- Ballarat Oncology and Haematology Services

WA
- Fiona Stanley Hospital

https://anzup.org.au/clinical-trial/keypad/





UNICAB

ANZUP 1802

Status: Open & recruiting

Location: Australia wide

Activated sites: 11

Patients recruited: 25 • **Patients required:** 48

This study aims to find how safe, tolerable and effective a new treatment called cabozantinib is for non-clear cell kidney cancer.

All patients will take cabozantinib orally every day, until the medication is no longer effective. There is no placebo (inactive treatment), which means that everyone who takes part in the trial will receive the active cabozantinib drug.

Cabozantinib is an anti-cancer drug that works by blocking cancer cell growth. Cabozantinib has previously been used in the treatment of many cancers, including clear cell kidney cancer and thyroid cancer. However, it has not been tested in people with non-clear cell kidney cancer.

Cancer trials can be undertaken in different settings. Depending on the trial, it may occur in a hospital, a clinic or the patient's home.

We are currently running the UNICAB trial at the following locations:

NSW
- Border Medical Oncology
- Calvary Mater, Newcastle
- Campbelltown Hospital
- Macquarie University
- St. George Hospital

QLD
- Royal Brisbane & Women's Hospital

SA
- Adelaide Cancer Centre
- Flinders Medical Centre

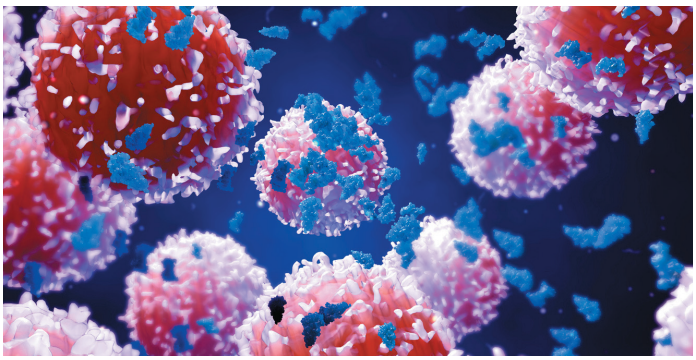
VIC
- Goulburn Valley Hospital, Shepparton (teletrial)
- Eastern Health
- Monash Medical Centre, Clayton

ANZUP collaborates with the Centre for Biostatistics and Clinical Trials (BaCT) to conduct the UNICAB Trial.
We thank and acknowledge Ipsen for providing product and funding to support our UNICAB Trial.

https://anzup.org.au/clinical-trial/unicab/

Spotlight on penile cancer

The penis is the male external genital organ. It is composed of three chambers of spongy tissue that contain smooth muscle and many blood vessels and nerves. The corpora cavernosa makes up two of the chambers located on both sides of the upper part of the penis. The corpus spongiosum is located below the corpora cavernosa and surrounds the urethra. The urethra is the tube through which semen and urine exit the body at an opening called the meatus. At the tip of the penis, the corpora cavernosa expands to form the head of the penis, or glans.

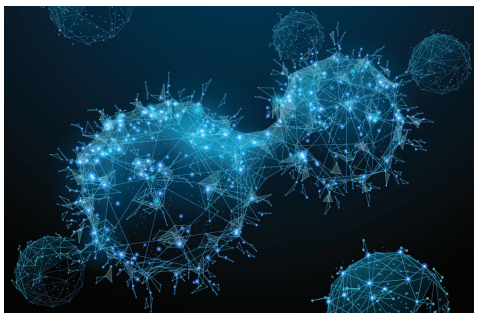


What is penile cancer?

Penile cancer is a rare type of cancer and occurs on the foreskin, on the skin of the penile shaft, or the glans (head) of the penis. It occurs mostly in uncircumcised men (men who still have foreskin around the head of the penis). Circumcision is the removal of the foreskin and may reduce the risk of penile cancer.

The stats*

Penile cancer is rare. In 2021 there were an estimated 155 cases of penile cancer diagnosed and 28 deaths from this disease. In 2013-2017, on average, 75.4% of males diagnosed with penile cancer survived 5 years after diagnosis. In 2021, the estimated age-standardised incidence rate of penile cancer is 1.1 cases per 100,000 males.



Penile cancer symptoms

People with penile cancer may experience a variety of symptoms. Symptoms may include:

- a growth or sore on the head of the penis (the glans), the foreskin or on the shaft of the penis that doesn't heal in a couple of weeks
- bleeding from the penis or under the foreskin
- a hard lump on or under the foreskin
- an odorous discharge under the foreskin
- changes in the colour of the skin on the penis or foreskin
- thickening of the skin on the penis or foreskin that makes it hard to pull back the foreskin
- pain in the shaft or tip of the penis
- swelling at the tip of the penis
- a rash on the penis or a constant red patch of skin that does not resolve
- lumps in the groin due to swollen lymph nodes.

155 men

Were estimated to be affected by penile cancer **in Australia in 2021.**

Reference

*https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/summary

Spotlight on penile cancer

Causes of penile cancer

The cause of penile cancer is not known in most cases. However, there are several risk factors.

Infection with human papilloma virus is a risk factor for cancer of the penis. Some other conditions that affect the appearance of the skin of the penis can lead to cancer, so it's important to see your doctor if you notice white, red or scaly patches.

Other risk factors for penile cancer include:

- not being circumcised
- smoking tobacco
- increasing age
- certain skin conditions such as psoriasis
- HIV/AIDS
- premalignant lesions/conditions
- exposure to ultraviolet (UV) radiation.

Who treats penile cancer?

Based on your treatment options, you might have different doctors of various specialties on your treatment team. For penile cancer, the multidisciplinary team often includes a surgeon, a doctor called a urologist who specialises in urinary tract problems, a medical oncologist, and a radiation oncologist. Your healthcare team may also include a variety of other health care professionals, oncology nurses, social workers, pharmacists, counsellors and psychologists, dietitians, and others.

How is penile cancer treated?

Surgery is the main treatment for most men with penile cancers, but sometimes radiation therapy may be used, either instead of or in addition to surgery. Other local treatments might also be used for early-stage cancer. Chemotherapy may be given for some larger tumours or if the cancer has spread.

As well as medical treatment for penile cancer it is also important to adjust to living with the diagnosis. A specialist nurse, psychologist, social worker, a GP and support groups can all help and provide ways of coping.

Thinking about taking part in a clinical trial

Progress in treating penile cancer has been hindered by its rarity so it is difficult to recruit enough patients to penile cancer clinical trials.

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to receive state-of-the art cancer treatment, management and care that is not yet available to the wider public. Clinical trials are also the best way for a multidisciplinary team to learn better methods to treat this rare form of cancer.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor or contact ANZUP.

Although penile cancer is a relatively rare disease, its consequences can have profound effects for the men who experience it.

Evidence supports the view that factors such as embarrassment, fear, the potential impact on sexuality and a cancer in a sexual organ all impact on patients' seeking help, resulting in a delay in going to a healthcare professional. See your doctor early and ensure you talk about treatment and the effects on sexual health and fertility.

Penile cancer survivorship

Penile cancer falls within the rare cancer category. Due to the low number of people with rare cancers, the amount of research and clinical trials on these disease types are drastically less than those with common cancers.

With less research, we have less information about these cancers and less community awareness, therefore diagnosis remains slow and treatment availability is limited. All of this adds to the increased mortality rates for rare cancers.

Along with these challenges, non-Indigenous Australians, Aboriginal and Torres Strait Islander people are disadvantaged across an array of health and socioeconomic factors. This includes information and literature on survivorship amongst rural patients and Aboriginal and Torres Strait Islander People, which presents a priority for researchers.

Cancer in Aboriginal and Torres Strait Islander people of Australia

An average of **1,279** new cases of cancer a year in Indigenous Australians in 2009-2013

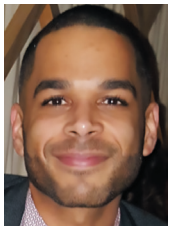
5 year relative survival from cancer was **50%** in Indigenous Australians in 2007-2014

3,626 Indigenous Australians alive at the end of 2013 who had been diagnosed with cancer

An average of **551 deaths** a year from cancer in Indigenous Australians in 2011-2015

https://www.aihw.gov.au/reports/cancer/cancer-in-indigenous-australians/contents/table-of-contents

Penile cancer survivorship in Western Australia amongst rural patients and Aboriginal and Torres Strait Islander people



DR. SIMEON NGWESO

Survivorship of many cancer types in the Aboriginal and Torres Strait Islander People, such as breast, prostate, colorectal, and lung cancer, is known. However, penile cancer survivorship amongst rural patients in Australia and Aboriginal and Torres Strait Islander People has not been published within the literature.

Dr. Simeon Ngweso recently undertook a study to review survivorship of penile cancer patients in Western Australia who were Aboriginal or Torres Strait Islander, or patients who were from rural communities, by performing a comprehensive, retrospective review of prospectively recorded penile cancer cases within the Western Australia Cancer Registry.

The research

Penile cancer is a very rare cancer and accounts for less than 1% of all cancers in males. A retrospective review of prospectively recorded penile cancer cases within the Western Australia Cancer Registry, between 1992 and 2017, was undertaken. The review found 186 cases of invasive penile cancer were recorded. Of this group, 62 patients (33.3%) were from rural WA, nine patients (4.8%) were Aboriginal, and five Aboriginal patients and 13 rural patients died from penile cancer. This review demonstrated that penile cancer patients from WA who were Aboriginal, or from rural WA, were at a greatly increased risk of death due to penile cancer.

Conclusion and next steps

Moving forward, more research is needed to understand disease characteristics amongst these vulnerable populations. Also, joint efforts amongst key stakeholders are necessary to address health discrepancies and improve outcomes. It is the responsibility of all health service organisations to consider and action their part in closing the gap in health inequalities experienced by Aboriginal and Torres Strait Islander people.

Trials in follow up

Once a clinical trial is finished, researchers scrutinise all the information collected during the course of the study. Reviewing all the data allows researchers to decide whether the results mean the new drug or device should continue to the next phase of clinical trial, or, when applicable, seek approval for broader use by the appropriate authorities. Once a new drug or device has been proven to be effective and safe, it may become part of standard treatment for the condition or disease.

Review and analysis of the information can take an extended period of time. So there may be a delay before the results of a clinical trial are known. This is definitely the case with larger trials that can involve thousands of people from many hospitals both in Australia and overseas. In large multi-centre trials, the examination of the data and outcomes may take place over several years.

If you have taken part in a trial and specified you wish to know the overall results of the trial, the researchers should make them available to you directly. Usually results of all completed studies will also be made available in papers or reports published in scientific journals.

ANZUP now has nine trials in follow-up across four of the below the belt cancer types – bladder, testicular, prostate and kidney cancer.

ANZUP Trials

1. ENZAMET – Prostate Cancer ANZUP 1304

Enzalutamide is a new hormone treatment taken as tablets. Previous trials have proven that enzalutamide improves survival and quality of life in men with prostate cancer that has stopped responding to standard hormone treatments and chemotherapy.

This large, international randomised trial was undertaken to determine if treatment with enzalutamide can improve survival and quality of life in men starting hormone treatment for newly diagnosed prostate cancer that has spread beyond the prostate. The trial was led from Australia by ANZUP in collaboration with the NHMRC Clinical Trials Centre. It involved 1,125 men from Australia, New Zealand, Canada, the US, Ireland, and the UK.

In 2020 the ENZAMET trial won all three of the Australian Clinical Trials Alliance (ACTA) Awards. The ENZAMET trial was awarded the 2020 ACTA Trial of the Year Award, the ACTA STInG Award for Excellence in Trial Statistics and the Consumer Involvement Award.

This landmark Australian led clinical trial, ENZAMET, has now shown that hormone therapy with a drug called enzalutamide can improve the survival of some men with advanced, hormone-sensitive prostate cancer.

Findings from the ENZAMET trial, led by ANZUP, have shown that men with this sort of cancer who receive enzalutamide with standard treatment have a 33% improvement in survival compared to men receiving standard treatment alone and a 60% improvement in the time it takes to detect the cancer growing again. These results were much better than it was thought they might be when the trial began.

The ANZUP investigator initiated studies were financially supported by Astellas, who also provided enzalutamide.

2. ENZARAD – Prostate Cancer ANZUP 1303

ENZARAD is a randomised phase 3 trial of enzalutamide in androgen deprivation therapy with radiation therapy for high risk, clinically localised, prostate cancer.

Enzalutamide is a new hormone treatment taken as tablets. Previous trials have proven that enzalutamide improves survival and quality of life in men with prostate cancer that has stopped responding to standard hormone treatments and chemotherapy. This large, international randomised trial will determine if treatment with enzalutamide can improve survival and quality of life in men starting radiation and hormone therapy for prostate cancer that does not seem to have spread beyond the prostate.

The trial has been led from Australia by ANZUP in collaboration with the NHMRC Clinical Trials Centre. The trial accrued 802 men from 69 sites across Australia, New Zealand, Canada, the US, Ireland, and the UK. Recruitment closed on 30th June 2018.

The ANZUP investigator initiated studies were financially supported by Astellas, who also provided enzalutamide.

3. TheraP – Prostate Cancer ANZUP 1603

Lutetium-177 PSMA radionuclide therapy (Lu-PSMA) is a new treatment for advanced prostate cancer. Lu-PSMA is a radioactive molecule that specifically attaches to cells with high amounts of PSMA on the surface of the cells. This allows the radioactivity to be delivered mainly to the prostate cancer cells wherever they have spread, while sparing most normal tissues. Previous small studies of Lu-PSMA showed promising activity in patients with advanced prostate cancer.

This randomised study has compared Lu-PSMA, with a type of chemotherapy called cabazitaxel, which is the standard treatment for advanced prostate cancer when other treatments have stopped working. Half the participants received Lu-PSMA and half received cabazitaxel. This trial enrolled 200 participants in Australia.

ANZUP was able to report interim results of the TheraP clinical trial at the American Society of Clinical Oncology (ASCO) Annual Scientific Virtual Meeting on Friday 29 May 2020.

A favourable response, defined by reduction of PSA by 50% or more, occurred in 66% of men assigned to receive Lu-PSMA compared to 37% with cabazitaxel. Results of the trial also demonstrated the treatment had less severe side effects than chemotherapy.

Patient follow-up is ongoing with initial results suggesting the new treatment may delay progression of prostate cancer.

TheraP is a partnership between ANZUP Cancer Trials Group and the Prostate Cancer Foundation of Australia (PCFA) with support from the Australian Nuclear Science and Technology Organisation (ANSTO), Endocyte, It's a Bloke Thing, Movember and CAN4CANCER.

4. PCR-MIB - Prostate Cancer ANZUP 1502

Opened in mid-2016, this trial is aimed at managing bladder cancer that has spread into the wall of the bladder. A combination of chemotherapy and radiotherapy is the current standard treatment.

This study aims to assess if it is safe and effective to add an additional new drug called pembrolizumab to the standard therapy of chemotherapy and radiation therapy.

Pembrolizumab is a new treatment that "takes the brakes off" the immune system, allowing it to attack cancers more effectively. Studies of pembrolizumab in widespread bladder cancer have shown benefit, with cancer shrinkage observed in about two thirds of people, and in some cases long periods of disease control. At present, pembrolizumab, is approved for use in Australia for the treatment of advanced melanoma in adults.

5. UNISoN – Kidney Cancer ANZUP 1602

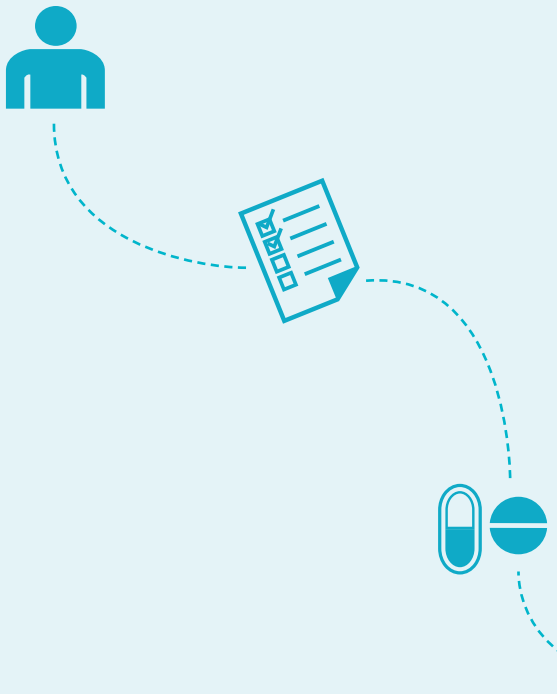
In this clinical trial ANZUP will test whether new immune treatments can help people with rare kidney cancer ('non-clear cell' cancer).

Non-clear cell kidney cancer represents approximately 25% of people with kidney cancer; and because it is rare there are no treatments currently reimbursed in Australia.

The UNISoN trial is now closed to recruitment and is in follow up. This trial is investigating immune treatments in two different ways; firstly the trial is investigating how well one immune treatment (nivolumab) works alone. If this is unhelpful by itself, then people can continue taking nivolumab but also add in a 2nd immune treatment (ipilimumab). The trial will also discover how many people will benefit from one drug alone, and by doing detailed laboratory testing of people's cancer samples, we hope to also learn who will only benefit from taking both treatments together.

Nivolumab and ipilimumab have been used alone or together in many cancers, so the side-effects are well known and should be manageable. Immune treatments help some people with cancer, especially those with melanoma, common (clear cell) kidney cancer, lung and bladder cancer. Unfortunately they are much less effective in other cancers (like pancreas, prostate and brain cancers). Nivolumab and ipilimumab have not been tested in people with non-clear cell kidney cancers, so ANZUP is delighted to ask this question, and hopes to help people with this rare disease.

We thank and acknowledge BMS for providing the study drug and funding to conduct the UNISoN trial.



Co-badged Trials

6. proPSMA – Prostate Cancer

Prostate cancer is the most commonly diagnosed cancer in Australian men. If detected early, when disease has not spread, there is a high chance of cure. Relapse, however, is not uncommon despite careful selection of patients prior to surgery or radiotherapy. This, in part, reflects a failure to detect disease spread at baseline due to limited accuracy of current scanning techniques. More accurate scanning may improve outcomes by redirecting patients with disease spread from unsuccessful local treatments to more appropriate management.

This clinical trial will investigate a new type of scan which provides whole body images of prostate cancer spread. Early experience suggests that this new technology, called PSMA PET/CT (prostate specific membrane antigen positron emission tomography/computed tomography), is superior to current scanning techniques. PSMA PET/CT has capacity for wide availability at relatively low cost. Performing a single better test rather than several less accurate scans will also be cheaper, improve patient experience and expose patients to lower amounts of radiation.

This is a randomised study at multiple centres around Australia comparing PSMA-PET/CT to conventional imaging. If the initial work-up does not demonstrate tumour spread, patients will cross-over to the other imaging arm. We hope to prove that PSMA-PET/CT has superior diagnostic performance, should be used as a first-line test for staging prior to surgery or radiotherapy and will result in significant changes to patient management. Results of this trial will be used to support funding of this new technology in Australia and internationally.

The trial has now closed to recruitment and enrolled 300 participants in Australia.

7. FASTRACK II – Kidney Cancer

Surgery is the standard treatment for primary kidney cancer. However, in some cases, surgery is either not possible or other health problems make surgery high risk. This study involves a relatively new, highly precise multidirectional radiotherapy technique called Stereotactic Ablative Body Radiotherapy (SABR) which will be applied to all participants.

The aim of the study is to test the ability of the technique to control cancer within the kidney for those people for whom surgery is not an option, and to examine the side effects of the treatment, including how it may affect your kidney's function.

This study is led by TROG and co-badged by ANZUP Cancer Trials Group and is now closed to recruitment and is in follow up.

8. NMIBC-SI - Bladder Cancer

Non-muscle invasive bladder cancer (NMIBC) makes up approximately 70-80% of all bladder cancer diagnoses. NMIBC is bladder cancer that has not yet invaded through the wall of the bladder. Treatment is generally intended to reduce the risk of the bladder cancer recurring or progressing to muscle invasive disease. Treatment involves endoscopic resection to the bladder tumours followed by potential intravesical chemotherapy or immunotherapy.

Although treatments can significantly reduce the risk of recurrence and progression, there are both benefits and harms that are likely to vary between treatment options. However, little is known about the impact of these treatments on patients' quality of life.

Phase I of the project involved qualitative research to develop a draft Non-Muscle Invasive

Bladder Cancer Symptom Index (NMIBC-SI).
The second phase of the project aims to evaluate the psychometric properties of the NMIBC-SI.
This was conducted across two field tests:

- Field Test 1 was a cross-sectional study design asking participants to complete the draft NMIBC-SI questionnaire either on paper or lectronically. The purpose of Field Test 1 is to produce a shorter version of the NMIBC-SI by eliminating items with poor psychometric properties.
- Field Test 2 used a prospective longitudinal study design to evaluate the clinical validity of the final version of the NMIBC-SI. Participants were asked to complete the NMIBC-SI along with comparative questionnaires at different time-points during their treatment. The purpose of Field Test 2 is to assess the reliability, validity and responsiveness of the final version of the NMIBC-SI to ensure it is fit for purpose in clinical research.

ANZUP was running this trial in collaboration with Cancer Australia and Cancer Council NSW. This study is being sponsored by the University of Sydney.

This study was funded by Cancer Australia and Cancer Council NSW. It was sponsored by USYD and co-badged with ANZUP.

For more information on our trials in follow up go to our website https://anzup.org.au/clinical-trials/follow-up/

ANZUP's 2021 Below the Belt Research Fund Recipients

ANZUP brings together a leading multi-disciplinary network of oncology, surgical, medical, radiation, nursing, psychology and allied health professionals from within the urogenital cancer field to conduct vital research through clinical trials.

Clinical trials are essential for discovering new treatments for diseases, as well as new ways to detect, diagnose, and reduce the chance of developing the disease. Clinical trials can show researchers what does and doesn't work in humans that cannot be learned in animals or in the laboratory, and at the same time test for any potential side effects.

Clinical trials are expensive, often costing millions of dollars. ANZUP receives some funding from the Australian Government, and this provides useful support but comes nowhere near covering our basic costs. And importantly, government infrastructure support funds cannot be used to run clinical trials. Every clinical trial we do needs to have its own funding. This is why ANZUP has fundraising events.

Some of our fundraising goes to support researchers who do not have other means to support their research. And other funds raised through the Below the Belt events supports ideas that are not yet fully fledged clinical trials but might evolve into them. This is one way we continue to grow ideas for future work.

The Below the Belt Research Fund has supported many members in the development of investigator-initiated studies. This year, it has provided much needed seed funding to support four ANZUP members to progress new trial ideas to the point of becoming full scale studies. We would like to congratulate the recipients and following you can read about three of these studies.

DR CIARA CONDUIT,
MEDICAL ONCOLOGIST,
PETER MACCALLUM
CANCER CENTRE

Ciara Conduit:

Exploring the activity of pseudoephedrine in treating retrograde ejaculation following retroperitoneal lymph node dissection in survivors of testicular cancer (PREPARE)

Testicular cancer (TC) is one of the most common cancers diagnosed in young men in Australia. While most men can expect a positive outcome, treatment can result in long-term side effects.

Sometimes after retroperitoneal lymph node dissection (RPLND; surgery involving the lymph nodes at the back of the abdomen), important nerves controlling ejaculation can become disrupted. This results in retrograde ejaculation (RE), where sperm flows back into the bladder instead of through the penis after orgasm. It is sometimes called a dry orgasm. Although RE is not harmful or painful, it may affect sensation during orgasm and result in infertility (difficulty conceiving a pregnancy). While RE may resolve spontaneously in some men, it becomes a chronic problem for others and existing treatments are not standardised, nor always helpful or successful.

We plan to conduct a pilot study exploring the effectiveness of an oral medication, pseudoephedrine (an ingredient in 'Cold and Flu' tablets), to improve RE following RPLND. As pseudoephedrine causes tightening of the bladder muscle, it prevents sperm flowing back into the bladder and thus helps sperm move through the penis. It is therefore a potentially effective treatment for RE. Whilst some studies in men with RE due to other causes have shown pseudoephedrine may be helpful, it is not known how effective this approach is for men with RE after RPLND.

We are currently undertaking a study to help understand how common RE is after RPLND, and how it affects men's health-related quality of life (HRQoL). To follow up, we would like to recruit men with RE following RPLND and explore the effectiveness of pseudoephedrine as a treatment and improve our understanding of the impacts that RE has on HRQoL for survivors of TC.

DR MEGAN CRUMBAKER,
ST. VINCENT'S HOSPITAL SYDNEY

Megan Crumbaker:

A Phase II study of high dose testosterone in combination with carboplatin in men with metastatic castrate-resistant prostate cancer

Prostate cancer that has spread beyond the prostate and its nearby areas is usually incurable and targeted with treatment that lowers testosterone, called ADT. ADT is associated with several side effects, including some that worsen over time on treatment. Though effective initially, prostate cancers generally become resistant to ADT eventually. This resistance allows the cancer to grow, causing symptoms, such as pain, and shortened lifespan.

Research shows that prostate cancer cells in the lab can adapt to ADT in ways that make them vulnerable to attack from high testosterone levels. Recent prostate cancer trials used pulses of testosterone in men with ADT-resistant cancer to try to shrink the cancer and improve men's overall wellbeing. The research found that the treatment is safe, associated with improved quality of life and has anti-cancer effects. Based on this research and other research into the effect of testosterone on resistant prostate cancer cells, we hypothesise that adding a particular chemotherapy drug, carboplatin, will enhance the effectiveness of testosterone treatment without compromising quality of life.

We have treated 9 men with the combination of testosterone and carboplatin. Many of the patients on this pilot study report feeling much better due to an increase in their testosterone levels. The treatment has also stopped the growth of some men's cancer. We would like to use funding from this grant to expand the study to other cancer centres to improve access to this novel treatment, assess the effectiveness of the treatment, and determine whether a larger trial comparing it against other prostate cancer treatments would be worthwhile.

DR JOSHUA KEALEY,
MASTER OF SURGERY,
MONASH UNIVERSITY,
UROLOGY REGISTRAR

Joshua Kealey:

ACCEPT-U – Australian Multicentre Prospective Registry to Evaluate Practice and Patient Outcomes in Upper Tract Urothelial Carcinoma

Upper tract urothelial carcinoma (UTUC) is a rare cancer of the lining of the kidneys and ureter. Whilst UTUC is similar to bladder cancer it is often more advanced at diagnosis, more challenging to treat and more likely to cause death. Diagnosis requires a combination of laboratory tests, imaging and endoscopic procedures. Treatments are based on cancer stage and presence of metastasis. Treatment ranges from surgical removal of the kidney and ureter, for those in whom cure is attainable, to palliative treatments where cure is not possible.

Due to the small number of people diagnosed with UTUC it is challenging to study individual treatments and outcomes in large trials. Often patients diagnosed with UTUC have multiple medical comorbidities and are excluded from trials, which makes results difficult to extrapolate to these groups. Whilst some data is collected in generic government cancer registries it is too limited to be of specific clinical use. There is also little known about the compliance with international guidelines to ensure that Australian patients are receiving the highest level of care regarding their UTUC.

We propose an Australian UTUC registry to assess the patterns of care in Australia. We aim to enrol patients after their diagnosis of UTUC. The ways in which patients present, undergo investigation, treatment and follow-up will be recorded and analysed. By analysing the complete journey of patients diagnosed with UTUC we aim to identify areas of improvement and provide feedback to clinicians to ensure the best possible outcomes. A comparison of individual treatments and their outcomes will also aim to provide some clarity around treatment decisions. We will combine this database with the previously created bladder cancer cystectomy database (ACCEPT) to ensure that all urothelial cancers are covered by this multicentre registry.

Below the Belt Pedalthon
RIDING FOR UROGENITAL CANCERS

SUPPORTING ANZUP
Cancer Trials Group Limited

REGISTER TODAY!

FIGHT CANCER BELOW THE BELT

Ride or support and help fight prostate, testicular, bladder, penile and kidney cancer

FRIDAY 9 SEPTEMBER 2022
SYDNEY MOTORSPORT PARK

LIKE CYCLING?

We're back and ready for you, your colleagues and networks to take on the ultimate team challenge.

Join the fight and ride with us in September at the iconic Sydney Motorsport Park. The date will be released soon, so stay tuned.

The Sydney Pedalthon is a cycling event for all riders – the keen cyclist, the novice or those looking for a new sporting challenge. Teams of up to six take on the task of riding as many laps as possible within 3 hours and with a sprint challenge for the speed demons in the final hour.

DON'T LIKE CANCER?

A diagnosis of cancer can turn a life upside down particularly when the best treatment is not known. The Pedalthon was founded to raise awareness of below the belt cancers and provide ANZUP with the critical funds to improve the lives of more than 27,000 people diagnosed in Australia event year.

Clinical trials help us move research forward to develop the next step in treatment while giving patients the very best possible care.

Every cent raised by the Pedalthon goes directly towards clinical trial research, which means straight into the hands of experts committed to treating prostate, bladder, kidney, penile and testicular cancer better.

We need your help to find more trials and make a difference.

"Every dollar raised through the Below the Belt Pedalthon for the Below the Belt Research Fund goes back to support research. Do you know of many other charities with 100% investment of fundraising back into their cause?"

ANZUP Chair,
Professor Ian Davis

"[This] event gets bigger and better and I am looking forward to cheering on everyone as they roll around Eastern Creek raceway raising money for a great cause! I look forward to seeing familiar and also welcoming new faces out there!"

Kaarle McCulloch, Pedalthon Ambassador, World Champion Track Cyclist and Olympian.

For more information go to **www.belowthebelt.org.au** or email **belowthebelt@anzup.org.au**

How can you get involved?

Support comes in all shapes and sizes.

Whatever you are interested in doing to support ANZUP, let us know and we will help support you on the journey.

Participate in a fitness challenge – Get involved with a fun run, triathlon, walkathon - the options are endless! – and represent ANZUP.

Sponsor a fundraiser – Donate to a friend or family member participating in a sports festival.

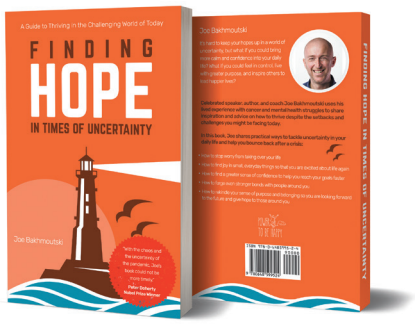
Hold an event – Be it a morning tea, a raffle, a barbie, trivia night, or book club, we can support you to run your own fundraising event.

Donate In Memoriam – Honour your loved one with a contribution in their name or asking for donations in lieu of funeral flowers.

Give in Lieu of a Gift – Donate towards a special occasion in lieu of a traditional gift. For example, a wedding, birthday or retirement celebration. If it is your special occasion, why not ask for donations instead.

Provide in-kind support – In-kind donations include providing the budget for a specific staff member, meeting room use, auctionable goods for fundraising, advertising and creative support, and can help us deliver more interesting and educational information.

Community fundraising



Purchase a book and support below the belt cancer research

It's hard to keep your hopes up in a world of uncertainty, but what if you could bring calmness and confidence into your daily life? In 'Finding Hope in Times of Uncertainty: A Guide to Thriving in the Challenging World of Today', Joe Bakhmoutski, author, podcaster and testicular cancer survivor, is a proud and passionate supporter of ANZUP.

Joe Bakhmoutski is the host of the Simplify Cancer Podcast where he interviews oncology experts and cancer survivors to share insights and inspiration to live a better life beyond cancer. After going through testicular cancer three years ago, Joe made it his mission to help others feel more calm, confident and in control of their lives. He is a proud and passionate supporter of ANZUP's research work and is donating $5 dollars from each copy of his latest book "Finding Hope in Times of Uncertainty:

In his book he shares practical ways to tackle uncertainty in your daily life and help you bounce back after a crisis. Order your book today at **https://www.belowthebelt.org.au/support-us/findinghope**

Finding the Comedy in Cancer Podcast – Living with Testicular Cancer

On Joe Bakhmoutski's Simplify Cancer Podcast, he talks candidly to ANZUP ambassador, comedian, and testicular cancer survivor Michael Shafar about living with testicular cancer, why they both support ANZUP and the importance of clinical trials. Have a listen and a laugh about a very serious subject – testicular cancer. Episode 079: Finding the Comedy in Cancer - Simplify Cancer.

Host Your Own Fundraiser and Help us Fight Cancer, Below the Belt

Run, ride, go without your daily coffee, host a garage sale, or bake your heart out. The sky is the limit when it comes to Hosting Your Own fundraiser.

No matter where you are across Australia or New Zealand, or around the world, you can use your skills and interests to get involved and help us fight below the belt cancers.

So far, through our Below the Belt events we have raised over $1.95 million and funded 32 new cancer research projects. Get involved today and help us support more projects to improve the lives and outcomes of those living with below the belt cancers.

Every fundraiser, no matter how big or small, makes a difference

It's easy to create a 'host your own' fundraiser and make a difference.

Organise an event

Bring together family, friends and colleagues and host a lunch or night out. Whether it is a corporate golf day, dress down day, trivia night, comedy performance, dinner, or a high tea, we will be there every step of the way to make sure your event is as fun, raises funds and is memorable as ever.

Honour a loved one

Remember a loved one with an in-memoriam gift. Organise a group collection in lieu of flowers or give a one-off personal donation. Each gift in memory of your loved one will help future cancer research.

Donations instead of a gift

Do you have a birthday or wedding coming up? Ask your friends and family to support ANZUP cancer trials research with a gift that keeps on giving. Every gift funds more research to improve treatments and outcomes for people living with a below the belt cancer.

To organise your next fundraising event, go to www.belowthebelt.org.au/hostyourown

A thank you

The Hillcrest Foundation supports ANZUP's Kidney Cancer project

ANZUP would like to thank and acknowledge the Hillcrest Foundation who provided much needed funding to continue important scientific research on the blood and tissue samples collected as part of ANZUP's kidney cancer UNISoN Trial. ANZUP will now be able to further investigate tumour tissue and blood samples, generously donated by patients who participated on the trial, to help us find better treatments for those with kidney cancer in the future. This funding was made possible through Perpetual's IMPACT Philanthropy Application Program.

UNISON STUDY CHAIR, ASSOCIATE PROFESSOR CRAIG GEDYE

Don't forget this May you can get involved in Below the Belt #YourWay

To find out more view the back cover or visit **www.belowthebelt.org.au/yourway**

Thanks to our Partners, Corporate and In-kind Supporters

Corporate Supporters

We are very fortunate to have our corporate supporters and partners who enable ANZUP to better support our members and ultimately, patients and their families. Our 2022 corporate supporters include:

Astellas, AstraZeneca, Bayer, Bristol Myers Squibb, Ipsen, Janssen,Pfizer Oncology.

In-Kind Supporters

We acknowledge and thank the following organisations for the generosity they have shown by providing their services pro-bono.

AFI Branding, The Saturday Paper and FC Lawyers.

Below the Belt

SUPPORTING ANZUP CANCER TRIALS

Fight Cancer Below the Belt

Join us in the fight to improve the treatments and outcomes of those with below the belt cancers

Host your own

Bring together your family, friends and colleagues and host a fun day or night out, or any other event.

#Yourway 1-31 May 2022

Set yourself a challenge and sweat it out for below the belt cancers.

Pedalthon

Ride to fight cancer.
Sydney: Friday 9 September

www.belowthebelt.org.au

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