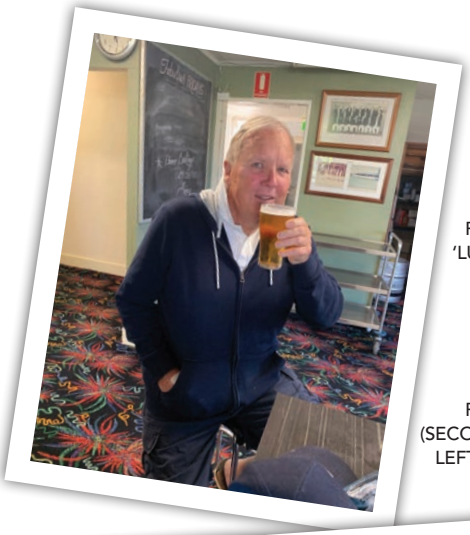
A clinical trial and a lucky life

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.