ANZUP Clinical Trials

By Kalli Spencer

The Australian and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group was formed in 2008, and is comprised of a multidisciplinary team of doctors, nurses, allied health care professionals, scientists, researchers, and community representatives, all working in areas related to urogenital cancer. Their aim is to improve outcomes for people affected by these cancers by exploring and defining priority areas in below the belt cancer research. They investigate which data deserves attention, which treatments hold promise for the future, which drugs should be tested in clinical trials and most importantly, they try to understand the main areas of concern of patients. In this week's blog we will feature some of ANZUP's clinical trials which are currently in the recruitment phase.

- **DASL-HiCaP** (Darolutamide Augments Standard Therapy for Localised Very High-Risk Cancer of the Prostate)

Darolutamide is a tablet that blocks the effects of testosterone. Testosterone is responsible for prostate cancer growth and spread. The purpose of this study is to see if 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. This is a randomised controlled trial, which means that, in addition to best standard treatments, half the participants on the study will receive darolutamide, and the other half will receive placebo. The trial is being led from Australia and the plan is to enrol 1,100 men from Australia, New Zealand, Canada, the US, Ireland, and the UK. Eligibility criteria include men aged 18 years or older with either very high-risk localised prostate cancer planned for primary radiation therapy, or very high-risk features with PSA that remains persistently raised or rises within one year following radical prostatectomy and suitable for radiation therapy.

- **ENZA-p** (Enzalutamide with Lu PSMA-617)

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 [CRPC]). 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 and 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 ENZAp 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. The trial team plans to enrol 160 participants across Australia. Eligibility criteria include men with metastatic CRPC (mCRPC) not previously treated with docetaxel for castration-resistant disease, suitable for treatment with enzalutamide and Lu-PSMA. Acceptance into the trial will be assessed based on a screening GaPSMA PET and FDG PET scan.

- **GUIDE**

The purpose of this study is to see if a prostate cancer marker in the blood (mGSTP1) can be used to guide docetaxel 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. The study team believe results will tell them if having these treatment breaks guided by mGSTP1 can improve how men feel during treatment while still treating the prostate cancer effectively. The target population is men with mCRPC receiving docetaxel chemotherapy, with a detectable mGSTP1 at baseline. (This is 80% of all men starting treatment with docetaxel for mCRPC)

- **NINJA** (Novel Integration of New prostate radiation therapy schedules with adjuvant Androgen deprivation)

This trial aims to compare two emerging schedules of radiotherapy in the treatment of unfavourable intermediate or high-risk prostate cancer with no evidence of metastatic disease. Participants will be randomly assigned to one of two radiotherapy schedules. In schedule 1 (called Stereotactic Body Radiotherapy – see previous blog for more details) 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. Trial participants will also receive at least 6 months of androgen deprivation treatment (testosterone blocking tablets). It is hoped this research will potentially improve the accuracy and quality of radiotherapy treatment in prostate cancer.

- **UpFrontPSMA**

PSMA on prostate cancer cells can be targeted with Lutetium-177 PSMA (Lu-PSMA) and kill 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 has shown to be effective in some patients with metastatic prostate cancer. The emitted radiation only travels about 1mm, which means it mainly causes the killing 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 results for Lu-PSMA used to treat 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 destroying cancer cells and potential cure.

Some of the benefits of being involved in a clinical trial include access to a new treatment before its available to others; becoming more active in one's treatment journey; more frequent health check-ups and medical care; helping others get better treatment in the future; and access to information, resources, and support groups. Health care providers should inform all eligible patients about these trials and patients have a choice after hearing all the facts whether to enrol into the trial or not. Clinical trials are essential for the discovery of ground-breaking treatments which will continue to save countless numbers of lives.

About the Author

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Kalli is an internationally renowned Urological Surgeon, specialising in oncology and robotic surgery. He trained and worked in South Africa, before relocating to Australia where he has worked at Macquarie University Hospital and Westmead Hospital. His passion for what he does extends beyond the operating room, through publichealth advocacy, education and community awareness of men's health, cancer and sexuality.

Kalli has been involved with the Prostate Cancer Foundation of Australia for many years, advocating for improved cancer care and facilitating community prostate cancer support groups.