ANZUP Cancer Trials Group Limited

ANZadapt (ANZUP 2101) Trial News

www.anzup.org.au

Welcome!

Thanks for your participation in ANZadapt. A big thank you to all sites and investigators for your continued support and hard work towards this exciting study.
We have recruited our first 29 patients onto the trial.

With Box Hill Hospital - Eastern Health (VIC) and ICON Cancer Centre (ADE) coming on board, we have a total of 11 sites open to recruitment.
We have one site to open, St George Hospital in Sydney.

Study Team Introduction

Study Chair: A/Prof Craig Gedye
Deputy Chair: Dr Laurence Krieger

ANZUP Team (study sponsor):
Chair: Prof Ian Davis
CEO: A/Prof Samantha Oakes
Project Manager: Archana Nair

HMRI Team (trial coordination):
Head of Clinical Trial Operations: Naomi Knoblauch
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"Thanks everyone for being part of the r-evolution in this long-overdue study! Farmers and veterinarians have been applying the principles of 'integrated pest management' and 'treatment refugia' for decades to maintain and extend the effectiveness of herbicides and pesticides, it's fantastic to finally be proving the survival benefit of evolutionary therapy in cancer treatment!"

STUDY CHAIR A/Prof Craig Gedye

Recruitment summary (to 21 June 2024)

Site	Screened	Randomised
Calvary Mater Newcastle	8	6
GenesisCare North Shore	7	5
Chris O'Brien Lifehouse	2	1
Mater Cancer Care Centre	10	5
Border Medical Oncology	5	4
Royal Adelaide Hospital	3	2
ICON Cancer Centre	1	1
Sydney Adventist Hospital	2	2
Fiona Stanley Hospital	3	3
Total:	**41**	**29**

STUDY DEPUTY CHAIR
Dr Laurence Krieger

WHAT'S NEW?

Protocol v1.3 (dated 26 April 2024) has been approved by the lead Human Research Ethics Committee. Sites are in the process of seeking RGO approval for implementation of the protocol amendment; currently, all but one site has received RGO approval. A number of useful changes have been implemented.

1. More flexible PSA threshold for inclusion

After your feedback from the Trial Management Committee held on 13 December 2023, inclusion criteria No.7 has now been updated to "a PSA concentration of ≥ 2ng/mL" better reflecting routine clinical practice in Australia. This will assist what many sites reported as a recruitment barrier where a PSA concentration of ≥ 10ng/mL was needed.

2. 'Resetting' the PSA baseline

For participants on the adaptive treatment arm, clinical or radiological progression may occur while the patient is on a treatment pause This may occur when the PSA level remains below the pre-treatment baseline. In this unusual situation, the team has agreed that the participant should be assigned a 'new' PSA baseline, the e PSA level at the time of restarting the treatment due to clinical or radiological progression.

3. Drugs to Use with Caution

We've updated this section to be simpler and match eviQ guidance for each drug.

Reminders:

- Enzalutamide is a CYP3A4 inducer, and case reports suggest fentanyl and oxycodone are hyper-metabolised and potentially ineffective.
- Spironolactone may reduce the efficacy of abiraterone resulting from the ability of spironolactone to bind and activate the androgen receptor, causing abiraterone resistance.

4. Switching to alternate agent; strategy stays the same

Each patient and their doctor will choose to use abiraterone or enzalutamide at the beginning of the study. However, some patients might find that the chosen drug is intolerable. PBS rules allow a change to the alternate agent in cases of intolerance. A switch from Abiraterone to Enzalutamide or vice versa is permitted as per standard of practice in the context of intolerable side effects, but the treatment strategy – adaptive or continuous - should continue unchanged.

5. Safety follow up visit

To simplify the participant's journey, the Safety follow up visit has now been combined with End of Treatment visit and should occur within 4-6 weeks after study treatment end date.

6. ANZadapt Patient Information Brochure and Simple PICF

To improve communications with prospective participants, a simplified and much shorter PICF has been created and approved by the HREC. A **simple brochure is also available for prospective patients** to aid recruitment. Both have QR codes that link to the existing patient video. You can watch the video using the QR Code below:

TIPS & HINTS

Screening and Enrolment

To make the patient's recruitment as simple as possible a bone scan and/or CT scan that has been conducted as part of standard of care, can be used as the baseline scans, provided that the patient is randomised within 42 days following the scans.

It is mandatory to have conventional imaging as per the protocol, as we are using PCWG3 criteria for assessing disease progression. ^{99}Tc bone scans and conventional CT scans are needed as part of the screening assessments, then every 12 weeks on study.

- PSMA PET scans cannot be used for the trial. We hope that one day PET scans might replace conventional scans, but for now we have to use the traditional scans for clinical trials
- Bone scan and CT are not required to be repeated at end-of-treatment visit if progressive disease has been confirmed within the last 4-6 weeks using WBBS and/or CT CAP.

Inclusion criterion 6: It is acceptable to have the first PSA test outside of the screening window showing a rise in PSA, as long as the patient has progressive disease at study entry, as confirmed by the second rising PSA result.

Exclusion criterion No.11: Prior cyproterone, flutamide, bicalutamide and nilutamide are permitted, provided they are ceased > 6 weeks before the first treatment visit.

There are two stratification factors: choice of AA or ENZ; presence of visceral (e.g. liver, lung) metastases. Please confirm and double check when you enter stratification details in the eDC before randomising a patient on study.

Randomisation

Randomisation should occur after all the mandatory screening assessments have been completed and eligibility confirmed as per the protocol, and before patient is administered study treatment.

Preference is to randomise the patient on or as close as possible to Visit 1 since the study outcomes are tied to the randomisation date.

Screen Failure

The minimum data entry required for a screen failure is the 'Consent' form and the 'Eligibility' form.

Translational biospecimens

Collection of translational biospecimens for future translational science is a critical part of the study. We are most interested in tracking the evolution of the prostate cancer in each participant, so plasma samples suitable for circulating tumour DNA (ctDNA) analyses must please be collected at baseline and every 12 weeks for exploratory analysis from all patients. This is a mandatory requirement of the study.

Tumour blocks may not be available for patients where surgery or biopsy occurred more than a decade ago, but please still check with the pathology lab and retrieve if possible. The tumour blocks will be extremely helpful in understanding the evolution of each person's cancer and testing the idea that adaptive treatment slows this evolution.

TIPS AND HINTS, cont……

PSA progression when on the Study

PSA progression is defined as per PCWG3 criteria; defined as:

- PSA rising >25% and >2ng/mL from the lowest PSA level (the nadir), but also,
- …while the participant patient is on continuous treatment with AA/ENZ for at least 8 weeks.

SAE reporting

SAEs must be reported from the time of treatment initiation up to 30 days after completion of study treatment or 30 days after the EOT visit, whichever comes first.

In collaboration with

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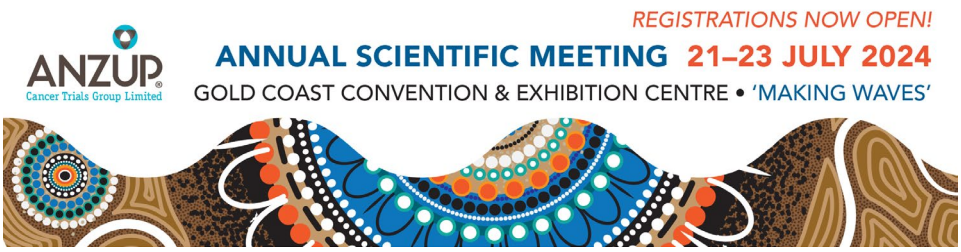

ANZadapt key contacts

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