ANZUP Cancer Trials Group Limited

WOMBAT Trial News

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Welcome to the first WOMBAT newsletter

Thank you for your continued invaluable contribution and support of the WOMBAT (ANZUP 2201) trial. We are pleased to announce that we currently have 9 sites collaborating to this trial.

Study Chair: Professor Anthony Joshua

"We look forward to understanding if we can improve both the utility of darolutamide as well as the quality of life of people on the drug by using bipolar androgen therapy – we are appreciative of the contributions of the participants to date as well as the organising committee"

What is WOMBAT?

Working Out M0 Bipolar Androgen Therapy (WOMBAT) - ANZUP 2201

Single-arm phase II trial to determine the utility of the addition of bipolar androgen therapy to intermittent darolutamide upon PSA progression on darolutamide alone for M0CRPC as measured by metastasis free survival (time from commencing BAT to evidence of metastasis or death) and to determine if this treatment is worthy of further study.

Study schema

Key Inclusion Criteria:

- Histologically confirmed prostate adenocarcinoma
- ECOG performance status 0-1
- PSA progression while on darolutamide despite castrate serum testosterone (<1.7nmol/L)
- PSA >1 ng/mL

Key Exclusion Criteria:

- Neuroendocrine or small cell prostate cancer
- M1 disease on CT/WBBS
- Significant cardiac or thrombotic disease

Interventions:

Eight-week cycles

Day 1: Testosterone enanthate

Days 29-56: darolutamide

Ongoing ADT

Primary Objective:

MFS on conventional imaging (RECIST / PCWG3)

Secondary Objectives:

- Safety and tolerability
- Health-related Quality of Life (EORTC QLQ-C30, EORTC QLQ-PR25)
- PSA response rate
- Time to PSA progression
- Metabolic effects (Serum PINP, plasma CTX, bone densitometry)

Tertiary Objective:

Exploratory biomarker analysis to assess associations of outcomes with cell-free DNA alterations, AR-V7 status and circulating tumour DNA methylation changes.

Study team introduction:

Sponsor: Australian and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group Ltd
Study Chair and Coordinating Principal Investigator: Prof. Anthony Joshua
Study Co-Chair and Co-Coordinating Principal Investigator: A/Prof. Megan Crumbaker
Collaborative Group Chair: Prof. Ian D. Davis, Chair ANZUP Cancer Trials Group

Coordinating Centre: The George Institute for Global Health

Contact us:

Email: WOMBAT@georgeinstitute.org.au which is the trial mailbox for all your study related questions or trials@anzup.org.au for any sponsor related queries.

Study Update

Active Sites

- St. Vincent's Hospital Sydney (Anthony Joshua)
- Sydney Adventist Hospital (Gavin Marx)
- Royal Adelaide Hospital (Hsiang Tan)
- GenesisCare North Shore (Laurence Krieger)
- Cabrini Health (David Pook)
- Grampians Health Ballarat (Sharad Sharma)
- ICON Cancer Centre Chermside (Jeff Goh)
- Eastern Health-Box Hill Hospital (Angelyn Anton)
- The Border Cancer Hospital (Kay Xu)

Pending Activation

- The Canberra Hospital (Ganes Pranavan)

Enrolment Update

We are aiming to enrol 69 patients. Please reach out to the WOMBAT project team with any potential patients. Let's work together to achieve this goal! Please see below for the current enrolment breakdown. A huge thank you and congratulations to all involved for your hard work in reaching this milestone!

Site	In Screening	Screen Failures	Registered
Royal Adelaide Hospital	0	0	**3**
Grampians Health Ballarat	1	0	**1**
Cabrini Health	0	2	**2**
Eastern Health-Box Hill Hospital	0	0	**1**
Totals	**1**	**2**	**7**

Reminders

Protocol Amendment: Protocol version 2.0 and PISCF version 2.0 was HREC approved on 29Jan2025.

Protocol Clarification Memo (PCM): Please note that a PCM has recently been approved by HREC and will be circulated this week. The content of the PCM is outlined below.

- Participants to **stop darolutamide administration up to 48 hours prior to C1D1**
- **During treatment cycles: darolutamide may be stopped** on days 54 to 55 **to allow a break of up to 48 hours** of darolutamide dosing prior to day 1 of the following cycle's testosterone dose.
- **Inclusion criteria #4:** "PSA progression while on darolutamide defined as three rising PSA (1 baseline and 2 consecutive rises) levels at least 1 week apart despite castrate testosterone level (<1.7nmol/L)." adjusted to: "PSA progression while on darolutamide defined as three rising PSA (1 baseline and 2 consecutive rises) levels at least 1 week apart despite castrate testosterone level (<1.7nmol/L). **Patients with a minor subsequent PSA fall, provided there was no intervening therapy since the three consecutive rises, are eligible."**
- **Exclusion criteria #4:** "Current or prior treatment with enzalutamide, abiraterone, apalutamide, or cytotoxic chemotherapy. Prior first generation ARSI such as bicalutamide, flutamide, nilutamide are permitted." Adjusted to: "Current or prior treatment with enzalutamide, abiraterone, apalutamide, or cytotoxic chemotherapy. **Patients with pelvic nodal metastases (below the aortic bifurcation) <2 cm in short axis at original diagnosis who ceased cytotoxic chemotherapy (docetaxel) at least 12 months prior to C1D1 are eligible.** Prior first generation ARSI such as bicalutamide, flutamide, nilutamide are permitted."

Clarification on the schedule of assessments: C2D1 & C3D1 assessments that can be conducted within the 3 days prior to day 1 of the cycle are all respectively labelled with footnote "o". Please ensure that all other assessments are conducted on day 1.

Eligibility and enrolment

- **pre-screening log** to track potential participants before screening. Once a patient provides **informed consent**, they should be immediately entered into the database, which also captures **screen failures (Refer to eCRF Completion Guidelines for additional details).**
- If a patient meets all eligibility criteria, the final forms in the **database** are **"Eligibility"** and **"Registration."** The system collates information from previous screening forms into the **Eligibility** form, where the complete **inclusion and exclusion criteria** are assessed/displayed. **The screening result is displayed on-screen, confirming whether the patient is eligible.**
- If eligible, the patient is registered as participating in WOMBAT, and the system displays the **deadline for the first dose**. The **Registration** must be completed within **7 days prior to the start of treatment.**

Data Entry Requirements

- Prioritise timely data entry into REDCap to facilitate ongoing data monitoring, ensuring accuracy and completeness throughout the trial
- Take necessary follow-up measures, such as data corrections, to maintain the integrity and quality of the study data

Adverse Events (AEs)/ Serious Adverse Events (SAEs)

Please ensure that all AEs/SAEs are reported in a timely manner following the previous advised reporting requirements.

Monitoring

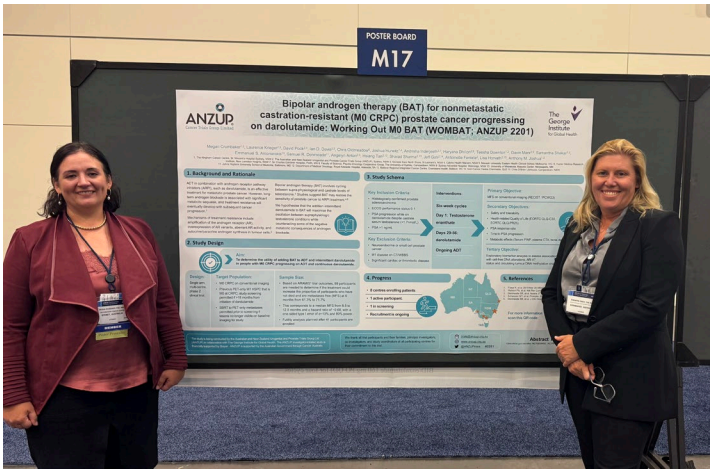
Please note that all monitoring visits for WOMBAT are to be conducted remotely, as outlined in the protocol. The first monitoring visit for your site should be scheduled within 10 business days from C1D1 of the first patient.

WOMBAT Lab Kits

All activated sites have now received lab kit supplies for three patients up to Cycle 3. If additional kits are needed, please submit the completed Re-Supply Request Form to the WOMBAT Coordinating Centre.

Note: If in doubt, please reach out to the contacts outlined above.

WOMBAT at ASCO GU



Bipolar androgen therapy (BAT) for nonmetastatic castration-resistant (M0 CRPC) prostate cancer progressing on darolutamide: Working Out M0 BAT (WOMBAT ANZUP 2201)

Presented by A/Prof. Megan Crumbaker (pictured with ANZUP CEO Adj. Professor Sam Oakes)

ANZUP ASM

Registrations and abstracts now open!

WOMBAT key contacts

- **Clinical trial operations, E:** WOMBAT@georgeinstitute.org.au
- **Coordinating PI: Anthony Joshua E:** Anthony.Joshua@svha.org.au
- **Sponsor queries (payments, contracts) E:** trials@anzup.org.au
- **Trial information:** https://anzup.org.au/clinical-trial/wombat/