TRIALS IN PROGRESS - P3BEP (ANZUP 1302):
An international randomized phase 3 trial of accelerated versus standard BEP chemotherapy for individuals aged 11-45 years with intermediate and poor-risk metastatic germ cell tumours

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1. Background and rationale

- Bleomycin, Etoposide, Cisplatin (BEP) administered as 4 x 3-weekly cycles is standard first-line treatment for patients with metastatic germ cell tumours (GCT) with poor prognostic features.
- High-dose chemotherapy and more complex regimens (e.g. VIP, T-BEP) have failed to improve cure rates and are more toxic.
- Accelerating regimens of standard chemotherapy to 2-weekly rather than 3-weekly improved cure rates in other malignancies.
- Results from an Australian single-arm phase I/II trial[1,2] and a UK trial[3] confirmed that accelerating standard chemotherapy for germ cell tumours is safe, feasible, and active: The 5-year PFS was 94% and 50%, and 5-year OS was 94% and 92%, for intermediate and poor prognosis patients, respectively[2].

2. Aim

To determine if accelerated BEP is superior to standard BEP as first-line chemotherapy for intermediate and poor-risk metastatic germ cell tumours.

3. Study Design

Design: Open-label, randomized, stratified, 2-arm, 2-stage multi-center, phase 3 clinical trial.

Target Population: Participants aged 11 – 45 years, with intermediate or poor-risk metastatic germ cell tumours for first line chemotherapy.

Sample Size: 150 (stage I) and 500 (stage II) patients gives >80% power at 5% level of significance to detect a 21% improvement in response rate from 59% with standard BEP to 80% with accelerated BEP (stage I), and 7% absolute improvement in 2yr PFS from 81% with standard BEP to 88% with accelerated BEP (stage II), respectively.

4. Study Objectives

Primary
Progression free survival

Secondary
- Response following treatment completion
- Adverse events
- Health related quality of life
- Treatment preference
- Delivered dose intensity of chemotherapy
- Overall survival

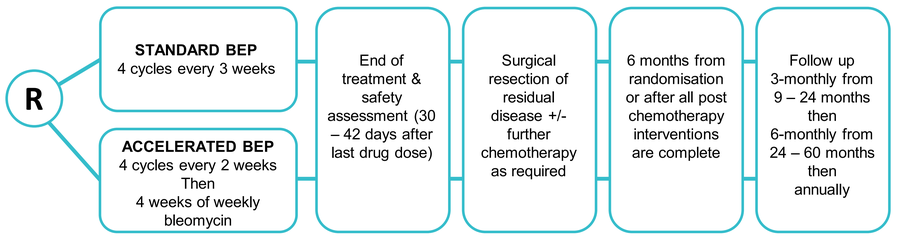
Tertiary:
Correlative biomarker studies including microRNA.

5. Study Schema

Screened → Randomised 1:1 → BEP Chemotherapy → Initial Response Assessment → Post Chemotherapy → Final Response Assessment → Follow Up

Eligibility:
- Intermediate or poor risk GCTs
- First line chemotherapy
- Adequate organ function

Stratification:
- IGCCC risk group
- Primary site
- Brain metastases
- Induction chemotherapy
- Age
- ECOG status
- Gender
- Study site



BEP doses:
- Etoposide (E) 100mg/m^2 D1-5
- cisplatin (P) 20mg/m^2 D1-5
- Peg G-CSF D6 **or** Filgrastim daily
- Bleomycin (B) 30000 IU IV weekly (age ≥ 16 years) **or**
- Bleomycin (B) 15000 IU /m^2
- (age < 16 years)

Week	1	2	3	4	5	6	7	8	9	10	11	12
Standard BEP (21-day cycle)	EP B	B	B	EP B	B	B	EP B	B	B	EP B	B	B
Accelerated BEP (14-day cycle)	EP B	B	EP B	B	EP B	B	EP B	B	B	B	B	B

6. Study Progress

Enrolment opened	**Feb 2014**
Sites open to recruitment (196)	**23 ANZ 17 UK 156 USA**
Patients recruited	**N=287**
Interim analysis (N=76)	**Safety acceptable**
Stage I analysis (N=150) Including formal comparison of response rate	**Activity acceptable**
Stage II analysis (N=500)	**Expected in 2029**

7. Contact Us

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Clinical trial identifiers: NCT02582697, ACTRN12613000496718

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In collaboration with:

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