An international randomized phase 3 trial of accelerated versus standard BEP chemotherapy for adult and paediatric male and female patients with intermediate and poor-risk metastatic germ cell tumours: P3BEP (ANZUP protocol 1302)

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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 has 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-centre, phase 3 clinical trial.

Target Population: Participants of all genders 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.

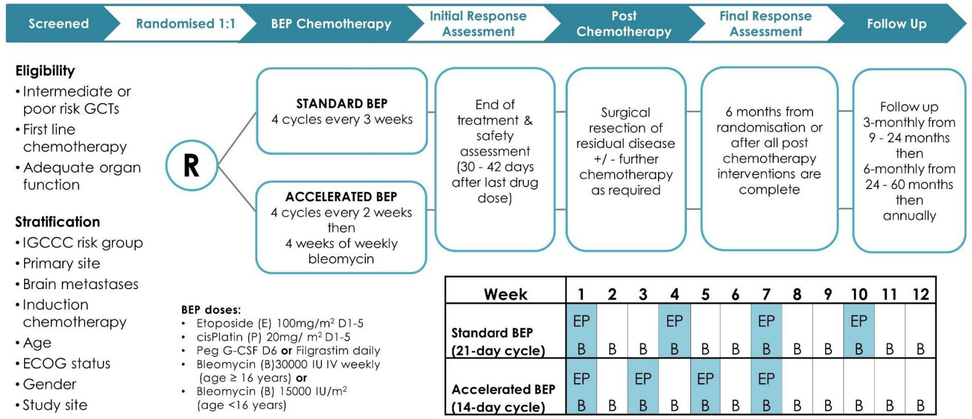
4. Study Objectives

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



BEP doses:
- Etoposide (E) 100mg/m² D1-5
- cisPlatin (P) 20mg/ m² D1-5
- Peg G-CSF D6 **or** Filgrastim daily
- Bleomycin (B)30000 IU IV weekly (age ≥ 16 years) **or**
- Bleomycin (B) 15000 IU/m² (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 (189)	**23 ANZ 17 UK 51 USA**
Patients recruited	**N = 241**
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 2028**

7. Contact Us

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SCAN ME

Clinical trial identifiers: NCT02582697, ACTRN12613000496718

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In collaboration with:

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