P3 BEP (ANZUP 1302): An international randomized phase 3 trial of accelerated versus standard BEP chemotherapy for male and female adults and children with intermediate and poor-risk metastatic germ cell tumours (GCTs) (TPS5102)

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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 (eg 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 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.

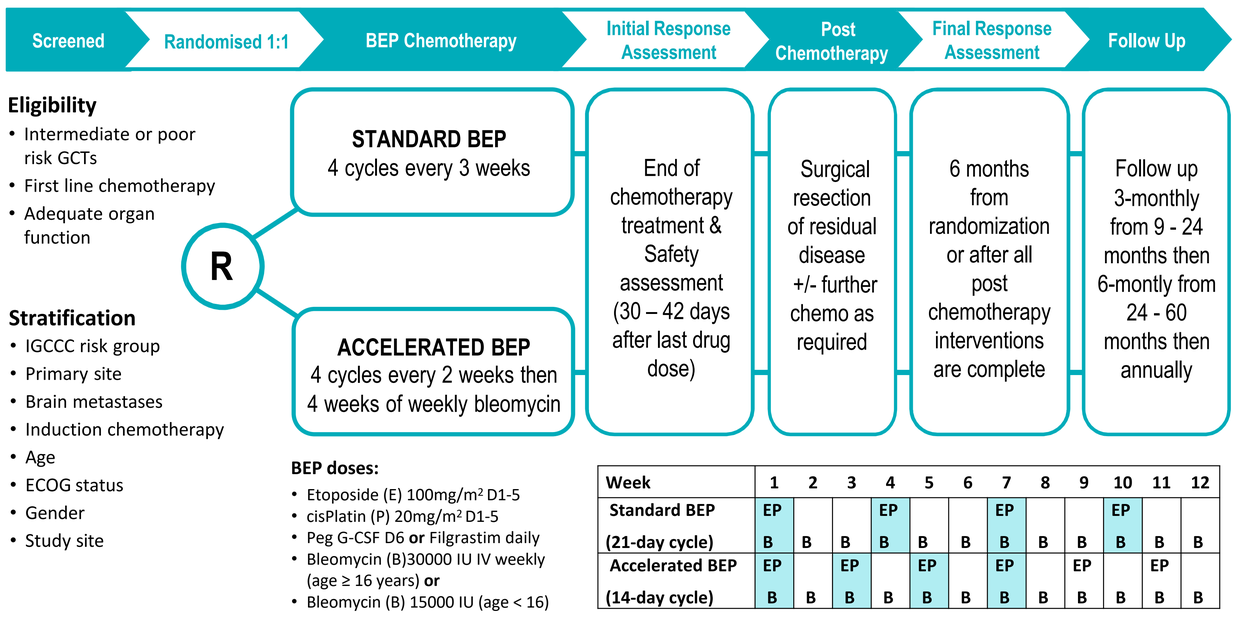
4. Study Objectives

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

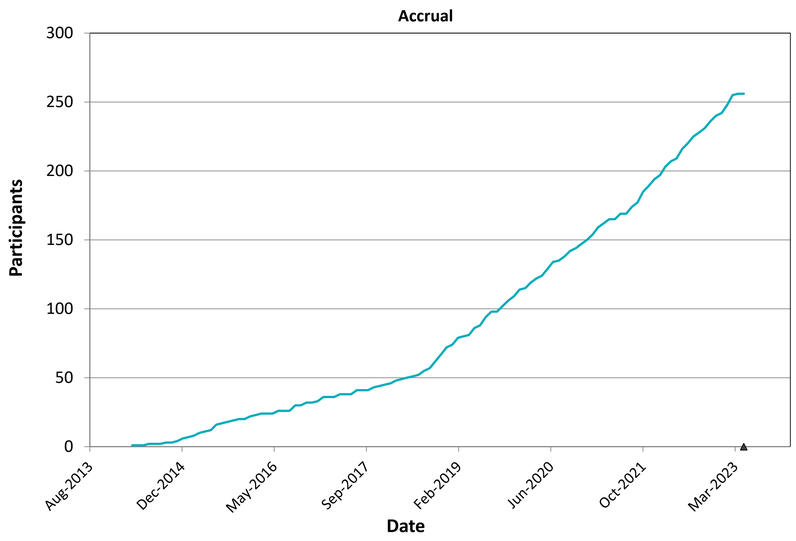


Week	1	2	3	4	5	6	7	8	9	10	11	12
Standard BEP (21-day cycle)	EP B	B	B	EP B	B	B	EP B	B	B	EP B	B	B
Accelerated BEP (14-day cycle)	EP B	B	EP B	B	EP B	B	EP B	B	EP B	B	EP B	B

6. Study Progress

Enrolment opened:	Feb 2014
Sites open to recruitment (190):	23 Australia and New Zealand 17 UK 150 USA
Patients recruited:	N = 256
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

Overall Accrual Summary



7. Contact us

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Clinical Identifiers:

NCT02582697
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References:

1. P.S. Grimison, et al. Annals of Oncology 2014; 25: 143-148. 2. N. Lawrence, et al. Annals of Oncology 2016; 27:2303-2303. 3. Y. Rimmer, et al. British Journal of Cancer 2011;105:766-72

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In collaboration with: