An international randomised 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 1302)

Shalini Subramaniam[1,17], Guy C. Toner[2,17], Martin R. Stockler[1,17], Andrew Martin[1,17], Farzana Pashankar[3], Lindsay Frazier[4], Danish Mazhar[5], Kate Ford[1], Euan Walpole[7,17], Amanda Gwendolyn Stevanovic[8,17], David Wyld[9], Simon Troon[10,17], Fritha J. Hanning[11,17], Alison Birtle[12,17], Matthew Wheater[13], Robert Huddart[14], Jeffery White[15], Sheri Spunt[16] Peter S. Grimison[1,6,17] on behalf of the Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP)

[1]NHMRC Clinical Trials Centre, Sydney, Australia, [2]Peter MacCallum Cancer Centre, Melbourne, Australia, [3]Yale School of Medicine, USA, [4]Dana Farber Cancer Institute, USA, [5]Cambridge University Hospital Paediatrics, Cambridge, UK, [6]Chris O'Brien Lifehouse, Sydney, Australia, [7]Princess Alexandra Hospital, Brisbane, Australia, [8]Nepean Cancer Care Centre, Kingswood, Australia, [9]Royal Brisbane and Women's Hospital, Brisbane, Australia, [10]Fiona Stanley Hospital, Perth, Australia, [11]Auckland City Hospital, Auckland, New Zealand, [12]Royal Preston Hospital, Preston, UK, [13]University Hospital Southampton, Southampton, UK, [14]Royal Marsden Hospital, London, UK, [15]Beatson West of Scotland Cancer Centre, Glasgow, UK, [16]Lucile Packard Children's Hospital Stanford, Palo Alto, USA, [17]Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP), Sydney, Australia

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 have failed to improve cure rates and are more toxic.

Accelerating regimens of standard 3-weekly chemotherapy to 2-weekly cycles has improved cure rates in other malignancies.

Results from an Australian phase I/II trial[1,2] and a UK trial[3] confirmed that accelerating standard chemotherapy for GCT 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 GCT.

3. Study Design

Design: **Open label, randomised, stratified, 2-arm, multicentre, 2-stage, phase 3 trial.**

Target Population: **Participants aged 11 to 45 years with intermediate or poor-risk metastatic GCT arising in testis, ovary, retroperitoneum, mediastinum considering first-line chemotherapy.**

Sample Size: **150 (stage I) and 500 (stage II) patients gives >80% power at 5% level of significance to detect a 20% 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.**

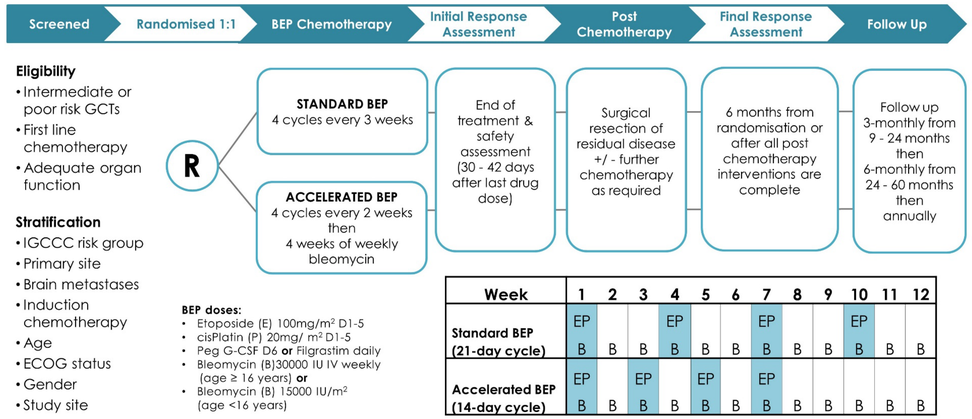
4. Study Objectives

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 or Correlative
Associations between biomarkers and their correlation with clinical outcomes.

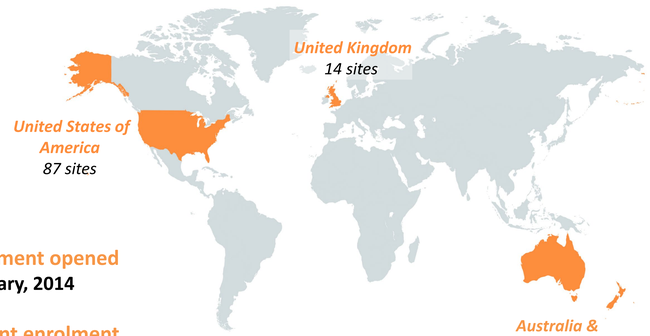
5. Study Schema



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
February, 2014

Current enrolment
113 patients randomised

7. Contact Us

P3BEP@ctc.usyd.edu.au

www.anzup.org.au

@ANZUPtrials

Clinical trial identifiers: **NCT02582697, ACTRN12613000496718**

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In collaboration with

References: 1. Grimison PS, *et al.* Annals of Oncology 2014; 25: 143-148.; 2. Lawrence N, *et al.* Annals of Oncology 2016; 27; 2302-2303; 3. Rimmer, Y, *et al.* British Journal of Cancer 2011;105:766-72

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