P3 BEP: Randomised phase 3 trial of accelerated versus standard BEP chemotherapy for patients with intermediate and poor-risk metastatic germ cell tumours

(ANZUP protocol 1302)

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1. Background and Rationale

- Bleomycin, Etoposide, Cisplatin (BEP) administered 3-weekly x 4 remains standard first-line treatment for intermediate- and poor-risk metastatic germ cell tumours.
- 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 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, randomised, stratified, 2-arm, 2 stage multi-centre phase 3 clinical trial.
- **Target Population:** Males and females 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 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.

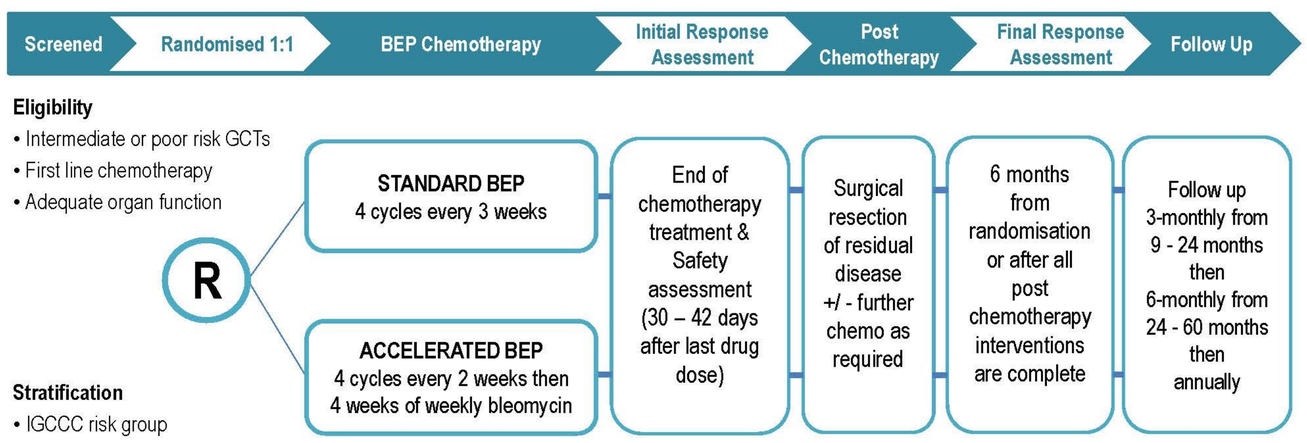
4. Study Objectives

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: Correlative biomarker studies including serum 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	B	B	B	B

6. Study Progress

Enrolment opened	Feb 2014
Sites open to recruitment (189)	23 ANZ 17 UK 149 USA
Patients recruited	N=211
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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Acknowledgments

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References

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3. Y. Rimmer, et al. British Journal of Cancer 2011;105:766-72

This study is being conducted by the Australian and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group Ltd in collaboration with the NHMRC Clinical Trials Centre at the University of Sydney, Cancer Research UK, Australian and New Zealand Children's Haematology/Oncology Group (ANZCHOG), Children's Oncology Group USA, and 189 sites in ANZ and UK and USA. ANZUP is supported by the Australian Government through Cancer Australia. The trial is co-funded by Cancer Council Australia and Cancer Australia (APP1159837). Sydney Catalyst Translational Cancer Research Centre supported by Cancer Institute NSW has financially supported the collection of blood and tissue for translational research.

In collaboration with: