GUIDE: A randomized non-comparative phase II trial of biomarker-driven intermittent docetaxel versus standard-of-care docetaxel in metastatic castration-resistant prostate cancer (ANZUP 1903)

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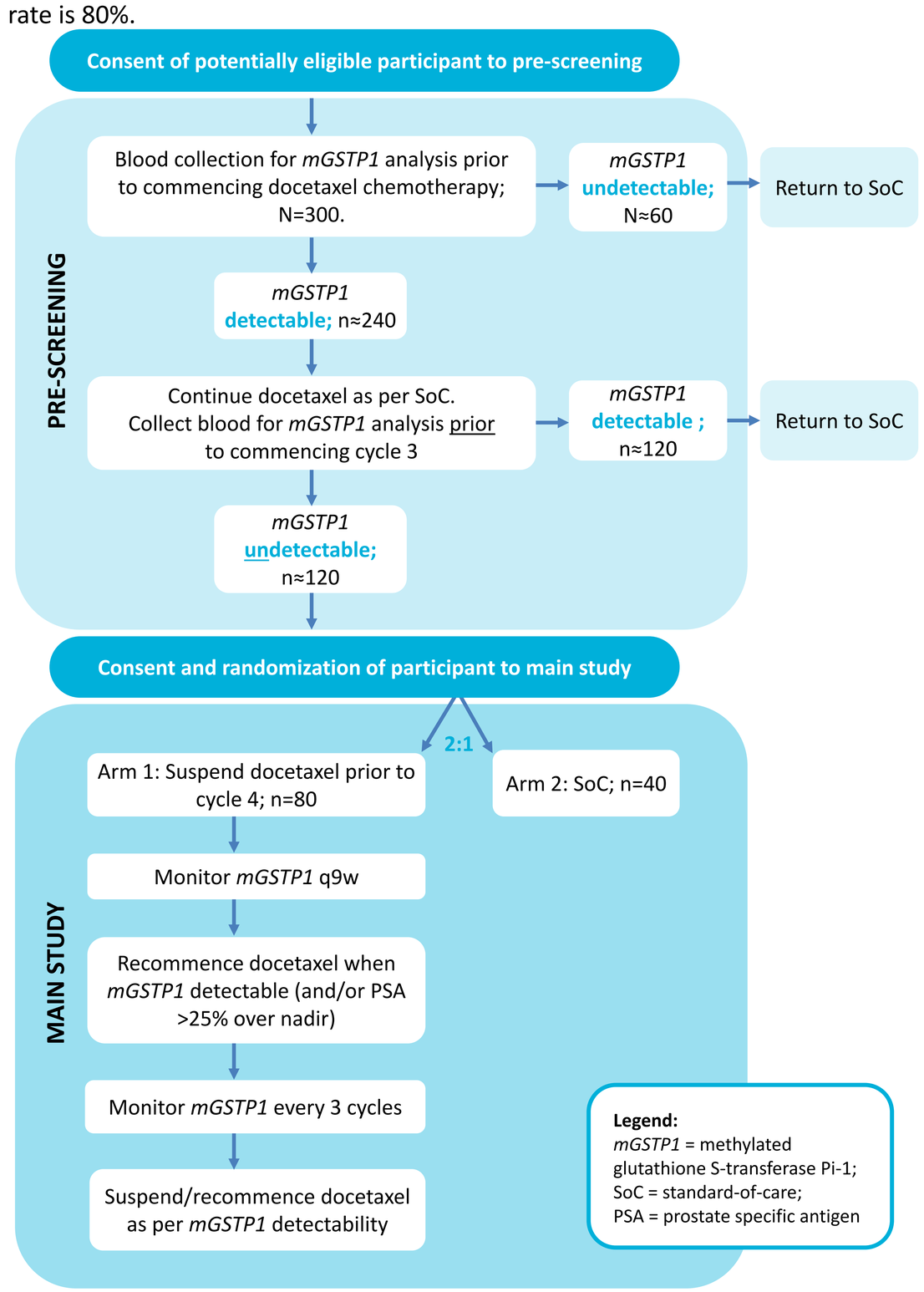
1. Background and rationale

- Docetaxel improves survival in metastatic castration resistant prostate cancer (mCRPC)[1] but is associated with toxicities which impact tolerability, particularly for patients who may be older and often with multiple co-morbidities[2].
- Biomarker-driven de-escalation of docetaxel chemotherapy may allow improved balance of cancer control and quality of life against toxicity.
- A fall in circulating methylated glutathione S-transferase Pi-1 (*mGSTP1*) DNA after 2 cycles of chemotherapy for mCRPC is associated with improved overall survival[3].

In this ongoing trial, we aim to determine the **efficacy and safety** of intermittent docetaxel chemotherapy guided by **circulating plasma *mGSTP1*** in individuals with metastatic CRPC.

2. Study Design, Schema, Population

Design: GUIDE is a randomized, two-arm, non-comparative phase 2 clinical trial.
Target population: individuals with progressing metastatic CRPC, defined by PCWG3, who are planned to commence docetaxel chemotherapy (prior docetaxel is allowed if administered in the mHSPC setting and at least 2 years prior to study enrolment).
Sample size: Allowing for 10% of dropout prior to radiographic progression, at least 77 participants are required to receive intermittent docetaxel. Therefore, 120 people with undetectable *mGSPT1* after two cycles of docetaxel will be randomised at 2:1 ratio between the arms. The undetectable *mGSPT1* rate after two cycles is expected to be 50%; therefore, 240 people with detectable *mGSPT1* at baseline will be required in pre-screening. At baseline, the detectable mGSTP1 rate is 80%.



4. Study Progress

- **Primary Endpoint:** Radiographic progression-free survival (rPFS)
- **Secondary Objectives:**
  - Time on treatment holidays
  - Safety
  - Patient-reported outcomes, evaluated using EORTC QLQ-C30 and FA-12, FOP and modified PRO-CTCAE
  - Overall survival
  - Resource use and cost associated with treatment

4. Study Progress

- Recruitment commenced in November 2021.
- Actively recruiting at eight Australian sites, including four regional hospital networks.

5. References

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ClinicalTrials.gov Identifier: **NCT04918810**
Website: **www.anzup.org.au**
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