



GENESCREEN 5-FU

GENOTYPE-GUIDED PERSONALISED
FLUOROPYRIMIDINE DOSING:
FEASIBILITY AND IMPLEMENTATION
PILOT STUDY

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BACKGROUND AND RATIONALE

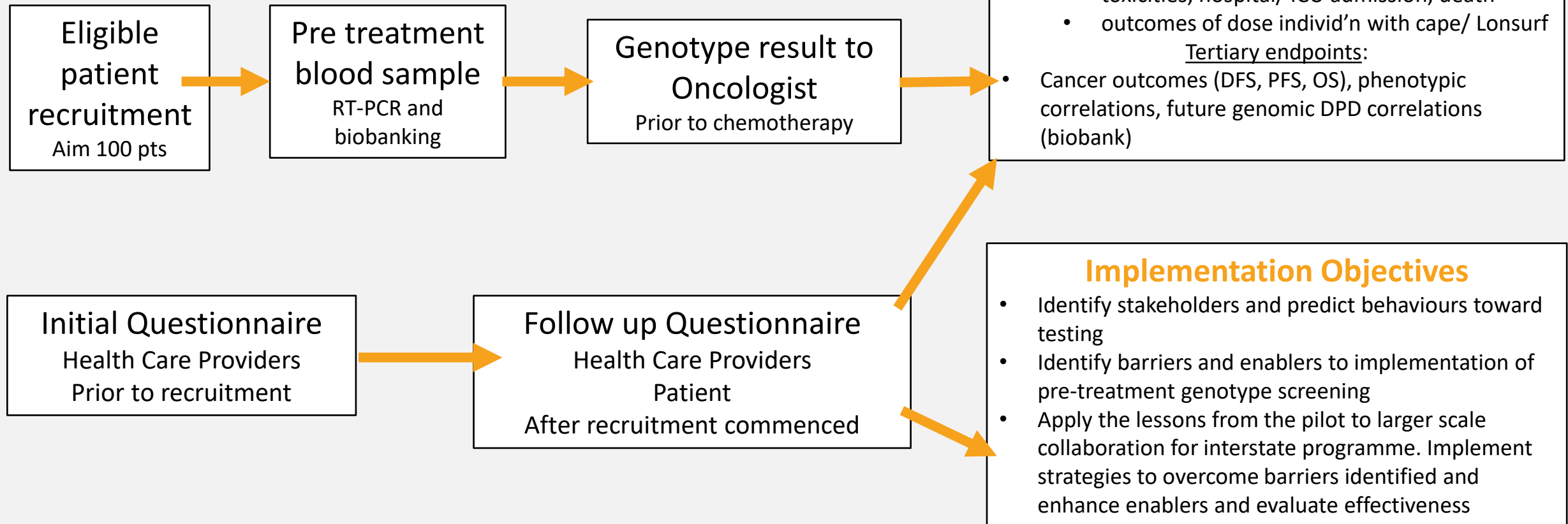
- Fluoropyrimidine (FP) chemotherapy (5FU, capecitabine, Lonsurf)
 - Colon, Upper GI, Breast and Head and Neck cancers (>10,000 Australians/ year) (30% toxicity)
 - DPD enzyme critical for metabolism and excretion
 - DPD deficiency → excess FP → toxicity (hospitalization, ICU, death) (Up to 60% of toxicity)
 - DPYD gene responsible for DPD production (8% Caucasian population have functional variant)
 - Up to 50% of DPD deficient toxicity due to 1 of 4 DPYD gene variants
- Netherlands, UK, France
 - DPD enzyme and DPYD genotype screening PRIOR to delivery of FP chemotherapy
 - Safer prescribing, less toxicity, cost effectiveness
- **Can this be offered in Australia?**
- **What are the barriers and enablers to delivering this service in Australia?**

Henricks et al 2015, Pharmacogenomics
Henricks et al 2018, Lancet Oncology
Muelendijks et al 2015, Lancet Oncology
Deenen et al 2016, Journal Clinical Oncology

METHODS, AIMS AND OBJECTIVES

PART ONE: GeneScreen 5-FU Feasibility Study

- HNELHD and CCLHD (six sites)



IMPLEMENTATION METHODS

- Rationale: Pre-screening adopted in UK and Europe
- Martens *et al*, 2020 conducted analysis following introduction of testing in Netherlands
 - Enablers: Clear protocols and instructions for ordering/ reporting
 - Barriers: lack of consensus on test approach, long turn around time
- **Theoretical Domains Framework**

HCP Questionnaires:

Domains: skills, knowledge, beliefs (actions/ consequences), intent (actions/ consequences)

Patient Questionnaire:

Domains: knowledge, memory/ attention, beliefs

- Adjustments to approach (HCP, patients, laboratory) based upon outcomes (clinical and implementation)
- Implementation Evaluation in Larger Scale Program
 - Incorporation of Discrete Choice Experiment and Health Economics Analysis

FUTURE PROJECTIONS AND QUESTIONS

PART TWO: Larger Scale GeneScreen 5-FU Programme

NSW, Vic, Others. Aim 1000+ patients

Clinical Objectives

- Chemo safety data
- Dose reduction data (capecitabine and Lonsurf)
- Cancer outcomes

Implementation Objectives

- Inclusion of hosp executives and health system managers
- Discrete Choice Experiments
- Implementation analysis

Health Economics Objectives

- Cost effectiveness analysis compared to historical cohorts
- DCEs

Future Research Objectives

- Genomic research (related DPD genes/ DPD activity markers)
- Genetic variants related to specific ethnic groups