The HSCT-BIOME Trial:

A hybrid phase 0/1 trial evaluating oral capsule faecal microbiota transplantation for preventing HSCT-associated complications

The Supportive Oncology Research Group

Anna Li[1,2], Joanne M Bowen[1], Feargal J Ryan[3], Samuel P Costello[4], Robert Bryant[4,5], Angie Yong[6], Cindy Lee[6], David Yeung[6], Daniel Thomas[2,6], Craig Haifer[7], Hannah R Wardill[1,2]

1 School of Biomedicine, Faculty of Health and Medical Sciences, The University of Adelaide, 2 Precision Cancer Medicine Theme, South Australian Health and Medical Research Institute, 3 Lifelong Health Theme, South Australian Health and Medical Research Institute, 4 BiomeBank, 5 Basil Hetzel Institute, 6 Department of Haematology, Royal Adelaide Hospital, SA Health, 7 Department of Gastroenterology, St Vincent's Hospital

INTRODUCTION AND STUDY AIMS

- Changes in the gut microbiota during haematopoietic stem cell transplantation (HSCT) are increasingly linked to the development of various complications
- Faecal microbiota transplantation (FMT), a method of delivering a healthy gut microbiota to a recipient, offers potential in promoting gut microbiota stability and improving HSCT outcomes
- The HSCT-BIOME Trial is designed to determine the tolerability and safety of orally-administered, encapsulated FMT **delivered peri-HSCT**, and test its ability to reduce the incidence/severity of complications.

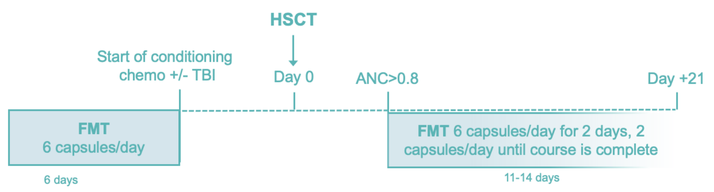
STUDY OBJECTIVES

1. Determine safety and tolerance of peri-HSCT encapsulated FMT
2. Determine if peri-HSCT encapsulated FMT reduces the proportion of participants that develop severe gastrointestinal toxicity
3. Determine if peri-HSCT encapsulated FMT reduces symptom burden in people undergoing HSCT

STUDY DESIGN

Stage 1 | **Safety run-in trial**: Open label with N=5 participants to identify any treatment-emergent (TE)-AEs (CTCAE v5) and confirm adherence to the protocol.

Stage 2 | **Efficacy trial**: Double-blind, placebo-controlled trial to determine the clinical efficacy of peri-HSCT delivered encapsulated FMT with N=51 participants randomised 2:1 FMT or placebo.



STUDY CONDUCT

PARTICIPANT CRITERIA
Male and female >18 years old
Scheduled for autologous-HSCT +/- TBI
No pre-existing GI disease

FMT PRODUCTION
Facilitated by BiomeBank in line with TGA guidelines
Donor stool anaerobically prepared and lypholised

STUDY SITES
Royal Adelaide Hospital, Adelaide, South Australia
St Vincent's Hospital, Sydney, New South Wales

PRIMARY OUTCOMES

Primary outcomes will be assessed by measure of:

- Safety using CTCAE v5
- Severe gastrointestinal toxicity:
  - Stool consistency by the Bristol stool chart
  - Frequency of stool excretion

Final assessments taken one month post FMT

Table 1: Study assessment schedule

Assessment	Before prophylactic FMT	After prophylactic FMT	Day of HSCT (day 0)	During in-patient stay	Before recovery FMT	After recovery FMT	Day +21	1 month after
Patient demographics								
Comorbidities								
Medications								
Diagnosis/treatment details								
ECOG performance status								
Adherence								
Bristol stool chart (BSC)			Daily					
Frequency			Daily					
Body weight				2-3x weekly while in patient				
Symptom burden			*	*	*	*		*
Adverse events ^								

BIOSPECIMEN COLLECTION

Blood and stool samples will be collected longitudinally throughout stage 2 of the study for exploratory analysis

Table 2a: **Blood** collection schedule

Before starting pre-HSCT FMT	Day of chemotherapy infusion	Day 0 (HSCT)	Post HSCT period	Day of discharge	~35*
X	X	X	A maximum of 5x weekly aligning with routine blood draws	X	X

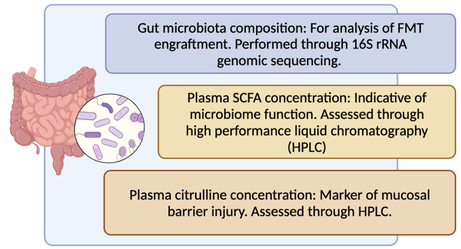
Table 2b: **Stool** collection schedule

Before starting pre-HSCT FMT	Day of chemotherapy infusion	Day 0 (HSCT)	Post HSCT period	Start of FMT #2	End of FMT#2	~35*
X	X	X	A maximum of 5x weekly while in patient**	X	X	X

SECONDARY OUTCOMES AND EXPLORATORY ANALYSIS

Secondary outcomes:

- Symptom burden using ESAS-r-SC
- Incidence of fever and BSI
- Use of supportive care interventions including:
  - Antibiotics
  - TPN
  - Loperamide
  - Opioid analgesics
- Duration of hospital stay



STATISTICS

Safety: TE-AEs and SAEs in each group

Adherence: Completion of full FMT course

Effectiveness: Proportion of participants that reach primary endpoint

Compared using chi-squared test in accordance with approval SAP

CONCLUSIONS, NEXT STEPS & ACKNOWLEDGEMENTS

- **FMT is a promising HSCT adjunct to mitigate complications; however, its clinical utility is limited to narrow indications i.e. treatment-resistant/refractory GvHD.**
- **The HSCT-BIOME study will be the first clinical trial conducted of peri-HSCT delivered capsule FMT for prevention of HSCT-associated complications.**
- **Peri-HSCT delivery promotes microbial composition prior to and following HSCT for greater protective effect.**
- **Study to begin recruiting in Q4 of 2024**

Contact hannah.wardill@adelaide.edu.au for more information.

BiomeBank
the hospital research foundation
finding cures improving care
THE UNIVERSITY of ADELAIDE