The CANnabinoids in CANcer (CANCAN) trial:

A randomised, double-blind, placebo-controlled trial of medicinal cannabis in alleviating the symptom burden in people with cancer

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The Supportive Oncology Research Group

INTRODUCTION AND STUDY AIMS

- Cannabis use is growing among people with cancer for the management of symptoms and side effects of treatment
- 80% of clinicians report being asked by their patients about medicinal cannabis, but <30% feel equipped in how to guide their patients appropriately, owing to poor quality evidence[1]
- Medicinal cannabis predominantly contains the active compounds, cannabidiol (CBD) and ∆9-tetrahydrocannabinol (THC), which augment the endocannabinoid system (ECS)
- Gut function is highly dependent on the ECS, with evidence of medicinal cannabis alleviating mucosal inflammation and associated symptoms in non-cancer settings (e.g. IBD)[2]
- Given centrality of gastrointestinal mucositis (GI-M) to numerous symptom sequelae (Figure 1):

The CANCAN trial hypothesises that medicinal cannabis is well positioned to minimise GI-M and associated symptoms

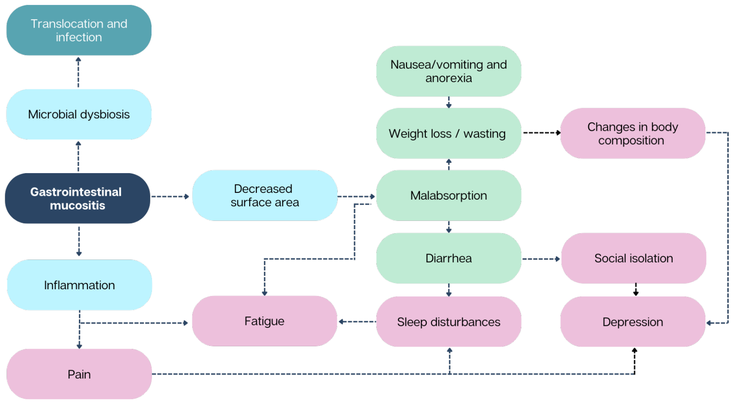

Figure 1 – Centrality of GI-M in intestinal and extra-intestinal symptoms

PROTOCOL DETAILS

Design: Phase II, double-blinded, randomised, placebo-controlled trial conducted at 3 sites in South Australia

Participants: N=176 scheduled to receive mucotoxic chemotherapy, including FOLFOX, FOLFIRI, CAPOX, capecitabine for advanced cancer. Key exclusion criteria:

- Cannabis dependence/misuse (CUDIT>7) or recreational use >once/week in the month leading up to the trial
- History or presence of unstable CVD, psychosis or other psychiatric disease, hepatic dysfunction, intolerance to cannabis products
- Pregnant, planning pregnancy or lactating
- Pre-existing oral disease or disability impacting mucosal absorption

Intervention: CBD (300 mg/day) and THC (5-20 mg/day, patient to self-titrate in 5 mg increments) administered as a sublingual wafer. Wafers taken daily for 3 cycles of chemotherapy. Supplied by iX BioPharma

Comparator: Placebo sublingual wafer (1:1 randomisation)

Primary outcome: GI-M burden defined by the AUC for Mucositis Daily Questionnaire Scores over study duration

INNOVATIONS

eConsent enabled by Consentic®
↑ Participant satisfaction and understanding of risks/benefits

High emphasis on PROMs
Better positioned to capture *burden* not severity of side effects

ePROM collection with PersonifyCare
Friendly reminders, simple dashboard, real-time data access (for study team)

STUDY OUTCOMES

Specimen collection

- Blood, stool, and saliva collection for translation studies

PROMs

- Symptom burden (ESAS-r-SC, FAACT)
- Depression/anxiety (HADS)
- QoL (EORTC-QLQ-C30)
- Financial toxicity (FACIT-COST)

Clinical/other outcomes

- Adverse events (NCI CTCAE)
- Incidence of hospitalisation
- Incidence of chemotherapy dose reductions or breaks
- Cumulative dose of chemotherapy given
- % of intended chemotherapy dose received
- Tumour response (RECIST)
- Overall and progression-free survival (12 and 24 months)
- Supportive care interventions used

STATUS

- **Protocol accepted by HREC**
- **Recruitment anticipated Q2 2024**
- **ANZCTR registration: ACTRN12622000419763**

Wardill, HR. *et al*. (2024). Supporting gut health with medicinal cannabis in people with advanced cancer: potential benefits and challenges. *Br J Cancer* 130, 19–30.

Acknowledgements
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References
[1]Braun, I. M, et al. (2018). *J Clin Oncol*, 36(19), 1957-1962
[2]Naftali, T, et al. (2021). *PloS One*, 16(2), e0246871