PILOT AND DEFINITIVE RANDOMISED DOUBLE-BLIND PLACEBO CONTROLLED TRIALS OF EVALUATING AN ORAL CANNABINOID-RICH THC/CBD CANNABIS EXTRACT FOR SECONDARY PREVENTION OF CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING

Antony Mersiades¹, Annette Tognela², Paul Haber³, Martin Stockler^{1 3 4 5}, Nicholas Lintzeris^{6 7}, John Simes¹, Iain McGregor⁸, Jan Oliver⁹, David J Allsop⁸, Craig Gedye¹⁰, Adrienne Kirby¹, Rachael L Morton¹, Anh D Tran¹, Karen Briscoe¹¹, Peter Fox¹², Nicole Wong¹, Anna Walsh¹, Anjali Bhardwaj¹, Carmel Hahn⁴, Peter Grimison^{1 4}

¹ NHMRC Clinical Trials Centre, University of Sydney, NSW, Australia, ² Department of Medical Oncology, Macarthur Cancer Therapy Centre, NSW, Australia, ³ Sydney Medical School, University of Sydney, NSW, Australia, ⁴ Chris O'Brien Lifehouse, NSW, Australia ⁵ Concord Cancer Care Centre, Concord, NSW, Australia, ⁶ Division of Addiction Medicine, University of Sydney, NSW, Australia ⁷ Drug and Alcohol Services, South East Sydney Local Health District, Sydney, NSW, Australia, ⁸ Lambert Initiative for Cannabinoid Therapeutics, University of Sydney, NSW, Australia, ⁹ Sansom Institute for Health Research, University of South Australia, SA, Australia, ¹⁰ Department of Medical Oncology, Calvary Mater Newcastle, NSW, Australia, ¹¹ Mid-North Coast Cancer Institute, Coffs Harbour Hospital, NSW, Australia, ¹² Central West Cancer Care Centre, Orange Health Service, NSW, Australia

BACKGROUND

Up to half of patients receiving chemotherapy of moderate or high emetic risk experience CINV despite optimal anti-emetic prophylaxis¹. Limited evidence suggests cannabinoid medicine in the form of tetrahydrocannabinol (THC) may reduce CINV, and addition of cannabidiol (CBD) may improve efficacy and tolerance².

AIM

To determine if an anti-emetic regimen incorporating oral THC/CBD is more effective than guideline-consistent anti-emetic regimen alone for the secondary prevention of CINV, during any 3 consecutive cycles of chemotherapy (A, B or C).

DESIGN

Multicentre, double-blind, placebo-controlled, phase II/III randomised trial.

ELIGIBILITY

Key inclusion criteria:

- 1. Adult with any malignancy receiving moderate to highly emetogenic intravenous chemotherapy (Day 1) in a 14 or 21-day cycle
- 2. CINV despite guideline consistent anti-emetics
- 3. Planned for ≥2 further consecutive cycles of the same regimen
- 4. ECOG performance status ≤2

Key exclusion criteria:

- 1. Unable/unwilling to comply with driving restriction
- 2. Unable/unwilling to abstain from cannabis use (drug test at study entry)
- 3. Disease related nausea and vomiting requiring daily anti-emetic use
- 4. Oral chemotherapy
- 5. Planned radiotherapy (brain, abdomen, pelvis)
- 6. Contraindication to cannabinoid treatment

OBJECTIVES (ENDPOINTS)

Primary:

Proportion of patients with a complete response (no emesis and no use of rescue medications) during the overall phase (0-120 h) of cycle A/B

Secondary:

Proportion of patients during the acute (0-24 h), delayed (24-120 h) and overall (0 – 120 h) phases of Cycles A, B and C with:

- i. complete response
- ii. no emesis
- iii. no significant nausea
- iv. no use of rescue medications

Number of emetic episodes during 0-120 hours of cycles A, B and C

Tertiary:

Health system resource use and costs

Quality of life and cost-effectiveness

STATISTICAL CONSIDERATION

A sample size of 80 patients, allocated 1:1 to either study drug followed by placebo or placebo followed by study drug, will have 80% power at a 2-sided significance level of 10% to detect a 20% difference in the proportion of patients with complete response between the two treatments (McNemar's test).

STUDY PROGRESS

As of May25th, 52 of 80 participants have been recruited to the pilot study.

Table 1 – Cancer characteristics					
Primary	Stage				Total
	I	II	III	IV	
Breast	2	9	4	3	18
Colorectal			2	5	7
Pancreas			2	4	6
Lung	1		2	1	4
Gastro-oesophageal			1	3	4
Unknown				3	3
Ovary			1	1	2
Cervix		1		1	2
Endometrial			1		1
Testes			1		1
Sarcoma				1	1
Lymphoma				2	2
Total	27		22		52

Table 2 – Baseline characteristics	
Characteristic	N (%)
Gender	
Female	39 (75%)
Male	13 (25%)
Age group	
18-29 years	1 (2%)
30-49 years	16 (31%)
50-69 years	32 (62%)
>70 years	3 (6%)
Previous cannabis	19 (37%)
Alcohol consumption	21 (40%)
Motion sickness	10 (19%)
Previous pregnancy	34 (87%)
Nausea during pregnancy	19 (56%)
Chemotherapy	
Moderately emetogenic	28 (54%)
Highly emetogenic	24 (46%)

REFERENCES

1. Gilmore JW, et al. Antiemetic guideline consistency and incidence of chemotherapy-induced nausea and vomiting in US community oncology practice: INSPIRE Study. Journal of oncology practice / American Society of Clinical Oncology 2014;10:68-74
2. Smith LA, et al. Cannabinoids for nausea and vomiting in adults with cancer receiving chemotherapy (review). Cochrane Database of Systematic Reviews 2015, Issue 11. Art. No.: CD009464

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