Medicinal cannabinoids – Research in Palliative Care

Professor Phillip Good

Palliative and Supportive Care

Mater Health Services and St Vincent's Private Hospital Brisbane

Clinical Problem – Advanced Cancer/Palliative Care

- multiple symptoms: pain, nausea & vomiting, anorexia/cachexia, fatigue, depression, anxiety
- unmet needs for symptom control
- strong patient demand for cannabinoids
- strong government push
- weak clinical evidence base

Reasons for use

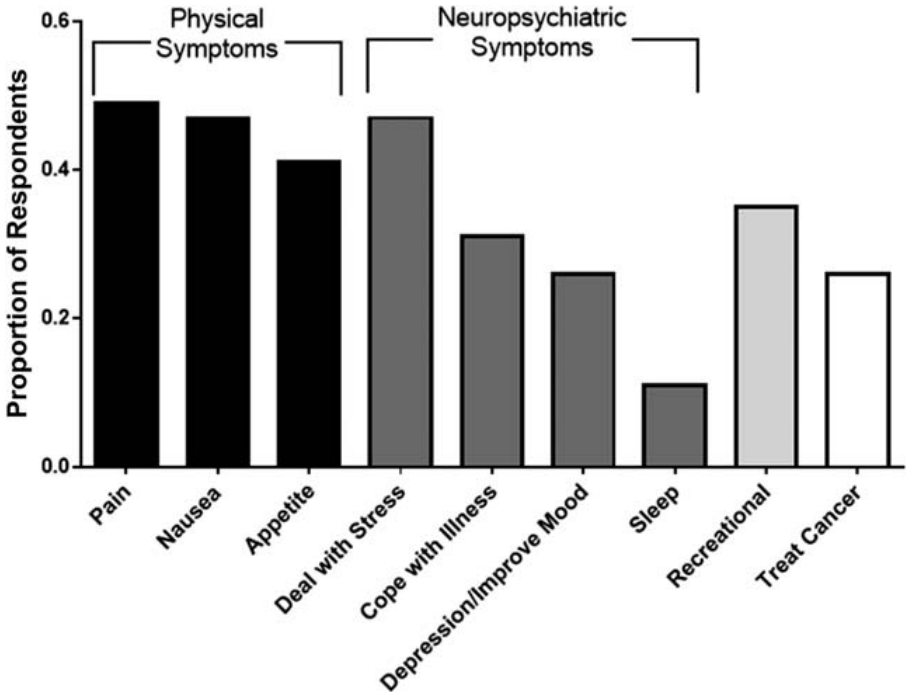

Figure 3. Reasons for cannabis use among the survey respondents. The reasons for use were not mutually exclusive responses. Overall, the respondents used cannabis for physical symptoms (165 of 219 [75%]), for neuropsychiatric symptoms (139 of 219 [63%]), recreationally (76 of 219 [35%]), and to treat cancer (58 of 219 [26%]).

Preferences

Table 2 Patient preferences for modes of delivery in a hypothetical clinical trial of medicinal cannabis for anorexia, appetite loss and taste change from advanced cancer (*n* = 204)

Preferred mode	*n*†	%†
Tablets or capsules	144	71
Mouth spray	84	42
Vaporiser	83	41
Eating	76	37
Drinking	68	33
Topical	53	26
Suppositories	16	8

†Participants could select >1 preference from the list given.

Guidance

Australian Government
Department of Health
Therapeutic Goods Administration

Guidance
for the use of
medicinal cannabis
in the treatment of
palliative care patients
in Australia

Version 1, December 2017

"Given the low number and generally poor quality of studies available to guide clinicians, it is recommended that patients be encouraged where possible to enrol in clinical trials of medicinal cannabis in palliative care"

Research Program – MRFF 2018

JOURNAL OF PALLIATIVE MEDICINE
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Mary Ann Liebert, Inc.
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Original Article

An Open-Label Pilot Study Testing the Feasibility of Assessing Total Symptom Burden in Trials of Cannabinoid Medications in Palliative Care

Phillip D. Good, MBBS, PhD,[1–3] Ristan M. Greer, PhD,[2]
Georgina E. Huggett, RN,[1,2] and Janet R. Hardy, BSc, MD[1,2]

Good et al. BMC Palliative Care (2019) 18:110
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BMC Palliative Care

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STUDY PROTOCOL Open Access

Oral medicinal cannabinoids to relieve symptom burden in the palliative care of patients with advanced cancer: a double-blind, placebo controlled, randomised clinical trial of efficacy and safety of cannabidiol (CBD)

Phillip Good[1*], Alison Haywood[2,3], Gauri Gogna[4], Jennifer Martin[5,6], Patsy Yates[7,8], Ristan Greer[9] and Janet Hardy[10]

2a. RCT of CBD oil vs placebo

-blinded, dose escalation

-73 participants in 17 months

Trials

2b. RCT of CBD/THC oil (10mg/ml) vs placebo

-blinded, dose escalation

- 23 participants in 10 months

STUDY PROTOCOL Open Access

Oral medicinal cannabinoids to relieve symptom burden in the palliative care of patients with advanced cancer: a double-blind, placebo-controlled, randomised clinical trial of efficacy and safety of 1:1 delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD)

Janet Hardy[1], Alison Haywood[2,3], Gauri Gogna[4], Jennifer Martin[5,6], Patsy Yates[7,8], Ristan Greer[9] and Phillip Good[10*]

Research Program – MRFF 2018

3. Qualitative study

-exploring the views of participants and non-participants towards medicinal cannabis

-25 on trial, 11 non-trial

1. Open Label

Objectives: pilot study to test protocol designed to assess dose tolerance and adverse effects of CBD and THC as single agents prior to definitive placebo controlled trials.

Aim: to target symptom burden as a whole

Design: prospective, two-arm, open label trial of escalating doses of CBD and THC oil.

Setting: palliative and Supportive Care service within Mater Health Services in Brisbane.

Participants: patients with advanced cancer and cancer-related symptoms.

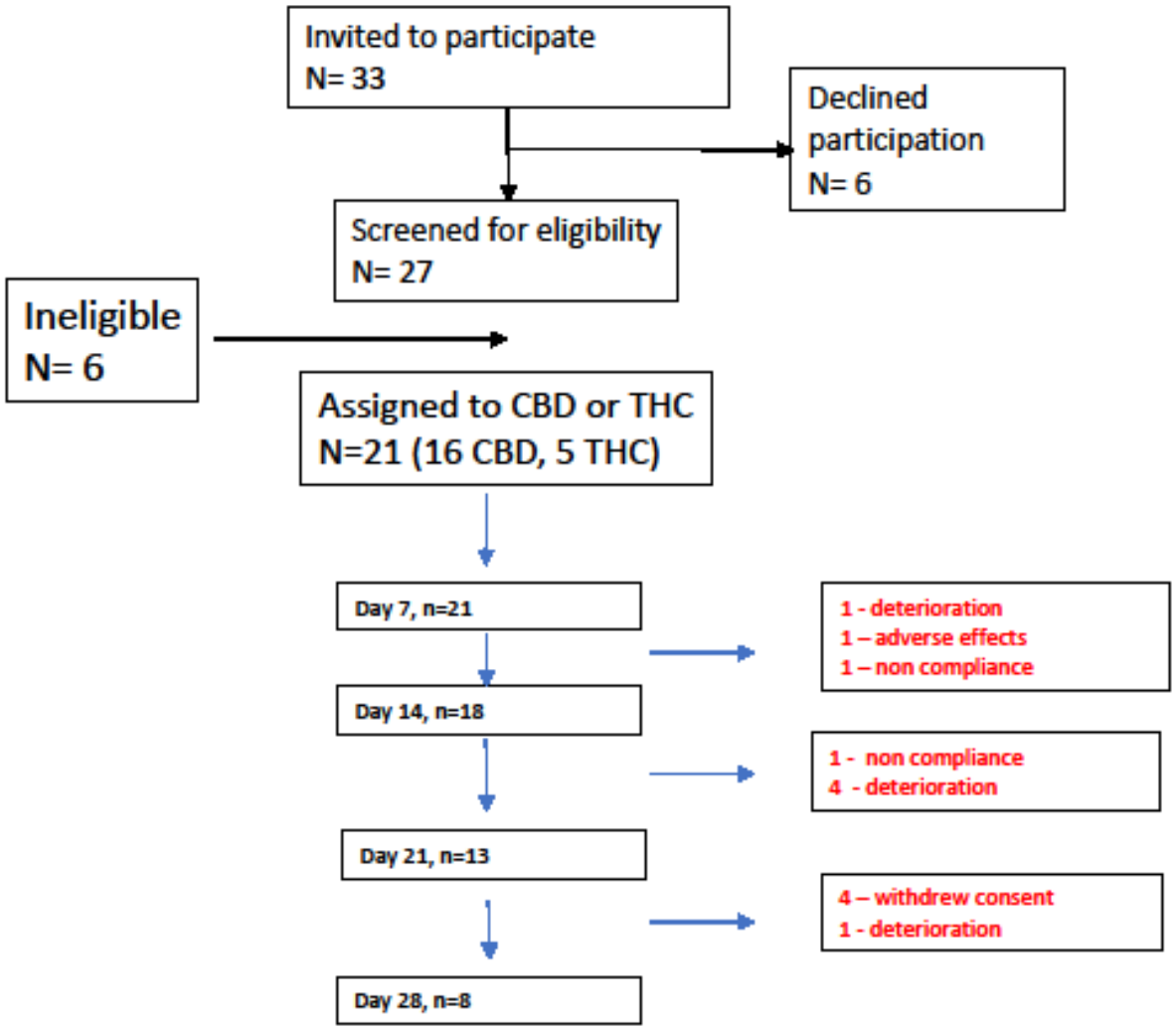
Main outcome research measures: change from baseline of the Total Symptom Distress Score (TSDS) as measured by the Edmonton Symptom Assessment Scale (ESAS) at day 14.

MODIFIED EDMONTON SYMPTOM ASSESSMENT SYSTEM (m-ESAS-Can)

Please circle the number that best describes how you felt over the past 24hrs:

No pain	0 1 2 3 4 5 6 7 8 9 10	Worst possible pain
Not tired	0 1 2 3 4 5 6 7 8 9 10	Worst possible tiredness
Not nauseated	0 1 2 3 4 5 6 7 8 9 10	Worst possible nausea
No shortness of breath	0 1 2 3 4 5 6 7 8 9 10	Worst possible shortness of breath
Not drowsy	0 1 2 3 4 5 6 7 8 9 10	Worst possible drowsiness
Best appetite	0 1 2 3 4 5 6 7 8 9 10	Worst possible appetite
Not anxious	0 1 2 3 4 5 6 7 8 9 10	Worst possible anxiety
Not depressed	0 1 2 3 4 5 6 7 8 9 10	Worst possible depression
Best feeling of wellbeing	0 1 2 3 4 5 6 7 8 9 10	Worst possible wellbeing

Figure 1. Consort diagram



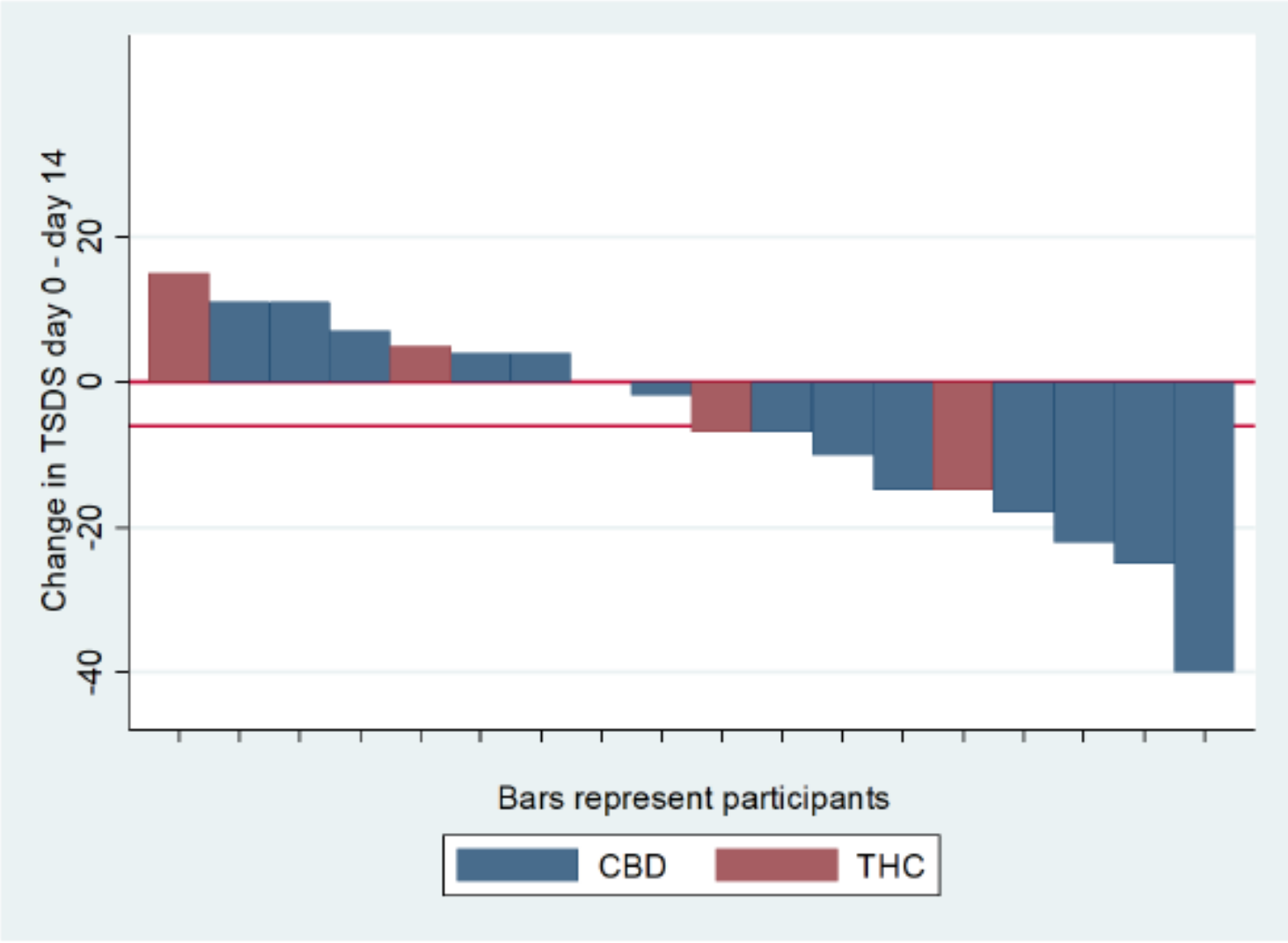
Baseline characteristics

Sex – M/F %	**33.3/66.7**
Age - mean, (SD)	57.5 (12.4) years
OME (median, range)	140mg (0-800mg)
THC urine test positive – N (%)	4 (19%)
Drug allocation – CBD/THC	16/5
AKPS (median, range)	70 (50-90)
TSDS (mean, SD, range)	41.1 (16.52, 14-64)
Cancer – n (%)	Breast 7 (33%) Prostate 4 (19%) Colorectal 3 (14%) Gynaecological 2 (10%) Pancreas 2 (10%) Haematological 1 (5%) Bone / soft tissue 1 (5%) Unknown Primary 1 (5%)

Results

- 21 participants enrolled (CBD, n=16; THC, n=5)
- 18 participants (86%) completed day 14.
- 9/ 21 (43%) met the definition of response (≥6 point reduction in TSDS).
- median maximum tolerated doses were – CBD, 300 mg/day (range 100 to 600mg); THC, 10 mg/day (range 5 to 30mg).
- mean (SD) change in ESAS TSDS from baseline to day 14 was -5.8 (14.7), n=18, p=0.11).
- significant decrease on the emotional ESAS sub scale (mean (SD) change -2.9 (4.6), n=18, p=0.01).
- no adverse event greater than grade 2 were reported.

Figure 2 – Waterfall plot of response per patient (n=18) at Day 14. The lower horizontal line represents a change in TSDS of -6, the defined primary endpoint of the study.



Changes in scores for individual ESAS items from day 0 to day 14 (n=18)

Variable	Mean change (95% CI)	Range
Pain	-0.61(-1.78 - 0.56)	-6 to 4
Tiredness	-0.17 (-1.50 - 1.17)	-8 to 6
Nausea	-0.56 (-1.91 - 0.79)	-5 to 6
Shortness of breath	-0.5 (-1.59 - 0.59)	-4 to 4
Drowsiness	0.22 (-0.92 - 1.37)	-4 to 5
Appetite	-0.94 (-1.90 - 0.01)	-4 to 2
Anxiety	-1.61 (-2.92 - -0.30)*	-7 to 3
Depression	-1.33 (-2.50, - -0.16)**	-8 to 3
Well being	-0.28 (-1.56 - 1.01)	-7 to 4

*p=0.02, **p=0.03

Impression of benefit, anxiety /depression and QoL (Day 14)

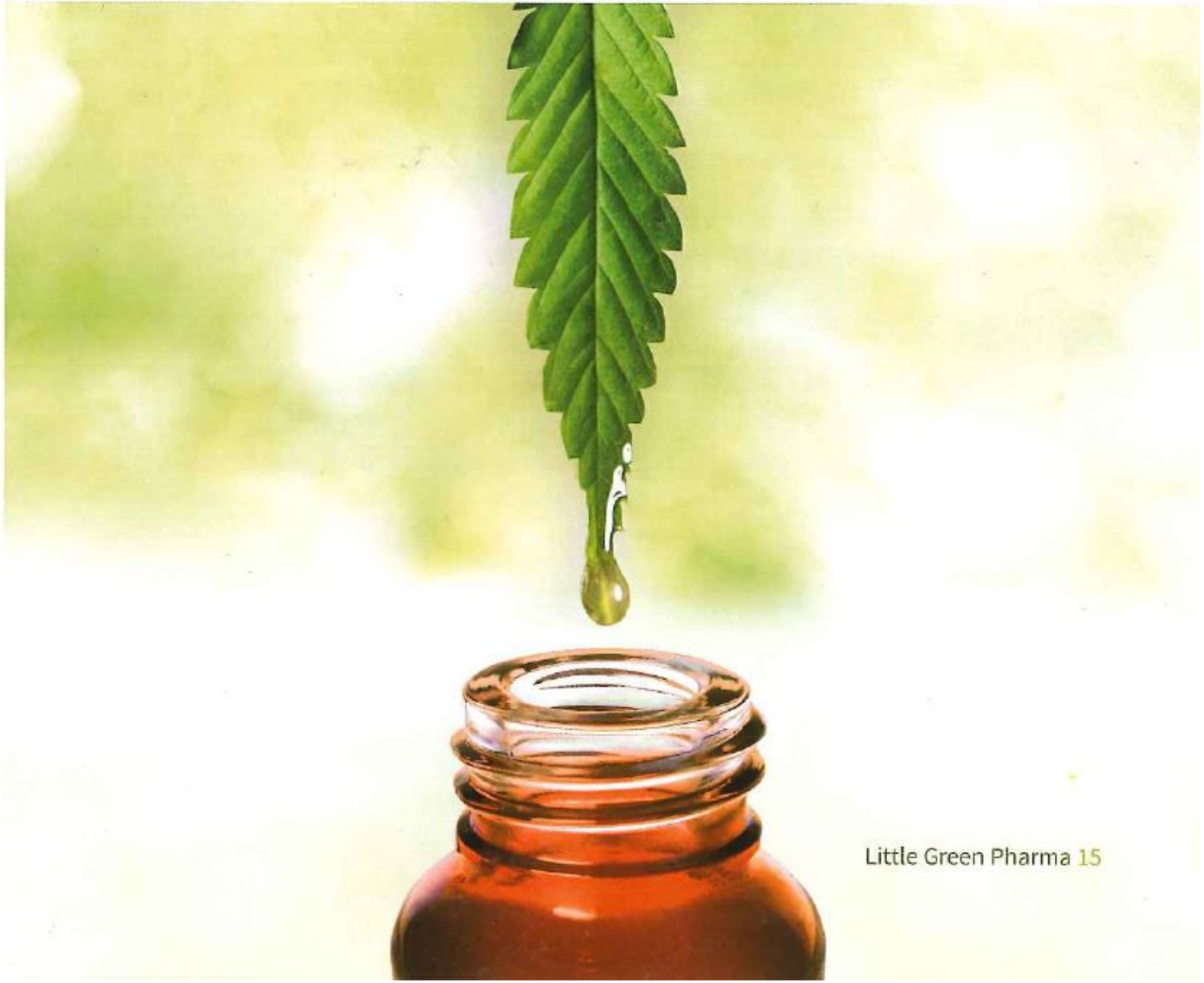
- 44.4% participants reported an overall improvement in their condition since starting cannabis.
- Clinician assessed scored 50% of patients as having had some improvement in their condition, with the remainder no change or worse.
- DASS-21 (17pp) median (range), baseline to Day 14
- Depression 3 (0-11) to 2 (0-18), p=0.04
- Stress score 6 (0-21) to 3 (0-20), p=0.046
- Anxiety score did not have a significant change
- Total scores - 13 (2-40) to 8 (0-50), p=0.047
- No change in overall quality of life as measured by the EORTC.

Number of Adverse Events graded worse than at baseline

Adverse Event[a]	Day 1-7	Day 8-14	Day 15-21	Day 22-28	Total: CBD and THC
Confusion	2	1	1		4
Somnolence	5	3	2	1	11
Personality change				1	1
Paranoia	1			1	2
Anxiety	2	2		1	5
Mood	1	3	0	2	6
Psychosis					0
Hypertension	1	3	2		6
Tachycardia	2	1	1		4
Sweating	1	1			2
Nausea	3	4			7
Vomiting	3	2	2	0	7
Abdominal Pain	3	3	0	0	6

Discussion

- Confirmed feasibility 86% were able to complete the primary outcome measure at Day 14
- The mean reduction in TSDS of 5.8 at day 14 suggests that our chosen outcome measure is appropriate
- A response rate of just under 50% is perhaps less than would have been anticipated in an open label study considering the anticipated placebo effect
- Improvement in emotional ESAS scores.
- The medication was generally well tolerated, the major adverse effect being drowsiness that seemed dose related and improved with a dose reduction.



Post-trial authorised prescriptions

- 53 participants completing day 28
- 23 (43%) requests for ongoing supplies
- GD-Cann C 100mg (CBD), NanaBis 8.33/8.33mg/mL (THC/CBD), NanaBidial 20/1mg/mL (CBD2THC),

  LG Classic 10/10mg/mL (THC/CBD),

  CannTrust 12.5/12.5mg/mL (THC/CBD
- cost issues

Authorised Prescriber

- GD Cann-C (MedCan1 study drug)

•(Cannabidiol 100mg/ml) – oil 25ml bottle

- LPG Classic 10:10 (MedCan2 study drug)

•(Tetrahydrocannabinol 10mg/ml : Cannabidiol 10mg/ml) – oil 50ml bottle

- LPG Classic 20:5

•(Tetrahydrocannabinol 20mg/ml : Cannabidiol 5mg/ml) – oil 50ml bottle

- NanaBis

•(Tetrahydrocannabinol 8.33mg/ml : Cannabidiol 8.33mg/ml) – Spray - 15ml bottle

- NanaBidial

•(Tetrahydrocannabinol 1mg/ml : Cannabidiol 20mg/ml) – Spray - 15ml bottle

- LGP Classic 50 (<0.2mg/50mg/ml THC/CBD) – 50ml bottle
- LGP Classic 1:20 (1mg/20mg THC/CBD) – 50ml bottle

ST VINCENT'S PRIVATE HOSPITAL
BRISBANE

Consent for unapproved therapeutic good use of Medicinal Cannabis

(Affix identification label here)

URN:

Family name:

Given name(s):

Date of birth: Sex: ☐ M ☐ F ☐ I

(A). Medicinal Cannabis Products

Product Name		
Contents	THC %	CBD %
Dose mg/day *(e.g 100mg BD)*		
Form *(e.g. oil, capsule)*		
Route		

(B). Potential Side Effects of Medicinal Cannabis

Treatment with medicinal cannabis can carry risks and side effects, including but not limited to:

Common

- Disorientation
- Dizziness
- Euphoria
- Confusion
- Drowsiness
- Dry mouth

Uncommon

- Depression
- Psychosis
- Allergic reaction *(hives, breathing difficulty)*

Less Common

- Somnolence *(sleepy)*
- Balance problems
- Hallucinations
- Nausea
- Paranoia
- Asthenia *(weakness)*
- Fatigue
- Anxiety
- Vomiting
- Diarrhoea
- Abdominal pain

(C). Informed Consent

- I, the patient understands, that the TGA has not evaluated the use of the unapproved good's safety, quality and efficacy in Australia
- I, the patient understand the possible benefits, risks and unknown side effects associated with its use
- I, the patient named on this form consent to the use of the named medicinal cannabis product
- I, the patient am aware the my doctor is required to report to the TGA on the progress of my treatment
- **I, the patient understand that I am not permitted to drive, attempt to put in motion, or be in charge of a motor vehicle and/or heavy machinery whilst using a product containing delta-9-tetrahydroccanabinol (THC), and that to do so constitutes an offence under section 79(2AA) of the transport Operations (Road Use Management) Act 1995**
  - *For more information*

    https://www.qld/gov.au/transprt/safety/road-safety/drink-driving/drugs/index.html

Name of patient. . . . . .

Signature. . . . . Date . . . . . .

I have explained the above information and I am of the opinion that the patients has understood the information sufficiently to give informed consent and agreement

Name of Doctor. . . . . .

Signature. . . . . Date . . . . . .

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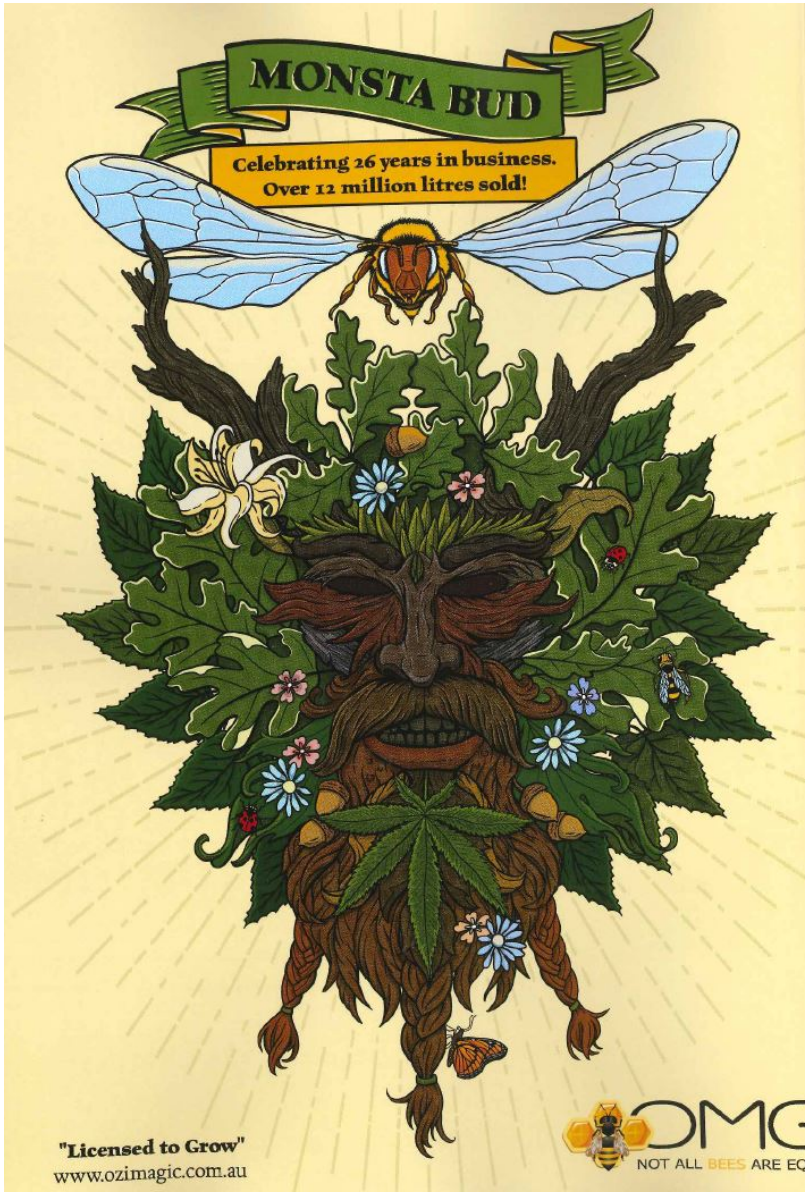
MedCan Post Trial (Medcan PT)

- Prospective audit of patients post trial on ongoing cannabis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