Current clinical trials of medicinal cannabis for cancer in Australia

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Visiting Medical Officer, Royal Prince Alfred Hospital, Sydney
Clinical Associate Professor, University of Sydney

Therapeutic Cancer Symposium
Medical Cannabis in the Cancer & Palliative Care Setting
Sir Charles Gairdner Hospital, Perth
19 October 2017
Personal introduction

• Staff Specialist in Medical Oncology
  • Chris O’Brien Lifehouse cancer hospital in Sydney
  • Focus on testis and upper gastrointestinal cancers
  • Also conduct outreach clinic in Dubbo, NSW
  • Coordinator of medical oncology training

• Clinical Associate Professor at University of Sydney (NHMRC Clinical Trials Centre)
  • PhD about quality of life assessment in cancer trials
  • Conduct national and international clinical trials of chemotherapy and supportive care for cancer, including anti-emetic trial for testis cancer
  • Lead a clinical trial of medicinal cannabis funded by NSW Health to prevent nausea and vomiting due to chemotherapy

• Member of Pharmaceutical Benefits Advisory Committee
  • Provide advice to Australian Government on medicines to be funded by PBS
What I will cover today

• Overview of medicinal cannabis for cancer care
  • History
  • Products and their mechanism of effect
  • Current evidence for use

• Importance of clinical trials of medical cannabis for cancer

• Current and planned clinical trials for cancer in Australia
History of cannabis as a medicine for cancer

• First reported medical use > 3000 years ago
• Siberian Ice Maiden: 5th century BC
• Traditional Indian medicine
  • Analgesic, sedative, anxiolytic, appetite introduced into UK by O’Shaughnessy in 1842
  • British physician working in India
  • Analgesic, anti-convulsant
• Fell out of favour in 1930s
  • Plant material too variable
  • Shelf-life short and unpredictable
  • Replaced by pure opiates and more reliable synthetic drugs
• Removed from UK/US Pharmacopeia 1932 & ’41
  • Prohibition 1930s

Kalant Pain Res Manage 2001
Resurgence in interest in cannabis as treatment for cancer over last 20 years

• Non-legal use in community: anecdotes

• Research since 1980s (esp. Israel)
  • Identified endogenous cannabinoids with influence on neurologic, immune, gastro-intestinal systems

• Synthetic THC developed
  • FDA approved: nausea and vomiting due to chemotherapy
  • Dronabinol 1986 (*also AIDS anorexia*, Nabilone 2010)

• Compassionate use allowed
  • California 1996 ... ... NSW 2014 (terminal illness)

• Clinical trials launched in NSW 2015

• **Medical** prescribing permitted in Australia 2016
Medline-indexed publications on cannabis or cannabinoids AND cancer have increased dramatically since 1970.

![Graph showing the increase in number of papers from 1970 to 2017. The number of papers increases significantly from 1990 onwards, peaking in 2017.]
Cannabis contains over 400 chemical compounds

- THC (psychoactive)
  - high affinity for CB1/CB2
  - plant: wide variation in concentration

- Cannabidiol (CBD)
  - low affinity for CB1/CB2 (agonist/antagonist)
  - counteracts psychoactive effects of THC
  - anxiolytic, anti-psychotic, analgesic (? due to anti-convulsant effect)

- Both highly lipid soluble
Cannabis may be endogenous, synthetic or derived from plants

- **Endogenous:** Endocannabinoids - *anandamide*
  - alter intracellular signalling
  - ? function is to modulate pain response

- **Synthetic cannabinoids**
  - synthetic THC: dronabinol, nabilone
  - many other forms (mostly illicit)

- **Phytocannabinoids**
  - derived from plants: Cannabis sativa
  - dried leaves and flowering heads (marijuana)
    - also resin of upper leaves & flowering beds (hashish)
Forms of phytocannabinoids (plant-derived cannabis)

• Inhaled leaf (smoked or vaporized)
  • *rapid onset but short duration* (2-4 hrs)
• Buccal spray: Nabiximols (*Sativex*)
  • 1:1 THC:CBD, *TGA registered for MS*

• Ingested forms
  • cannabis oil
  • oral drops
  • oral capsule (liposomal formulation)
  • *onset 30-90 mins, duration 4-12 hrs*

• Concentration of THC, CBD, other constituents vary widely but customisable
What is medical cannabis?

• TGA definition
  • therapeutic good containing $\geq 1\%$ THC, $\geq 2\%$ other cannabinoid
  • active ingredient manufactured only from cannabis plant
  • identifiable plant (macro, micro, chromatographic)
  • unadulterated
  • average content 90-110\% of stated
  • maintains standards of a therapeutic (European Pharmacopoeia)
    • known composition, likely effects (and side effects), activity in the body, patterns of excretion

• Prescribing restrictions
  • S8 if THC content $\geq 2\%$, S4 if THC content $< 2\%$

• Availability in Australia
  • Nabiximols (*Sativex*) is only TGA-approved product
  • SAS: Other commercial products for leaf, buccal, ingested forms

*TGA: Therapeutic Goods Order No. 93 (Standard for Medicinal Cannabis*
How cannabinoids work: $\text{CB}_1$ receptors focussed in brain & GI tract, $\text{CB}_2$ receptors in immune system

Expression of Cannabinoid Receptors

- $\text{CB}_1$ mRNA
  - Cortex, hippocampus
  - Basal ganglia
  - Hypothalamus
  - Cerebellum
  - Spinal cord
  - Dorsal root ganglia
  - Enteric nervous system
  - Adipocytes
  - Gastrointestinal tract
  - Endothelial cells
  - Liver

$\text{CB}_2$
- Expressed in immune cells and tissues: T cells, B cells, spleen, tonsil, and activated microglial cells

Medscape.com
How cannabinoids work: postulated non-psychototropic effects

Izzo et al. 2009
Medicinal cannabis for cancer care: How it could help cancer patients

• Relieve symptoms and improve quality of life
  • Chemotherapy-induced nausea and vomiting
  • Appetite stimulant & weight gain
  • Pain

• Control or cure cancer

• Anecdotes abound

• Current evidence is limited
Current evidence - nausea

“Cannabis-based medications may be useful for treating refractory chemotherapy-induced nausea and vomiting. However, methodological limitations of the trials limit our conclusions and further research reflecting current chemotherapy regimens and newer anti-emetic drugs is likely to modify these conclusions.”

Current evidence - nausea

- Early studies using smoked marijuana or oral THC
  - show limited efficacy
  - significant CNS adverse events at higher doses required to control chemotherapy-induced nausea and vomiting
  - compared cannabis-derived medicines to out-dated anti-emetic regimes or were too small to definitely influence clinical practice
Current evidence – chronic pain

Systematic review: Whiting et al JAMA June 2015

Figure 2. Improvement in Pain

### Cannabinoid vs Placebo by Study

<table>
<thead>
<tr>
<th>Study</th>
<th>Cannabinoid Events</th>
<th>Placebo Events</th>
<th>Odds Ratio (95% CI)</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abrams et al, 2007</td>
<td>13</td>
<td>6</td>
<td>3.43 (1.03-11.48)</td>
<td>6.51</td>
</tr>
<tr>
<td>Nabiximols</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GW Pharmaceuticals, 2005</td>
<td>54</td>
<td>59</td>
<td>0.86 (0.54-1.37)</td>
<td>19.02</td>
</tr>
<tr>
<td>Johnson et al, 2010</td>
<td>23</td>
<td>12</td>
<td>2.81 (1.22-6.50)</td>
<td>10.87</td>
</tr>
<tr>
<td>Langford et al, 2013</td>
<td>84</td>
<td>77</td>
<td>1.25 (0.81-1.91)</td>
<td>20.19</td>
</tr>
<tr>
<td>Nurmikko et al, 2007</td>
<td>16</td>
<td>9</td>
<td>2.00 (0.81-4.96)</td>
<td>9.84</td>
</tr>
<tr>
<td>Portenoy et al, 2012</td>
<td>22</td>
<td>24</td>
<td>0.90 (0.46-1.76)</td>
<td>14.04</td>
</tr>
<tr>
<td>Selvarajah et al, 2010</td>
<td>8</td>
<td>9</td>
<td>0.63 (0.14-2.82)</td>
<td>4.63</td>
</tr>
<tr>
<td>Serpell et al, 2014</td>
<td>34</td>
<td>19</td>
<td>1.97 (1.05-3.70)</td>
<td>14.91</td>
</tr>
<tr>
<td>Subtotal $I^2 = 44.5%, (P = .94)$</td>
<td>241</td>
<td>209</td>
<td>1.32 (0.94-1.86)</td>
<td>93.49</td>
</tr>
<tr>
<td>Overall $I^2 = 47.6%, (P = .64)$</td>
<td>254</td>
<td>215</td>
<td>1.41 (0.99-2.00)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Odds indicate 30% or greater improvement in pain with cannabinoid compared with placebo, stratified according to cannabinoid. The square data markers indicate odds ratios (ORs) from primary studies, with sizes reflecting the statistical weight of the study using random-effects meta-analysis. The horizontal lines indicate 95% CIs. The blue diamond data markers represent the subtotal and overall OR and 95% CI. The vertical dashed line shows the summary effect estimate, the dotted shows the line of no effect (OR = 1).
Current evidence – Anorexia - beneficial in HIV, very limited studies in cancer

**TABLE 3. Effect of Smoked Marijuana on Appetite and Weight Loss**

<table>
<thead>
<tr>
<th>STUDY</th>
<th>DESIGN</th>
<th>SUBJECTS</th>
<th>N</th>
<th>HOW ADMINISTERED</th>
<th>CONTROL</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foltin 1986(^1)</td>
<td>RCT/crossover</td>
<td>Healthy volunteers</td>
<td>9</td>
<td>Smoked</td>
<td>Placebo</td>
<td>Single marijuana cigarette had no effect on caloric intake, but 2 to 3 cigarettes were found to increase the average daily caloric intake</td>
</tr>
<tr>
<td>Hart 2002(^2)</td>
<td>Staggered double-dummy</td>
<td>Healthy marijuana smokers</td>
<td>11</td>
<td>Smoked</td>
<td>Oral THC and placebo</td>
<td>Both smoked marijuana and oral THC were found to increase food intake</td>
</tr>
<tr>
<td>Woolridge 2005(^3)</td>
<td>Cross-sectional questionnaire</td>
<td>HIV-positive outpatients</td>
<td>523</td>
<td></td>
<td></td>
<td>27% of patients surveyed used marijuana; 97% reported that marijuana improved appetite</td>
</tr>
<tr>
<td>Haney 2005(^4)</td>
<td>Staggered double-dummy</td>
<td>HIV-positive marijuana smokers with and without muscle wasting</td>
<td>30 (15 in each group)</td>
<td>Smoked</td>
<td>Oral THC and placebo</td>
<td>Smoked marijuana and oral THC improved caloric intake compared with placebo in the group with muscle wasting but not in the group without muscle wasting</td>
</tr>
<tr>
<td>Haney 2007(^5)</td>
<td>RCT/crossover</td>
<td>HIV-positive marijuana smokers</td>
<td>10</td>
<td>Smoked</td>
<td>Oral THC and placebo</td>
<td>Smoked marijuana and oral THC increased caloric intake and weight in a dose-dependent manner compared with placebo</td>
</tr>
</tbody>
</table>

Dronabinol
HIV - Comparable to smoked marijuana
Cancer – less effective than megestrol acetate
Marijuana Cures Cancer in 8 Month Old Baby

"My youngest patient, 8 months old, had a massive inoperable brain tumor"

The father chose cannabis treatment over chemotherapy, radiation and surgery

"The child's being called a miracle baby and I would have to agree that this is the perfect response that we should be insisting is frontline therapy for all children"

This child is not going to have long term side effects that come with chemotherapy and radiation

Kristina Marie was diagnosed with a terminal brain tumor

She refused Chemo and opts for Cannabis oil that is shrinking the tumor!

"The doctors told me I was going to die"

- Darren Miller

See what happened next...
Current evidence – anti-tumour effects
- NIH summary of laboratory/animal/preclinical studies

- Cannabinoids may cause anti-tumour effects by various mechanisms
  - induction of cell death and inhibition of cell growth
  - inhibition of tumour angiogenesis, invasion and metastasis

- Evidence of potential anti-tumour effects in cell cultures/xenografts
  - glioma, hepatocellular carcinoma, non-small cell lung cancer and breast cancer

- CBD may also enhance uptake of cytotoxic drugs into malignant cells
  - shown in mouse models of glioma

- Only 1 human study (Spanish, n=9)
  - patients with glioblastoma multiforme (GBM)
  - THC directly infused into tumour daily by subcutaneous catheter
  - small numbers and non randomised design
  - established safety but no conclusions re efficacy
    - Guzmán et al, Br J Cancer 2006
Adverse effects of cannabis

• Low-dose
  • mild euphoria, relaxation, sociability, reduced anxiety
  • temporal slowing

• High-dose
  • agitation, anxiety, depersonalisation
  • dry mouth and eyes
  • tachycardia
  • psychomotor function impairment
  • paranoia, hallucinations, psychosis

• Long-term
  • possible impaired verbal reasoning, memory, attention
  • addictive potential (< opioids), mild withdrawal syndrome
Current and planned research in Australia

1. Chemotherapy-induced nausea and vomiting
2. Anorexia in advanced cancer
3. Refractory advanced cancer
4. Gliomas
NSW government-sponsored clinical trial of a cannabis product for drug-resistant chemotherapy induced nausea and vomiting (CINV)

*Lead Investigator:*  
Clinical Associate Professor Peter Grimison  
Chris O’Brien Lifehouse and  
NHMRC Clinical Trials Centre, University of Sydney

*Sponsor:* University of Sydney

*Funding:* NSW Health

*Drug supply:* Tilray
About half of patients receiving chemotherapy of moderate or high emetic risk still experience significant nausea and/or vomiting despite optimal anti-emetic prophylaxis.

<table>
<thead>
<tr>
<th>STUDY</th>
<th>Aapro</th>
<th>Gilmore</th>
<th>Molassiotis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Setting</td>
<td>Europe</td>
<td>USA</td>
<td>UK</td>
</tr>
<tr>
<td>N</td>
<td>287</td>
<td>742</td>
<td>102</td>
</tr>
<tr>
<td>No emesis</td>
<td>63%</td>
<td>91%</td>
<td>79%</td>
</tr>
<tr>
<td>No nausea</td>
<td>48%</td>
<td>54%</td>
<td>43%</td>
</tr>
<tr>
<td>Complete response</td>
<td>60%</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Aapro, Ann Onc 2012; Gilmore, JOP 2014; Molassiotis, Supp Care Ca 2008
Preliminary data suggests preparations rich in cannabidiol (CBD) rather than THC may be effective and better tolerated

- CBD counteracts psychiatric effects of THC and has inherent anti-anxiety properties

- A preliminary RCT showed significant benefit of THC/CBD (Duran et al, 2010)
  - Addition of a spray containing THC and CBD in equal amounts to a standard anti-emetic regimen (Nabiximols, Sativex, GW Pharmaceuticals)
  - Improvement in complete response of CINV from 22% to 71%
  - Well tolerated despite transient psychiatric side effects
  - This data needs to be confirmed in a definitive RCT using a preparation available in Australia
Summary of trial design

• Pilot and definitive randomised double-blind placebo-controlled trials evaluating an oral cannabinoid-rich THC/CBD cannabis extract for secondary prevention of chemotherapy-induced nausea and vomiting
Study drug is oral THC/CBD

• Proprietary formulation (*Tilray*)
  • Oral capsule containing THC and CBD in 1:1 ratio
  • Aims to have similar pharmacokinetic properties to Nabiximols (*Sativex, GW Pharmaceuticals*)

• Initial doses administered in chemotherapy suite
• If well-tolerated then continue tds for 5 days at home
• Titrate to nausea control and adverse effects
• Daily telephone support, clinic review after day 5
Summary of pilot trial

Pilot double-blind randomised crossover phase 2 trial (n=80)

- Duration of accrual: 12 months
- Minimum duration of follow-up: 30 days after last study drug

Opportunity for post-study compassionate supply if preferred drug was study drug
Summary of definitive trial

Definitive double-blind placebo-controlled randomised parallel phase 3 trial (n=250)

- Duration of accrual: 2.5 years
- Minimum duration of follow-up: 30 days after last study drug
Summary of trial eligibility and endpoints

Eligibility:
Patients aged ≥ 18 years with known malignancy of any stage
Receiving moderate-to-highly emetogenic intravenous chemotherapy
Requiring ≥ 1 further cycles of chemotherapy
Experiencing significant CINV during previous cycle

Endpoints:
Complete response  Acceptability  Cost-effectiveness  
Adverse events  Resource use and costs  Pharmacokinetics  
Quality of life  Translational

Study powered to detect improvement in complete response from 22% to 42%

Aim to produce high quality data regarding effectiveness, cost-effectiveness, and safety that could be used in Australian regulatory and funding submissions
Key Exclusion Criteria

- Other causes of nausea and vomiting
  - Symptomatic CNS malignancy
  - Symptomatic gastrointestinal obstruction
  - Disease-related nausea and vomiting
  - Oral cytotoxic chemotherapy
  - Radiotherapy within 1 week of commencing therapy

- Contraindication to cannabinoid treatment
  - Unstable cardiac disease
  - History of epilepsy/recurrent seizures
  - History of schizophrenia, psychosis, severe personality disorder, suicidal ideation, or other significant psychiatric disorder (depression associated with underlying condition is OK)
  - Substance use disorder

- Unwilling/unable to refrain from driving and operating heavy machinery during study treatment and for 72 hours after last dose
Research team is a strong cross-disciplinary, multi-site, public-private, metropolitan-rural collaboration between leading academic researchers and consumers

<table>
<thead>
<tr>
<th>Collaborator</th>
<th>Investigators</th>
<th>Discipline/area of expertise</th>
<th>Role/Responsibilities</th>
</tr>
</thead>
</table>
| Chris O’Brien Lifehouse                          | Grimison Simes Stockler Horvath (HOD)          | Cancer Centre:                                    | • Lead investigator  
. Patient recruitment |  
|                                                  |                                                | - Medical Oncology                                 |                                                            |  
|                                                  |                                                | - Clinical trials                                 |                                                            |  
| Lambert Initiative for Cannabinoid Therapeutics, | Lintzeris McGregor Allsop Haber Dawson         | Clinical Trials Research                           | •Coordinate supply of study drug and placebo                |  
| University of Sydney                             |                                                | Psycho-pharmacology Pharmacovigilance Toxicology | • Protocol development                                     |  
|                                                  |                                                |                                                  | • Urine/blood kits & analyses                              |  
| NHMRC Clinical Trials Centre                     | Simes Stockler Grimison Wong Walsh              | Clinical Trials Research                           | Central coordinating centre:  
. Protocol development                                     |  
|                                                  |                                                |                                                  | . Feasibility assessment                                   |  
|                                                  |                                                |                                                  | . Site initiation                                           |  
|                                                  |                                                |                                                  | . Study management &                                        |  
|                                                  |                                                |                                                  | . Coordination                                              |  
|                                                  |                                                |                                                  | . Data management                                           |  
|                                                  |                                                |                                                  | . Quality assurance                                        |  
|                                                  |                                                |                                                  | . Statistical analysis                                     |  
|                                                  |                                                |                                                  | . Reporting, publication                                   |  

Research team is a strong cross-disciplinary, multi-site, public-private, metropolitan-rural collaboration between leading academic researchers and consumers

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</tr>
</thead>
</table>
| Calvary Mater Newcastle                          | Gedye         | Cancer Centre: - Medical Oncology - Clinical trials - Pharmacogenomics | • Patient recruitment  
• Pharmacogenomics                                               |
| University of SA                                 | Olver         | External expert on CINV trials                     | • Expert advice on study design & conduct                   |
| Chris O’Brien Lifehouse – Lifehouse Partnership Council | Hahn          | Consumer Advocacy & Review                          | Consumer advisory panel:  
• Input into protocol and PICF forms  
• Input into trial management, materials, reporting, publication and promotion. |
| Associated hospitals                             | Various       | Cancer Centre: - Medical Oncology - Clinical trials | Patient recruitment                                          |
NSW cancer centres are participating, with aim to recruit 330 patients over 3.5 years

- Chris O’Brien Lifehouse, and 9 other NSW metropolitan and rural sites
- Pilot study commenced recruitment in Nov 2016
  - Data safety and monitoring committee – no concerns
- Timeline predicts trial completion in 2020
Medicinal Cannabis for Anorexia in Advanced Cancer

Phase I/II dose-ranging study of the pharmacokinetics, dose-response parameters, and feasibility of vaporised botanical cannabis flower bud in advanced cancer

Lead Investigator:
Professor Meera Agar
Ingham Institute of Applied Medical Research, Sydney and Palliative Care Clinical Studies Collaborative (PaCCSC)

Sponsor: University of New South Wales
Funding: NSW Health

Drug supply: Bedrocan (Netherlands)

Sources:
https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=369767&isReview=true
Summary of study design for part 1

• Part 1 (currently enrolling)
  • enrol about 30 patients with advanced cancer
  • phase 1/2 design

• Objectives
  • Can a potential cannabis product be successfully given to patients by inhaling it as a vapour?
  • Is the potential cannabis product well tolerated by patients, that is, does it cause any unwanted side effects?
  • What is the ideal dose of the potential cannabis product and how often should it be given?

Sources:
https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=369767&isReview=true
Summary of study design for part 2

• Part 2 (proposed)
  • enrol about 250 patients with advanced cancer
  • phase 3 double-blind randomised placebo-controlled trial

• Objectives
  • Definitive information re efficacy and safety

Sources:
https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=369767&isReview=true
Study drug is vaporised cannabis flower bud

- **Bedrobinol (*Bedrocan BV*)**
  - Vaporised cannabis flower bud containing 13.5% THC and < 1% CBD
  - doses escalated every 1-2 days
    - mixed with placebo cannabis (terpene) to maintain consistent weight

- Administered at varying doses
  - one hour before meals, three times a day
  - for seven days unless side effects occur

Sources:
https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=369767&isReview=true
Key eligibility criteria

• Inclusion criteria
  • Advanced cancer
  • Anorexia for at least 2 weeks (appetite ≤ 4/10) despite treatment of cause
  • Age 18 years or above
  • Karnofsky performance status ≥ 40

• Exclusion criteria
  • Significant liver, renal or cardiac impairment
  • Cognitive impairment
  • Psychiatric disorders: severe depression or anxiety, personality disorder, history of psychosis, schizophrenia, and/or suicidal ideation
  • Acute delirium
  • Impaired pulmonary function which prohibits use of vaporiser
  • Abuse, dependence to alcohol, opioids, benzodiazepines or simulants
  • Recent use of cannabis or cannabinoids within < 30 days

Sources:
https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=369767&isReview=true
Assessments

• Pharmacokinetics (THC, CBD)
  • blood samples taken at 1, 5, 20, 40 and 60 minutes and 4 hours post inhalation after morning dose at each dose level

• Assessment of appetite, mood, quality of life
  • Questionnaires about hunger, satiety, quality of life, mood
    • FACT; SLIM; hunger, taste & smell survey; PHQ-9 and GAD-7
  • daily food record: MyFitnessPal
  • adverse effects
    • patient self-report, medical by NCI CTCAE
  • Health resource usage

• Feasibility

Sources:
https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=369767&isReview=true
NSW cancer centres are participating

• Part 1 of study (n=30) commenced recruitment in early 2017 for hospital inpatients
  • Sacred Heart Health Service in Sydney and Calvary Mater Newcastle hospital in NSW currently recruiting

• Part 2 of study (n=250) planned to commence in early 2018 in community
  • Multiple sites across NSW planned
Oral THC/CBD for treatment of refractory advanced cancer

Lead organisation: Olivia Newton-John Cancer Wellness & Research Centre

Funding: Pending

Drug supply: Cann Group (Australia)

Source:
Prof Niall Tebbutt, Olivia Newton-John Cancer Wellness & Research Centre
Summary of study design

• Double-blind randomised trial
  • 2:1 randomisation to THC/CBD or matching placebo

• Sample size of 100 patients
  • Detect reduction in proportion with > 10 point of global health status from 75% to < 45%

• Key eligibility criteria
  • Advanced cancer refractory to standard therapies
    • any tumour type/any histology
  • ECOG performance status of 0 to 2
  • Life expectancy of > 3 months

Source:
Prof Niall Tebbutt, Olivia Newton-John Cancer Wellness & Research Centre
Study drug is oral capsule containing 1:1 THC and CBD

• Cann Group
  • Oral capsule 5mg THC: 5mg CBD

• Daily administration
  • option to escalate; de escalate dosing depending on toxicity

Source:
Prof Niall Tebbutt, Olivia Newton-John Cancer Wellness & Research Centre
Study objectives

• Primary endpoint:
  • Overall quality of life

• Secondary endpoints
  • Use of other medications for symptom control: opioids/anti emetics
  • Toxicity
  • Tumour response rate
  • Progression free survival
  • Overall survival

Source: Prof Niall Tebbutt, Olivia Newton-John Cancer Wellness & Research Centre
Progress

- Planned to recruit 100 patients over 2 years at Olivia Newton-John Cancer Wellness & Research Centre

- *Awaiting funding*

*Source: Prof Niall Tebbutt, Olivia Newton-John Cancer Wellness & Research Centre*
Pilot trial assessing efficacy and safety of medicinal cannabis in patients with gliomas

*Sponsor:* Endeavour College of Natural Health, Brisbane

*Funding:* Commercial

*Drug supply:* FIT-Bioceuticals (overseas supply)

Summary of study

• Study population
  • Recurrent gliomas

• Pilot randomised trial
  • 120 patients

• Study drug is oral cannabis oil given at night
  • Arm 1 – 1:1 THC:CBD + standard treatment for 12 weeks
  • Arm 2 – 4:1 THC:CBD + standard treatment for 12 weeks
  • both arms allow dose escalation and titration

• Each arm compared to a self-selected control group

• Primary outcome: progression-free survival

Source: https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=373556&isReview=true
Progress

• Remains provisional
• Recruitment planned at Prince of Wales Hospital, Randwick
Summary of current and planned research in Australia

1. Chemotherapy-induced nausea and vomiting
2. Anorexia in advanced cancer
3. Refractory advanced cancer
4. Gliomas
Why do we need to do clinical trials of medicinal cannabis for cancer?

- Unmet need in cancer: symptoms (nausea, pain, anorexia), anti-cancer
- Preliminary evidence of benefit
  - particularly for chemotherapy-induced nausea and vomiting
  - also anorexia, anti-tumour effects (glioma)
- Community demand *driven by*
  - anecdotal reports and commercial interests
  - high use of non-sanctioned products
- Despite recent legislation and community demand, very little use of prescription medical cannabis in Australia
  - no widely available TGA-registered products
  - health departments reluctant to grant widespread approval
  - most doctors reticent to prescribe (lack of education, scepticism, reputation, paperwork)
  - unfunded
Why do we need to do clinical trials of medicinal cannabis for cancer?

• If high quality clinical trials prove that medical cannabis is helpful for cancer, then this could provide:
  • Evidence to support approval by the Therapeutics Goods Administration (TGA)
  • More confidence for state health departments and hospitals to more readily approve use of medical cannabis
  • Confidence by doctors to prescribe, and patients to use medical cannabis
  • Funding
What I have covered today

• Overview of medicinal cannabis for cancer care
  • History
  • Products and their mechanism of effect
  • Current evidence for use

• Importance of clinical trials of medical cannabis for cancer

• Current and planned clinical trials for cancer in Australia