
**Oral THC:CBD cannabis extract for refractory chemotherapy-induced nausea and vomiting (CINV): a randomised, placebo-controlled, phase 2 crossover trial**

P Grimison 1, A Mersiades 2, A Kirby 2, N Lintzeris 3, R Morton 2, P Haber 4, I Olver 5, A Walsh 2, I McGregor 6, Y Cheung 2, A Tognela 7, C Hahn 8, K Briscoe 9, M Aghmesheh 10, P Fox 11, E Abd 12, S Clarke 13, S Della-Fiorentina 14, J Shannon 15, C Gedye 15, S Begbie 16, J Simes 2, M Stockler 2

Affiliations

**Abstract**

**Background:** This multi-centre, randomised, double-blinded, placebo-controlled, phase 2/3 trial is aimed to evaluate an oral THC:CBD cannabis extract for prevention of refractory CINV. Here we report the phase 2 component results.

**Patients and methods:** Eligible patients experienced CINV during moderate-highly emetogenic intravenous chemotherapy despite guideline-consistent anti-emetic prophylaxis. Study treatment consisted of 1 cycle of 1-4 self-titrated capsules oral THC 2.5mg:CBD 2.5mg (TN-TC11M) three times daily, days 1 to 5 and 1 cycle of matching placebo in a crossover design, then blinded patient preference for a 3rd cycle. The primary endpoint was the proportion of participants with complete response during 0-120 hours from chemotherapy. 80 participants provided 80% power to detect a 20% absolute improvement with a 2-sided p-value of 0.1.

**Results:** 81 participants were randomised; 72 completing 2 cycles are included in the efficacy analyses and 78 not withdrawing consent are included in safety analyses. Median age was 56 years (range 29-80). 78% were female. Complete response was improved with THC:CBD from 14% to 25% (RR 1.77, 90% CI 1.12, 2.79, P = 0.041), with similar effects on absence of emesis, use of rescue medications, absence of significant nausea, and summary scores for the Functional Living Index-Emsis (FLIE). 31% experienced moderate or severe cannabinoid-related adverse events such as sedation, dizziness, disorientation; but 83% of participants preferred cannabis to placebo. No serious adverse events were attributed to THC:CBD.

**Conclusion:** The addition of oral THC:CBD to standard anti-emetics was associated with less nausea and vomiting but additional side effects. Most participants preferred THC:CBD to placebo. Based on these promising results, we plan to recruit an additional 170 participants to complete accrual for the definitive, phase 3, parallel group analysis.