(420) Demonstration of the safety and efficacy of CL-108 for moderate-to-severe pain with reduction of opioid-induced nausea and vomiting

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Opioid-induced nausea and vomiting (OINV) are the most common side effects of opioids used to treat moderate-to-severe acute pain. CL-108 [hydrocodone 7.5 mg/ acetaminophen 325 mg (HC/APAP) with promethazine 12.5 mg] is being developed as a strong analgesic with less OINV. We designed a randomized, double-blind trial to evaluate the analgesic efficacy of CL-108 compared to placebo (pbo) and the reduction of OINV compared to HC/APAP. The study was enriched by identifying adults with a propensity for nausea by history (on the Nausea-Prone Questionnaire) and/or direct observation after known pharmacologic exposure (on the Hydrocodone Challenge). After surgical removal of ≥ 2 impacted molar teeth, patients rated pain intensity on a categorical scale (PI-CAT). Patients with moderate or severe pain were randomly allocated to CL-108, HC/APAP, or pbo and used the PI-CAT hourly over 24 hours with nausea measured on a Nausea Intensity Scale and vomiting on a Vomiting Frequency Scale. They used Opioid Symptom Scales to evaluate other opioid side effects (eg, itchiness, dry mouth, dizziness, drowsiness, constipation). Patients remedicated every 4-6 hours and/or took supplementary analgesic or antiemetic as needed. Primary endpoints were $SPID_{24}$ (for analgesia) and a composite OINV prevention endpoint (no moderate/severe nausea, vomiting, or antiemetic use over 24 hours). 466 nausea-prone patients were evenly distributed among the treatment groups. Patients who used CL-108 reported significantly greater pain reduction (16.3) compared to pbo (3.2) and OINV incidence was significantly greater in patients who received HC/APAP than CL-108 (OR: 2.7; 95% CI: 1.8-4.1) (both $p < 0.01$). There were no differences between CL-108 and HC/APAP for other opioid-related side effects, no evidence of respiratory depression, and no serious adverse events. We conclude that CL-108 is a safe, effective analgesic for moderate-to-severe acute pain with significant reduction of opioid-induced nausea and vomiting. Supported by a grant from Charleston Laboratories.