Clinical Trial Results Summary
Study EN3225-003

Study Number: EN3225-003	
Title of Study: A Single-Center, Randomized, Double-Blind, Placebo-Controlled, Single-Dose Study of the Safety and Efficacy of Low-Dose Percocet® in Patients With Acute Pain Following Third Molar Extraction	
Investigators: Steven E. Christensen, D.D.S.	
Study Center(s): Jean Brown Research Center, Salt Lake City, UT 84124	
Publications (reference): None	
Studied period (years): 1 month	**Phase of development**: Phase 4
Objectives: The objectives of the study were to determine the analgesic efficacy and safety of low-dose Percocet® 2.5/325 mg in patients with acute pain following oral surgery.	
Methodology: This single-center study was conducted using a randomized, double blind, placebo-controlled, parallel-group design in patients with moderate or severe pain following oral surgery. After surgery was completed, patients experiencing persistent (not transient) moderate or severe pain (based on a categorical scale of none, mild, moderate, and severe) confirmed by a line-strike of at least 50 mm on a 100-mm Pain Intensity Visual Analogue Scale (PIVAS) were randomly assigned (1:1 ratio) to receive a single oral dose of either Percocet® 2.5/325 mg or placebo. Patients remained at the study site for the first 6 hours following study drug administration. Each patient was given two stopwatches. At the time of dosing, both watches were started. Patients were asked to stop the first stopwatch when pain relief was first perceived and to stop the second watch when meaningful pain relief was felt. Pain intensity and pain relief were recorded at baseline, 15 minutes, 30 minutes, 45 minutes, and hourly thereafter through Hour 6. Efficacy assessments were performed over 6 hours and safety evaluations were performed for up to 24 hours following study medication administration. Patients were allowed to discontinue from the study at any time.	
Number of Subjects (Planned and Analyzed): A total of 120 patients (60 per treatment group) were planned. Sixty patients were enrolled and treated (30 in each arm). Seventeen patients (6 placebo, 11 Percocet® 2.5/325 mg) completed the study. The reason for discontinuation for all 43 patients was lack of efficacy. All 60 treated patients were analyzed for efficacy and safety.	
Diagnosis and Main Criteria for Inclusion: Patients 18 to 60 years of age who were in generally good health; had one or more third molars extracted (up to four teeth); and had an initial pain intensity score following surgery of at least 50 mm (on a 100-mm PIVAS) and a categorical pain rating of moderate or severe (on a scale of none, mild, moderate and severe). At least one extracted molar was to be a partial or full bone impacted mandibular molar and have at least a moderate trauma rating (meaningful or significant bone removal, not an easy extraction).	
Test Product, Dose and Mode of Administration, Batch Number(s): Percocet® 2.5/325 mg (oxycodone hydrochloride 2.5 mg and acetaminophen 325 mg) capsule, single dose administered orally, lot numbers 313130NV (tablet) and 10978.01 (capsule)	
Duration of Treatment: A single dose	
Reference Therapy, Dose and Mode of Administration, Batch Number(s): Matching placebo capsule, single dose administered orally, lot number 07600.01	

Criteria for Evaluation:

Efficacy:

- 6-hour total pain relief (TOTPAR) (categorical and VAS)
- 6-hour sum of pain intensity differences (SPID) (categorical and VAS)
- Time to first perceptible pain relief
- Time to onset of meaningful pain relief
- Time to remedication
- Hourly pain relief scores
- Hourly pain intensity difference (PID) scores
- Patient-rated global pain assessment

Safety:

Adverse events

Statistical Methods:

Efficacy:

Efficacy analyses were performed on the intent-to-treat (ITT) population (patients who received study medication and had at least one post-dose efficacy evaluation, i.e., 15 minutes, without receiving rescue medication or vomiting before the evaluation) using the last-observation-carried forward (LOCF) approach for missing data. TOTPAR and SPID (categorical and VAS) over the first 6 hours of the study (0 to 6 hours) were analyzed using analysis of variance (ANOVA) with effects for treatment and baseline pain stratification (moderate or severe) included in the model. Pain relief scores and PID scores at each evaluation time point were analyzed using a model similar to that used for TOTPAR and SPID analyses. Time to first perceptible pain relief, time to onset of meaningful pain relief, and time to remedication were estimated using Kaplan-Meier product limit procedure. Treatment comparisons were conducted using log-rank test. The patient-rated global pain assessment was analyzed using Wilcoxon's rank-sum test. Efficacy analyses were repeated for subsets of patients with four teeth pulled and for patients with two or less teeth pulled.

Safety:

Safety analyses were performed on the safety population (patients who were randomized and received study medication) and repeated for the subsets of patients. Assessment of safety was based on incidence of adverse events (AEs).

SUMMARY:

During the enrollment period and while monitoring patient status, the sponsor recognized that the majority of enrolled patients were discontinuing from the study because they were not maintaining adequate pain relief over the 6-hour study period. Because of this occurrence and in accordance with the Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects), the sponsor terminated the study. At the time of study termination, only 60 patients had been enrolled, representing only ½ of the original planned sample size; this sample was not large enough to provide reliable conclusions.

Safety Results:

Nausea was the most frequently reported AE in both treatment groups, occurring in 2 of 30 patients in the placebo group and in 8 of 30 patients in the Percocet® 2.5/325 mg group. There were no reported deaths, safety-related discontinuations, or non-fatal serious adverse events (SAEs) in this study.