Safety and Efficacy of Sufentanil Sublingual 30mcg Tablets for the Treatment of Acute Pain Following Outpatient Abdominal Surgery

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Background

Day surgery, coming to and leaving the hospital on the same day as surgery as well as ambulatory surgery, leaving the hospital within twenty-three hours, is increasingly being adopted.[1] The number of outpatient surgery visits in the United States increased from 20.8 million in 1996 to 34.7 million in 2006, and with now more than 6000 ambulatory surgery centers (ASCs) in the United States, this trend is expected to continue.[2,3] Early discharge demands a rapid recovery and low incidence and intensity of surgery and anesthesia related side-effects such as pain, nausea and fatigue.[1] Patients must be fit enough and symptom intensity low enough to facilitate self-care, so there remains a clinical need for rapid-acting, potent analgesics that offer predictable offset and good tolerability. A sufentanil sublingual 30mcg tablet (ST30), dispensed using a single-dose applicator, is in development for treatment of moderate-to-severe acute pain in a medically-supervised setting (**Figure 1**). The product is designed to leverage sufentanil's unique pharmacodynamic properties and could offer potential analgesic advantages in ASCs or other venues requiring non-invasive, acute pain management.[4-6] The primary objective of this study was to compare the efficacy and safety of the sublingual Sufentanil Tablet (ST) 30 mcg to the sublingual Placebo Tablet (PT) for the short-term management of moderate-to-severe acute post-operative pain following abdominal surgery.

Figure 1. Sufentanil Sublingual 30mcg Tablet

Methods

Study Design

- The study was multicenter, randomized, double-blind and placebo-controlled for up to 48 hours, in adult patients undergoing abdominoplasty, open tension-free inguinal hernioplasty or laparoscopic abdominal surgery.
- Patients who met all inclusion and none of the exclusion criteria at screening, and following surgery, were randomly assigned at a 2:1 ratio to treatment with ST or PT.
- Before study staff could administer the first dose of study drug, patients must have reported a pain score of 4 or higher on a validated, 11-point numerical rating scale (0-10).

Methods (Cont)

Efficacy Assessments

- The primary efficacy variable (endpoint) was the time-weighted summed pain intensity difference to baseline over the 12-hour study period (SPID12).
- Key secondary endpoints included time-weighted summed pain intensity difference over the first hour of the study period (SPID1), total pain relief (TOTPAR), proportion of patients and healthcare professionals who responded "good" or "excellent" to the global assessments (PGA and HPGA) and proportion of patients who terminated early from the study due to inadequate analgesia.

Safety Assessments

- Safety assessments included spontaneously reported adverse events (AEs), vital signs (blood pressure, heart rate, and respiratory rate), oxygen saturation, and the use of concomitant medications.

Results

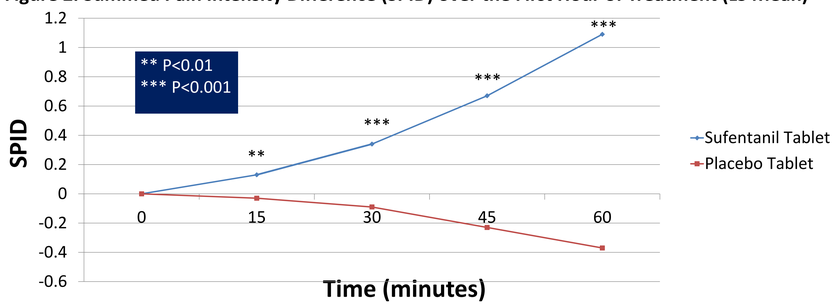
Baseline Demographics and Patient Disposition

- A total of 161 (107 ST and 54 PT) patients were randomized and received study drug. Average patient age was 41 years; 68% were female.
- Baseline demographics were evenly distributed between treatment arms with approximately 50%, 30% and 20% of the patients undergoing abdominoplasty, laparoscopic surgery and hernia repair, respectively
- Five times as many patients in the PT cohort terminated early from the study due to 'Lack of Efficacy' compared to the ST cohort (18.5% vs. 3.7%).

Efficacy

- Statistically significant SPID12 differences were observed in favor of ST over PT (25.8 vs. 13.1; p<0.001), demonstrating superiority for management of acute post-operative pain.
- Several secondary endpoints also met statistical significance in favor of ST including TOTPAR, PGA, HPGA and summed pain intensity/pain relief composite measure (p≤0.001 for all).
- **Figure 2** illustrates the differences in SPID over the first hour of treatment, with statistically significant separation between the two cohorts as early as 15 minutes from dosing (p<0.01).

Figure 2. Summed Pain Intensity Difference (SPID) over the First Hour of Treatment (LS Mean)



Results (Cont)

Safety

- AEs in general were mild to moderate in severity with the type and frequency observed typical of opioids in a post-operative setting
- Nausea, headache and vomiting were the most common treatment-emergent AEs across both treatment arms
- **Table 1** includes AE's ≥4% and considered "probably" or "possibly" related to study drug.

Table 1. Adverse Events Considered "Possibly" or "Probably" Related (≥4% in any group)

	Treatment Arm	
Adverse Event N (%)	Sufentanil Tablet (ST) (n = 109)	Placebo Tablet (PT) (n = 54)
Nausea	31 (29)	12 (22)
Headache	13 (12)	6 (11)
Vomiting	6 (6)	1 (2)
Dizziness	6 (6)	2 (4)
Somnolence	3 (3)	2 (4)
Pruritus	2 (2)	2 (4)

Conclusion

- **Efficacy and tolerability results from this study suggest that sufentanil 30mcg tablets dispensed sublingually via single-dose applicator may offer a viable alternative to IM or IV dosing in an ambulatory surgery population**
- **Nausea and headache were the most commonly reported AEs for both treatment arms**
- **Additional studies are indicated to assess potential applications within emergency medicine or other medically supervised venues**

References

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