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

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Background

Ambulatory surgery is defined as surgical and diagnostic intervention that does not require an overnight hospital stay. It has been increasingly adopted by patient populations in Europe owing to its safe, high quality, cost-effective and time saving approach to surgical intervention.[1] This considerable growth has been facilitated by the advent of short-acting anesthetics and minimally invasive procedures that have enabled healthcare professionals to perform multiple surgeries in a day.[2] Early discharge demands a rapid recovery and low incidence of surgery and anesthesia related side-effects such as pain, nausea and fatigue.[3] Patients must be fit enough and symptom intensity mild 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 (SST30), 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 distinct pharmacodynamic properties and could offer potential analgesic advantages in ambulatory surgery centers or other venues requiring reliable yet non-invasive, acute pain management.[4-6] The primary objective of this analysis was to compare the efficacy and safety of the Sufentanil Sublingual Tablet (SST) 30 mcg, by surgery type, to the sublingual Placebo Tablet (PT) for the 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 (LA) 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 SST 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 SPID over the first hour (SPID1), total pain relief (TOTPAR), early termination due to inadequate analgesia and the proportion of patients and healthcare professionals who responded "good" or "excellent" to the global assessment (PGA and HPGA).
- An a priori SPID12 subgroup analysis by type of surgery was also performed.

Safety Assessments

- Safety assessments included adverse events (AEs), vital signs including oxygen saturation and the use of concomitant medications
  - Sufentanil plasma concentrations at were also collected at 1, 12 and 24 hours

Results

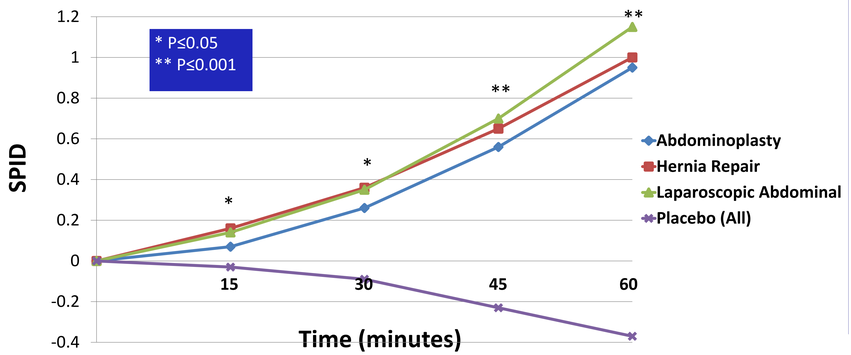
Baseline Demographics and Patient Disposition

- A total of 161 patients (107 SST and 54 PT) were randomized: mean age 41 years, 68% female
- Baseline demographics were evenly distributed with 80, 48 and 33 patients respectively, undergoing abdominoplasty, LA surgery and hernia repair.
- Baseline pain intensity scores were 6.5, 5.2 and 5.0 respectively for Abdominoplasty, LA surgery and hernia repair patients, respectively.

Efficacy

- The study met it's primary endpoint with statistically significant SPID12 differences observed in favor of SST over PT (25.8 vs. 13.1; p<0.001).
- Subgroup analysis by surgery type also yielded statistically significant (abdominoplasty; 30.8 vs 17.6 [p<0.001] and LA; 21.4 vs 8.2 [p=0.019] and numerical (hernia; 18.6 vs 7.7) improvements in pain intensity compared to placebo, though sample sizes were limited (**Fig 2**)
- Mean number of doses used over 12 hours ranged from 4.2 for abdominoplasty to 4.5 for LA surgery, with inter-dosing intervals for all cohorts ranging between 180-184 minutes

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 AEs by type of surgery "possibly" or "probably" related
- Mean sufentanil plasma concentrations were 39 and 44 pg/ml respectively at 12 and 24 hours

Table 1. Related Adverse Events by Surgery Type (reported by ≥ 3 patients)

Adverse Event N (%)	Abdominoplasty		Lap Abdominal		Hernia Repair	
	SST n=52	Placebo n=28	SST n=32	Placebo n=16	SST n=23	Placebo n=10
Nausea	22 (42)	7 (25)	3 (9)	4 (25)	6 (26)	1 (10)
Headache	10 (19)	5(18)	2 (6)	1 (6)	1 (4)	0
Vomiting	4 (8)	1 (4)	1 (3)	0	1 (4)	0
Dizziness	6 (12)	2 (7)	0	0	0	0
Somnolence	3(6)	2 (7)	0	0	0	0
Hypotension	5 (10)	2 (7)	0	0	0	0

Conclusion

- **Efficacy and safety results from this pivotal phase 3 study suggest that sufentanil 30mcg tablets dispensed sublingually via single-dose applicator may offer a viable alternative to IM or IV dosing in frequently performed abdominal surgery procedures**
- **Nausea and headache were the most commonly reported AEs across all surgery types**
- **Additional studies are indicated to further assess efficacy, tolerability and drug utilization patterns in a wider range of ambulatory surgical populations.**

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