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

Harold Minkowitz, MD[1]; Neil Singla, MD[2]; Timothy Melson, MD[3]; David Leiman, MD[4];Karen DiDonato, MSN, RN[5] Pamela Palmer, MD, PhD[5]

[1]Memorial Hermann Memorial City Medical Center, Houston, TX; [2]Lotus Clinical Research, Pasadena, CA; [3]Hellen Keller Hospital, Sheffield, AL; [4]Victory Medical Center, Houston, TX, [5]AcelRx Pharmaceuticals, Redwood City, CA

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 of surgery and anesthesia related side-effects such as pain, nausea and fatigue.[1] 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 ASCs or other venues requiring 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 spontaneously reported adverse events (AEs), vital signs including oxygen saturation, and the use of concomitant medications.

Results

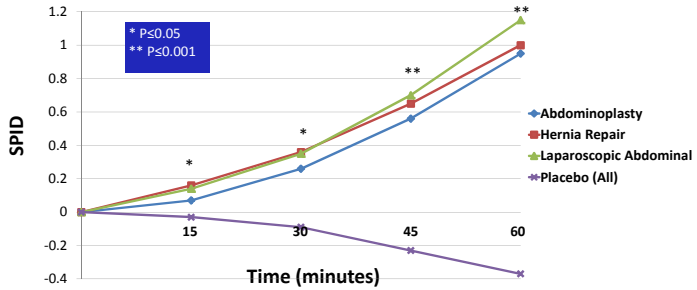
Baseline Demographics and Patient Disposition

- A total of 161 patients (107 SST and 54 PT) were randomized and received study drug; average age was 41 years, 68% were female.
- Baseline demographics were evenly distributed with 80, 48 and 33 patients respectively, undergoing abdominoplasty, LA surgery and hernia repair.
- Five times as many patients in the PT cohort terminated early from the study due to 'lack of efficacy' compared to the SST cohort (18.5% vs. 3.7%).

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.
- Figure 2 illustrates the differences in SPID by surgery type over the first hour of treatment.

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 to study drug and reported by ≥ 3 patients in any treatment arm

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 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 across a variety of ambulatory surgical procedures**
- **Nausea and headache were the most commonly reported AEs across all surgery types**
- **Additional studies are indicated to further assess safety and efficacy in at risk populations such as the elderly and those with renal or hepatic impairment**

References

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