Efficacy Subgroup Analysis by Age of Sufentanil Sublingual 30 mcg Tablets for the Treatment of Acute Pain following Outpatient Abdominal Surgery

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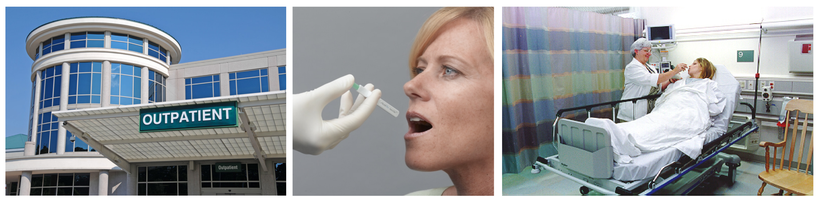
Background

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, with patients aged 45 to 64 years making up the largest cohort of procedures by number, followed by ages 15-44 years and 65-74 years, respectively.[2] Early discharge demands a rapid recovery and low incidence and intensity of surgery and anesthesia related side-effects such as pain, nausea and fatigue, so there remains a clinical need for rapid-acting, potent analgesics that offer predictable offset and good tolerability across all age groups. A sufentanil sublingual 30mcg tablet, 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.[3-5] 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 (NRS 0-10).

Efficacy Assessments

- The primary efficacy variable (endpoint) was the time-weighted summed pain intensity difference to baseline over the 12-hour study period (SPID12). Subgroup analysis by age (<65 years and ≥ 65 years) was also specified a priori as part of the statistical analysis plan
- Key secondary endpoints included SPID over the first hour of the study, total pain relief (TOTPAR) and proportion of patients and healthcare professionals who responded "good" or "excellent" to the global assessments of pain management (PGA and HPGA).

Methods (Cont)

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. Baseline demographics were evenly distributed and can be found in **Table 1.**
- Mean age was 41 years with less than 2% of all patients age 65 or older
- 'Lack of Efficacy' was the most common reason for early termination from the study with five times as many patients in the PT cohort terminating prior to 24 hours 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.
- Subgroup analysis by age also revealed that for patients less than 65 years old, there were statistically significant SPID12 differences favoring ST (25.2 vs. 12.9; p<0.001).
    - The sample size for patients ≥ 65 years was insufficient to support analysis
- Most secondary endpoints 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).

Table 1. Baseline Demographics

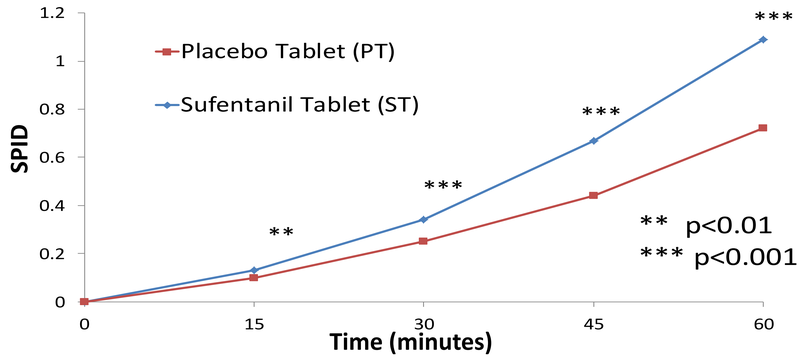
	Sufentanil Tablet 30 mcg (ST) n=107	Placebo Tablet (PT) n=54	Total
Age (years) - n (%)			
<65	106 (99.1%)	53 (98.1%)	159 (98.8%)
≥65	1 (0.9%)	1 (1.9%)	2 (1.2%)
Sex - n (%)			
Male	34 (31.8%)	18 (33.3%)	52 (32.3%)
Female	73 (68.2%)	36 (66.7%)	109 (67.7%)
Race - n (%)			
Asian	3 (2.8%)	1 (1.9%)	4 (2.5%)
Black	21 (19.6%)	10 (18.5%)	31 (19.3%)
White	76 (71.0%)	37 (68.5%)	113 (70.2%)
Other	7 (6.5%)	6 (11.1%)	13 (8.1%)
Surgery Type - n (%)			
Abdominoplasty	52 (48.6%)	28 (51.9%)	80 (49.7%)
Hernioplasty	23 (21.5%)	10 (18.5%)	33 (20.5%)
Laparoscopic Abdominal	32 (29.9%)	16 (29.6%)	48 (29.8%)

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 (29% vs 22%), headache (12% vs 11%) and vomiting (6% vs 2%) were the most common treatment-related AEs for the ST and PT treatment arms, respectively.

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



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, headache and vomiting were the most commonly reported AEs for both groups**
- **Previously published data with sublingual sufentanil 15mcg tablet suggests good efficacy and tolerability in patients ≥ 65 years, but additional studies with 30mcg are indicated to more fully characterize results in this subgroup of interest following outpatient surgery**

References

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