COMPREHENSIVE EFFICACY AND INTEGRATED SAFETY RESULTS FROM THE LATE-PHASE CLINICAL PROGRAM OF THE SUBLINGUAL SUFENTANIL TABLET 30 MCG

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Background

Following completion of a phase 3 clinical program that was sponsored by the U.S. Department of Defense, a New Drug Application for the sufentanil sublingual Tablet 30 mcg (SST 30 mcg; DSUVIA™) was recently submitted to the FDA. Four late-phase trials were performed; two randomized and placebo-controlled and two open-label. The proposed indication is for management of moderate-to-severe acute pain in medically supervised settings such as short-stay surgery or emergency department (ED), including field trauma. SST 30 mcg is dispensed by an HCP via pre-filled applicator and appears well-suited for short duration acute pain management because it acts rapidly (plasma-CNS equilibration time of 6 minutes), does not require an invasive route of delivery and possesses a predictable off-set, in part due to lack of active metabolites.[1,2] The primary objective of this analysis was to examine the comprehensive efficacy and integrated safety results from the four clinical trials conducted in ambulatory surgery and emergency medicine settings.

Figure 1. Sufentanil Sublingual Tablet 30 mcg

Methods

Study Design

- Two studies were randomized and placebo controlled in post-operative patients following bunionectomy (SAP202) or abdominal surgery (SAP301).
- Two studies were open-label and single-arm intended to evaluate SST 30 mcg in the ED (SAP302) and in older, post-operative patients, many with comorbidities (SAP303).
- Upon meeting all entrance criteria, patients were administered SST 30 mcg by a healthcare professional (HCP) no more frequently than hourly as needed to manage pain.
  - Rescue opioids (ie IV or oral morphine) were available on request.
- 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

- Primary efficacy variable was the time-weighted summed pain intensity difference to baseline over 12-hours for post-op studies (SPID12) and 1-hour for the ED study (SPID1)

Methods (Cont)

Safety Assessments

- Safety assessments included spontaneously reported adverse events (AEs), vital signs (blood pressure, heart rate, and respiratory rate), and oxygen saturation values.
- The Six-Item Screener was administered in the ED study pre and post dose to assess for potential cognitive impairment.[3]
- Screening laboratory analysis of BUN, creatinine, ALT, AST and total bilirubin were also analyzed in some studies to classify patients regarding renal and liver impairment status.

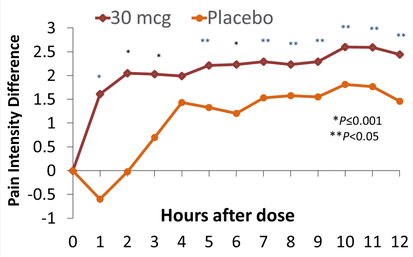
Results

Baseline Demographics & Efficacy

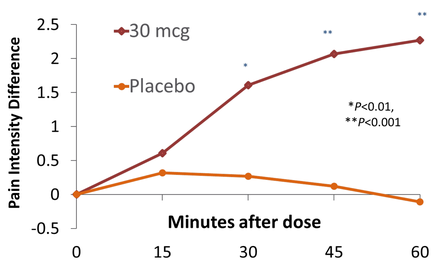
- A total of 480 patients were enrolled across all studies; baseline demographics in **Table 1**.
- Studies SAP202 and SAP301 demonstrated superiority of SST 30 mcg over placebo for the primary endpoint of SPID12 ($p=0.005$ and $p<0.001$ for bunionectomy and abdominal surgery populations, respectively); **Figure 2** includes PID over 12-hours (SAP301) and 1-hr (SAP202).
  - Statistically significant reductions in pain intensity vs placebo were evident within 15-30 minutes for SAP202 ($p<0.001$ at 30 min) and SAP301 ($p=0.002$ at 15 min).
- A single dose of SST 30 mcg resulted in approximately a 3-point drop in pain intensity within 60 minutes in the ED study (SAP302), with clinically meaningful analgesia in < 20 minutes
  - A clinically significant drop in pain intensity when administering 0-10 point numerical rating scale (NRS) to measure pain has been validated as 1.3[4]
- Mean SPID12 for all SAP303 patients was 36.04, with higher values observed in abdominal patients (39.27) compared to orthopedic patients (22.18).

Figure 2. Pain Intensity Difference by Evaluation Time Point – Pivotal Trials

a. SAP301 (Abdominal Surgery)



b. SAP202 (Bunionectomy)



Safety

- AEs in general were mild to moderate in severity with the most commonly reported (≥3%) in **Table 2.** There no statistical differences observed between active and placebo
- There were no clinically relevant mean changes from baseline in any vital sign throughout the study.

Results (Cont)

Table 1. Baseline Demographics of the Four Late-phase Trials

Study #	SAP202 (N=101)	SAP301 (N=163)	SAP302 (N=76)	SAP303 (N=140)
Mean Age, Yrs (range)	42.5 (18-76)	40.9 (18-69)	42.5 (21-77)	54.7 (40-84)
% Female	49%	68%	53%	54%
Race (%)	White 71% Black 23% Other 6%	White 70% Black 19% Other 11%	White 59% Black 34% Other 7%	White 84% Black 14% Other 2%
BMI, kg/m², mean (SD)	28.2 (6.3)	27.5 (4.8)	30.6 (9.0)	30.0 (6.8)

Table 2. Most Commonly Reported Adverse Events ≥ 3%

Adverse Events n (%)	SST 30 mcg Combined (N=363)	Placebo Combined (N=74)	Treatment P-value
Nausea	105 (28.9)	16 (21.6)	NS
Headache	29 (8.0)	10 (13.5)	NS
Vomiting	26 (6.3)	1 (1.4)	NS
Dizziness	21 (5.8)	3 (4.1)	NS
Somnolence	15 (4.1)	2 (2.7)	NS
Pruritus	11 (3.0)	2 (2.7)	NS

Conclusion

- **SST 30 mcg, while still under FDA review, may have benefit as a non-invasive analgesic modality in medically supervised settings requiring short-term treatment of acute moderate-to-severe pain**
- **A single dose of SST 30 mcg in the ED resulted in approximately a 3-point drop in pain intensity within 60 minutes, with clinically meaningful analgesia in < 20 min**
- **SST 30 mcg was well-tolerated; nausea and headache were the most common AEs**

References

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