A Phase 3, Open-label Study of Sufentanil Sublingual 30 mcg Tablets for the Treatment of Acute Pain in the Emergency Department

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Background

Pain is the most common reason people visit the Emergency Department (ED). Studies indicate however, that ED physicians often do not provide adequate analgesia to their patients as a result of time constraints, gender and age bias, opiophobia and insufficient knowledge of and formal training in acute pain management.[1] Novel classes of analgesics have recently been introduced, but many patients still suffer from acute pain in situations where immediate intravenous (IV) access may be unavailable.[2] A sufentanil sublingual 30mcg tablet (ST30), dispensed using a single-dose applicator, is in phase 3 development for treatment of moderate-to-severe acute pain in emergency medicine or battlefield trauma settings (**Figure 1**). The product is designed to leverage sufentanil's unique pharmacokinetic and pharmacodynamic properties and could offer potential analgesic advantages in venues requiring non-invasive, acute pain management.[3-5] The primary objective of this study was to evaluate the safety and efficacy of ST30 for the management of moderate-to-severe pain in ED patients.

Figure 1. Sufentanil Sublingual 30mcg Tablet

Methods

Study Design

- This is a multicenter, open-label, single-dose study in 40 (of 120 total) adult patients presenting to the Emergency Department ED with moderate-to-severe acute pain due to obvious trauma or injury.
- Upon meeting all entrance criteria, patients were administered a single dose of ST30 and remained in the study for up to 2 hours to accommodate safety and efficacy assessments.
- 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 1-hour study period (SPID1).

Methods (Cont)

Safety Assessments

- Safety assessments included spontaneously reported adverse events (AEs), vital signs (blood pressure, heart rate, and respiratory rate), oxygen saturation, the use of concomitant medications and a Six-Item Screener (SIS)
  - The Six-Item Screener was administered pre and post dose to assess for potential cognitive impairment[6]

Interim Results

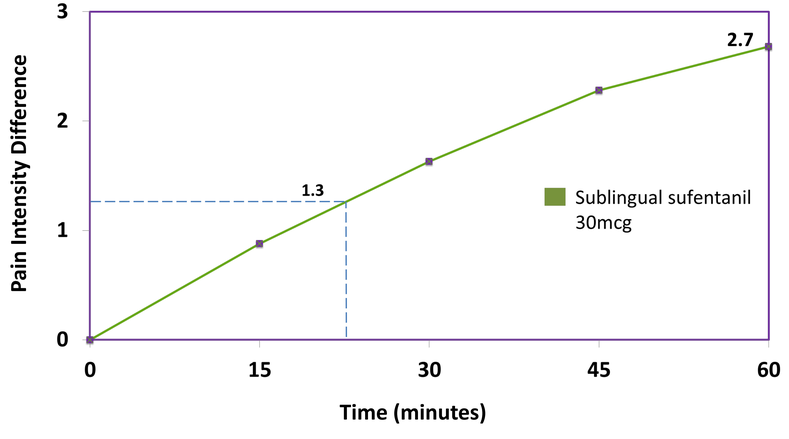
Baseline Demographics and Patient Disposition

- A total of 40 of the 120 planned patients have been enrolled to date.
- Mean age 42.4 years; 53% female
- Mean baseline pain intensity was 8.5/10 ("severe" pain)

Efficacy

- Substantial reductions in mean Pain Intensity (2.7/10) within the first hour have been recorded (**Figure 2**)
  - Literature has identified 1.3 as the minimum clinically significant change in Pain Intensity when administering a 10-pt NRS in the Emergency Department[7]
  - Mean PI decreases of 1.3 occurred within 15-30 minutes of administering one dose of sublingual sufentanil 30mcg
- The mean time-weighted Summed Pain Intensity Difference to baseline over the first hour (SPID1) is 1.87
- Only 1 patient thus far has terminated early (within the 1st hour of study) due to inadequate analgesia

Figure 2. Mean Pain Intensity Difference (PID) to Baseline over the First Hour of Treatment



Interim Results (Cont)

Safety

- No adverse events have been reported in 34/40 (85%) patients. Adverse events observed to date are listed in **Table 1.**
- AEs in general were mild to moderate in severity with nausea (5%) and somnolence (5%) the most common
- Early SIS results suggest no cognitive impairment caused by sublingual sufentanil 30mcg
  - mean pre-dose score was 5.7/6 vs 5.9/6 post-dose

Table 1. Interim Safety Results

Adverse Events	Sufentanil Sublingual 30mcg Total n=40 n (%)	Severity Rating
Nausea	2 (5%)	1 mild, 1 moderate
Somnolence	2 (5%)	mild
Feeling Hot	1 (2.5%)	mild
Dizziness	1 (2.5%)	mild
Disorientation	1 (2.5%)	mild
Facial Hypoesthesia	1 (2.5%)	mild
Pruritus	1 (2.5%)	mild
Vomiting	0 (0%)	NA

Conclusion

- **Early 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 analgesia in emergency medicine situations**
- **Nausea and somnolence have been the most commonly reported AEs to date (5% each)**
- **Additional patients, treated with multiple doses are indicated to more accurately characterize the safety and efficacy profile of this therapy in critical care situations**

References

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