

Efficacy and Safety of Sufentanil Sublingual Tablet 30 mcg for Management of Acute Traumatic Pain in the Emergency Department

James Miner, MD¹; Harold Minkowitz, MD²; Zubaid Rafique, MD³; Karen DiDonato, MSN, RN⁴; Pamela Palmer, MD, PhD⁴

¹Hennepin County Medical Center, Minneapolis, MN; ²Memorial Hermann Memorial City Medical Center, Houston, TX; ³Baylor College of Medicine, Ben Taub General Hospital, Houston, TX; ⁴AcelRx Pharmaceuticals, Redwood City, CA

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 patients as a result of time constraints, gender and age bias, opiophobia and lack of training in acute pain management.¹ Novel classes of analgesics have recently been introduced, but many patients still suffer from pain in situations where immediate intravenous (IV) access may be unavailable.² A sufentanil sublingual 30mcg tablet (ST30) is in phase 3 development for treatment of moderate-to-severe acute pain in emergency medicine and battlefield trauma (Figure 1). The product is designed to leverage sufentanil's unique pharmacokinetic and pharmacodynamic properties and could offer potential analgesic advantages in challenging venues.³⁻⁵ The primary objective of this study is to evaluate the safety and efficacy of ST30 for management of pain in an ED setting.

Figure 1. Sufentanil Sublingual Tablet 30 mcg



Methods

Study Design

- This was a multicenter, open-label study in 76 adults presenting to the ED with moderate-to-severe acute pain due to trauma or injury.
- Upon meeting entrance criteria, patients were either offered a single dose or multiple doses of ST30 and remained in the study as needed for safety and efficacy assessments.
- Patients must have reported a pain score of ≥ 4 on an 11-point numerical rating scale (NRS 0-10) before first dose of study drug.

Methods (Cont)

Assessments

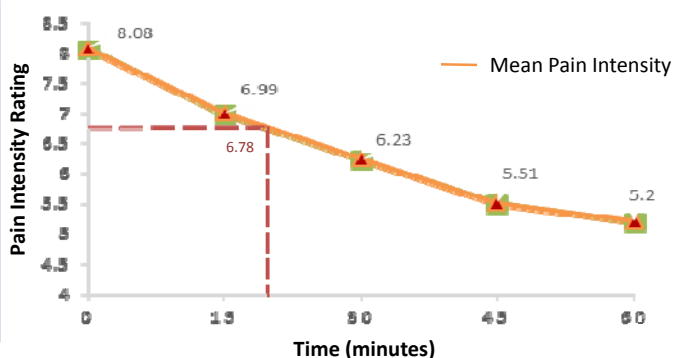
- Primary efficacy variable is the time-weighted summed pain intensity difference to baseline over the 1-hour study period (SPID1)
- Safety assessments included adverse events (AEs), vital signs, oxygen saturation and a Six-Item Screener (SIS)
- The Six-Item Screener was administered pre and post dose to assess for potential cognitive impairment.⁶

Results

Efficacy

- Forty patients were enrolled in the single-dose cohort and 36 in the multi-dose cohort; mean age 42 years, 61% were male
- Baseline pain intensity (mean) 8.1/10 ("severe" pain)
- Substantial reductions in Pain Intensity (mean 2.9/10) within the first hour were recorded (Figure 2)
- Literature has identified 1.3 as the minimum clinically significant change in Pain Intensity when administering an 11-pt NRS in the ED⁷
- Mean PI decreases of 1.3 occurred within 15-20 minutes of administering one dose of sublingual sufentanil 30mcg
- Only 4 patients in total terminated early (within the first 2 hours of the study) due to inadequate analgesia.

Figure 2. Pain Intensity Over First Hour



Results (Cont)

Safety

- No adverse events were reported in 60/79 (79%) patients.
- Observed AEs occurring in > 1 patient are listed in Table 1.
- AEs in general were mild to moderate in severity with nausea (9.2%) and somnolence (5.5%) the most common
- SIS results suggest no cognitive impairment caused by sublingual sufentanil 30mcg
 - Mean pre-dose score was 5.8/6 vs 5.9/6 post-dose

Table 1. Safety Results (AEs occurring in > 1 patient)

Adverse Events n (%)	Sufentanil Sublingual Tablet 30 mcg	Severity Rating
Nausea	7 (9.2%)	6 mild, 1 moderate
Somnolence	4 (5.5%)	All mild
Vomiting	3 (3.9%)	All mild
O ₂ Saturation Decreased	2 (2.6%)	All mild

Conclusion

- Efficacy and tolerability results from this study suggest that sufentanil 30mcg tablets dispensed sublingually may offer a viable alternative to IM or IV analgesia in ED situations
- Nausea, somnolence and dizziness were the most commonly reported AEs
- Additional, multi-dose studies are indicated to more accurately characterize the safety and efficacy profile of this therapy in Emergency Medicine

References

1. Motov SM. Problems and barriers of pain management in the emergency department: Are we ever going to get better? *J Pain Research* 2009;2:5-11
2. Sherry, S and Ham, B. Challenges and Solutions in Difficult Vascular Access. *Society of Critical Care Medicine* 2010; <http://www.sccm.org/Communications/Critical-Connections/Archives>. Accessed Feb 2016
3. Mather LE. Opioids: a pharmacologist's delight! *Clin Exp Pharmacol Physiol* 1995; 22:833-6.
4. Löttsch J. Pharmacokinetic-pharmacodynamic modeling of opioids. *J Pain Symptom Manage* 2005; 29(5 Suppl):S90-S103.
5. Scott JC, Cooke JE, Stanski DR. Electroencephalographic quantitation of opioid effect: comparative pharmacodynamics of fentanyl and sufentanil. *Anesthesiol* 1991; 74:34-42.
6. Christopher M. Callahan, MD, Frederick W. Unverzagt, PH.D, Liu L. Hui, PH.D, Anthony J. Perkins, Ms, And Hugh C. Hendrie, Mb, Chb; *Medical Care*: Volume 40, Number 9, Pp 771-781 ©2002 Lippincott Williams & Wilkins, Inc.
7. Bjur, Polly E., et al.. *Validation of a Verbally Administered Numerical Rating Scale of Acute Pain four Use in the Emergency Department. Academy Emergency Medicine.* 2003;10(6): 390-392.

Poster presentation at the European Society of Emergency Medicine, October 1-5 2016; Vienna, Austria