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

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Background

Acute pain management is challenging even in an ideal setting, and more so in a correctional system. Many inmates still suffer from acute pain post-operatively, while waiting to be evaluated and in the aftermath of emergency situations where violence may have erupted[1]. Opioids are often considered standard-of-care treatment for moderate to severe acute pain associated with trauma, however limitations of these therapies have been well-documented.[2,3] Morphine is associated with erratic onset of analgesia when delivered IM, and delayed side effects resulting from active metabolites, while fentanyl's rapid distribution and metabolism demands frequent re-dosing.[4,5] 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.[6] There remains a clinical need for rapid-acting, potent analgesics that do not require an invasive route of delivery. In collaboration with the U.S. Department of Defense (DoD), the Sufentanil Sublingual Tablet 30mcg (SST30) is in development for treatment of acute pain in the battlefield and emergency trauma settings (Figure 1). The product is designed to leverage sufentanil's unique pharmacokinetic and pharmacodynamic properties and could offer potential analgesic advantages in challenging venues.[7-9] The primary objective of this study was to evaluate the safety and efficacy of SST30 for management of pain in an Emergency Department (ED) setting.

Figure 1. Sufentanil Sublingual Tablet 30 mcg

Methods

Study Design

- This is a multicenter, open-label study in 76 adult patients presenting to the ED with moderate-to-severe acute pain due to trauma or injury.
- The first 40 patients (Single-Dose Cohort) were administered a single dose of SST30 and remained in the study for up to 2 hours to allow for safety and efficacy assessments.
- Subsequent 36 patients (Multiple-Dose Cohort) were allowed to re-dose after 1 hour and remained in the study for up to 5 hours 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 could be given.

Methods (Cont)

Assessments

- Primary efficacy variable was the time-weighted summed pain intensity difference to baseline over the 1-hour study period (SPID1). Pain Intensity (PI) by Time Point and Pain Intensity Difference (PID) were also assessed.
- Safety assessments included adverse events (AEs), vital signs, including oxygen saturation, and a Six-Item Screener (SIS)[10]
  - The Six-Item Screener was administered pre and post dose at the request of the DoD to assess for potential cognitive impairment.

Results

Baseline Demographics and Trauma Classification

Demographics

Category		Category	
Sex, male, %	61	BMI, %	
Age, years, mean	42	< 30kg/m²	61
Race, %		> 30kg/m²	39
Caucasian	45	ASA Classification, %	
African American	34	1	61
Native American	7	2	33
Ethnicity, %		3	7
Hispanic/Latino	16	Baseline Pain	8.1/10

Trauma Classifications

Injury Type	Number	Percent Total
Fractures	25	32.9%
Sprains/Strains	23	30.3%
Contusion/hematoma (soft tissue)	13	17.1%
Laceration	8	10.5%
Joint dislocation	4	5.3%
Burns	2	2.6%
Infections	1	1.3%

Efficacy

- 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 ED[10,11]
  - Mean decreases of 1.3 occurred within 15-30 minutes of first dose
- Mean Pain Intensity by Time Point reveals over 35% reduction by 60 minutes (Figure 3)

Figure 2

Pain Intensity Difference to Baseline

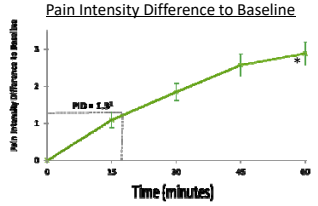
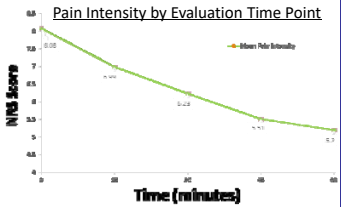


Figure 3

Pain Intensity by Evaluation Time Point



Results (Cont)

Safety

- Majority of patients experienced no side effects (Table 1)
- Nausea, somnolence and vomiting were the most common treatment-emergent AEs
- Six-item Screener SIS Cognitive Test results showed no cognitive impairment – 73 patients had either the same score or increased their score while only 2 patients had a decreased of 1 point compared to baseline.

Table 1. Adverse Events (≥ 2% of patients)

Adverse Event	SSTS 30 mcg
No Adverse Event	**79%**
Nausea	9%
Somnolence	5%[1]
Vomiting	4%
Oxygen Desaturation	3%[2]

1. All 4 patients with somnolence were rated as mild
2. Two patients experienced transient room air oxygen desaturations below 95% (88% and 94% which immediately improved with nasal cannula oxygen)

Conclusions

- Single dose of SSTS 30 mcg results in approximately a 3-point drop in pain intensity within 60 minutes, with clinically meaningful analgesia in < 20 minutes
- ARX-04 was well-tolerated in this clinical study, with most common reported AEs of nausea and somnolence.
- SIS Screen demonstrated no cognitive impairment
- Additional research is indicated to assess safety and efficacy in actual field-based environments

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