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Activity : Abstract
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TITLE:
A Randomized, Double-Blind Trial to Evaluate the Efficacy and Safety of the Sufentanil NanoTab® PCA System/15mcg Plus Rescue Morphine vs. Placebo Plus Rescue Morphine in Patients with Moderate-to-Severe Pain after Open Abdominal Surgery

AUTHOR(S):
Mike Royal, M.D.[1], Forrest G. Ringold, M.D.[2], Harold Minkowitz, M.D.[3], Tong-Joo Gan, M.D.[4], Keith Aqua, M.D.[5], Pamela P. Palmer, M.D.,Ph.D.[6].
[1]Clinical, AcelRx Pharmaceuticals, Inc., Redwood City, CA, USA, [2]Surgery, Surgical Associates of Mobile, Mobile, AL, USA, [3]Anesthesiology, Memorial Hermann Memorial City Hospital Medical Center, Houston, TX, USA, [4]Anesthesiology, Duke University Medical Center, Durham, NC, USA, [5]Atlantic Clinical Research Collaborative, Boynton Beach, FL, USA, [6]Medical, AcelRx Pharmaceuticals, Inc., Redwood City, CA, USA.

AFFIRMATIONS:

Affirmations (Complete):
*: I agree to the above statements
*: Yes
*: No animal subjects were involved in the research
*: Yes, I have IRB or IACUC approval

SESSION CATEGORY:
16.4 REGIONAL ANESTHESIA AND ACUTE PAIN - Pain - Clinical

QUESTIONNAIRE:

Questionnaire (Complete):
Please select: No, do not consider my abstract for the ANESTHESIOLOGY Journal Symposium
Please select: The presenting author is NOT a resident or fellow.
Will you be able to participate in the Resident Research Forum to be held on Saturday, October 12th at 1:00 PM? Not applicable

ABSTRACT:
INTRODUCTION
The Sufentanil NanoTab PCA System (SNPS) is a novel preprogrammed noninvasive product candidate in Phase 3 development that dispenses small (3 mm diameter) sufentanil 15 mcg microtablets sublingually with a 20-minute lockout period. Sufentanil possesses a high therapeutic index with minimal respiratory depressive effects relative to its analgesic effect in animal studies, a low incidence of cardiac instability and minimal pharmacokinetic differences based on age, liver or kidney function. While these attributes could be ideal in a post-operative opioid analgesic, its rapid redistribution from plasma following IV administration and short duration of action make it less than ideal for intravenous patient-controlled analgesia (IV PCA). IV PCA, particularly with morphine, is associated with limitations, including the use of

low therapeutic index opioids, the risk of pump programming errors, venous access failure, and reduced patient mobility from being “chained” to the IV pole.

METHODS

This randomized, double blind, placebo-controlled Phase 3 study was performed as one of two pivotal studies required for FDA approval of SNPS. The study objectives were to compare the safety and efficacy of SNPS to placebo (each with rescue IV morphine available p.r.n.) delivered via the SNPS device for the management of moderate-to-severe post-operative pain after open abdominal surgery. Up to 180 post-operative inpatients (18 years and older) were to be randomized 2:1 to ensure at least 106 in the SNPS group and 53 in the placebo group, respectively, received study drug, and provided data for analysis. The primary efficacy endpoint was the time-weighted sum of pain intensity differences over the 48-hour study period (SPID-48) using an 11-point numerical rating scale. Key secondary efficacy variables included pain intensity and pain relief scores (5-point categorical scale) over the study period, patient global assessments of method of pain control (4-point categorical scale), patient and nurse ease of care scores (using a validated Ease-of-Use questionnaire), and rescue medication consumption. Safety assessments included spontaneous adverse reaction reports, vital signs, medical history, physical examinations, oxygen saturation measurements, and concomitant medication usage.

RESULTS

The study was conducted at 13 US sites from March 2012 to January 2013. A total of 214 patients were screened and 178 were randomized 2:1 with 119 and 59 to the SNPS and placebo groups, respectively. A total of 80 patients (70.2%) of the SNPS group completed the 48h study period compared to 30 (51.7%) of the placebo group. Early drop-outs in the SNPS and placebo groups, respectively, were due to adverse events (AEs, 5.3% vs. 6.9%), lack of efficacy (16.7% vs. 31.0%), and other (7.9% vs. 10.3%). SNPS was superior to placebo for the SPID-48 primary endpoint (105.6 vs. 55.6, $p = 0.001$). Treatment-emergent AEs occurred in 64.0% and 67.2% of the SNPS and placebo patients, respectively. Adverse events with an occurrence greater than 5% in either the sufentanil group or the placebo group were nausea (30.7% and 41.4% respectively), fever (14.9% and 8.6% respectively), vomiting (8.8% and 6.9% respectively), itching (8.8% and 0.0% respectively), oxygen saturation decrease (6.1% and 1.7% respectively), and hypertension (2.6% and 5.2% respectively). There were no statistically significant differences between the groups for any AE except pruritus ($p = 0.017$ in favor of placebo) with all cases being mild in severity.

CONCLUSION

The Sufentanil NanoTab PCA System provides an attractive alternative to traditional IV PCA analgesia, is easy for healthcare professionals to set-up and for patients to use. Upon completion of the required studies, a new drug application will be submitted to FDA for review.

SUMMARY:

The Sufentanil NanoTab PCA System is a preprogrammed noninvasive product in development which delivers sublingual sufentanil 15 mcg tablets with a 20-min lockout. This novel system produced superior post-operative pain control compared to placebo. The only statistically significant difference in adverse events was pruritus in the sufentanil group.

Status: Complete