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TITLE:
Sufentanil NanoTab® PCA System vs. IV PCA Morphine for Post-Operative Pain: A Randomized, Open-Label, Active-Comparator Trial

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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

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ABSTRACT:
INTRODUCTION
IV patient-controlled analgesia (PCA) is commonly used to manage postoperative pain. However, it is associated with limitations, such as programming errors, reduced patient mobility, and frequent adverse events (AEs). While sufentanil has a high therapeutic index with minimal respiratory depressive effects relative to its analgesic effect, high cardiac stability and minimal pharmacokinetic differences based on age, liver or kidney function, rapid redistribution from plasma following IV administration and short duration make it less than ideal for IV PCA. The Sufentanil NanoTab PCA System (SNPS) is a novel preprogrammed noninvasive product in Phase 3 development designed to deliver sublingual sufentanil 15

mcg tablets with a 20-min lockout period. This study was designed to evaluate the ability of SNPS to produce comparable patient satisfaction with post-operative pain control to IV PCA with morphine 1 mg q6 min lockout (IV PCA).

METHODS

In a Phase 3 randomized, open-label, non-inferiority trial at 26 US sites, adult inpatients after major open abdominal or orthopedic surgery (knee or hip replacement) were randomized 1:1 to SNPS or IV PCA for up to 72h, stratified by age and type of surgery. The 48-hr Patient Global Assessment (PGA-48) using a 4-point scale (poor, fair, good, excellent), comparing the proportion of patients who responded “good” or “excellent” (collectively “success”) in each treatment arm was defined as the primary endpoint. Pain intensity and pain relief scores were obtained as secondary endpoints. Up to 390 patients were to be enrolled to ensure at least 176 patients per group received treatment and had available data for analysis (90% power to demonstrate therapeutic non-inferiority). A 95% confidence interval (CI) of the difference in success rate between two treatment groups was constructed and if the lower boundary of this CI was not less than -15%, SNPS would be considered non-inferior to IV PCA.

RESULTS

446 patients were screened, 359 were randomized, and 357 received study drug (ITT population: SNPS [n=177] and IV PCA [n=180]) with one patient in each group who did not receive study drug. The mean age for the SNPS group was 63.8 years (30.5% males) and IV PCA group was 64.0 yrs (40% males). Knee arthroplasty represented 32% of surgeries in
both groups. The primary efficacy analysis, PGA-48, included 355 patients (176 SNPS and 179 IV PCA). Overall, 78.5% vs. 65.6% of patients achieved PGA-48 “success” for the SNPS group vs. IV PCA group, respectively, demonstrating both non-inferiority based on the 95% CI ($p < 0.001$ using the one-side Z-test against the -15% non-inferiority margin) as well as statistical superiority in favor of the SNPS ($p=0.007$). The median number of sublingual sufentanil 15 mcg doses was 12, 24 and 39.5 over 12, 24 and 48 h of SNPS use. The SNPS group showed a better effect on early PID scores than IV PCA group with separation from IV PCA as early as 45 min and statistically significantly better PID scores at 1, 2, and 4h ($p < 0.01$). The proportion of patients reporting one or more adverse events (AEs) was similar for the SNPS group (86.4%) and the IV PCA group (90.6%) with the most frequently reported AEs: nausea (48.7% of all patients), pyrexia (18.8%), and anemia (16.8%). Most AEs were mild to moderate in severity. A total of 13 patients had 24 serious adverse events (SAEs) with 8 patients having 10 treatment-emergent SAEs. Three SAEs led to discontinuation of study drug (bile leak, atrial fibrillation, and anemia), all in the IV PCA group. The SNPS group had statistically significantly fewer patients experiencing oxygen desaturations ($p=0.028$) below 95% compared to the IV PCA group.

CONCLUSION

The Sufentanil NanoTab PCA System is a viable alternative to traditional IV patient-controlled analgesia modality. The System is preprogrammed (dose and lockout interval), and is easy for healthcare professionals to set-up and patients to use.

SUMMARY:

The Sufentanil NanoTab PCA System is a novel preprogrammed noninvasive product in Phase 3 development designed to deliver sublingual sufentanil 15 mcg microtablets with a 20-minute lockout period. The current study demonstrated the ability of the System to produce comparable patient satisfaction with post-operative pain control, faster onset, and reduced incidence of oxygen desaturation with post-operative pain control to IV PCA with morphine 1 mg q6 min lockout.