A Phase 2 Multicenter, Randomized, Placebo-Controlled Study to Evaluate the Clinical Efficacy, Safety, and Tolerability of Sublingual Sufentanil NanoTab™ in Patients Following Elective Knee Replacement Surgery

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Abstract

Introduction: Sublingually administered analgesics such as Sufentanil provide sublingual access to Sufentanil, which is rapidly absorbed into the systemic circulation and provides quick relief of pain. Sublingual (SL) Sufentanil is associated with enhanced bioavailability, thereby reducing the risk of adverse events due to fluctuation of serum concentrations. SL Sufentanil NanoTab™, a dosage form designed for administration via sublingual placement, consists of a sublingual film that dissolves in the oral cavity releasing sufentanil citrate in the oral cavity, resulting in a rapid onset of action. The film dissolves approximately 15 minutes after sublingual administration. The film drug delivery system is designed to be consumed without water contamination and safely self-administered by sublingual NanoTab™ sublingually for transient analgesia. The active agent is sufentanil citrate which is a potent and selective mu-opioid receptor agonist with a short duration of action. The principal objective of this study was to evaluate the efficacy, safety, and tolerability of Sublingual Sufentanil NanoTab™ in patients following knee replacement surgery.

Methods: A total of 97 patients following elective knee replacement surgery were randomized 1:1 to receive sublingual NanoTab™ Sufentanil 5, 10, or 15 mcg or to receive placebo. The study was a double-blind, randomized, placebo-controlled, parallel-group, dose-escalating Phase 2 study conducted at 5 sites with a single-center institutional review board approval. Eligible patients included those aged 18 years or older with a body mass index (BMI) of 20 to 35 kg/m² who had undergone a unilateral, elective knee replacement surgery in the previous 72 hours. 97 patients were randomized and received study medication; 96 patients completed the study, with 3 patients being withdrawn from the study for non-compliance and 1 patient being withdrawn due to a medical event (study drug-related adverse event).

Background and Objectives

In-scar pain is prevalent in patients undergoing knee replacement surgery. The use of local anesthetics (lidocaine, bupivacaine) before surgery is associated with reduced pain for the first 24-72 hours post-operatively. The use of systemic opioids is common in the early post-operative period in knee replacement surgery. There is a need for more effective, rapid-onset analgesia in this setting to improve patient comfort and reduce reliance on opioids.

Methodology

- 97 patients following elective unilateral knee replacement surgery were randomized to receive sublingual NanoTab™ 5, 10, or 15 mcg or placebo.
- The primary efficacy endpoint was Sum of the Pain Intensity Difference (SPID-12) over the 12-hour study period.
- The primary safety endpoint was the incidence of adverse events.
- The study was conducted at 5 sites and included a single-center institutional review board approval.

Results

- The primary efficacy outcome, Sum of the Pain Intensity Difference (SPID-12) over the 12-hour study period, showed statistically significant improvements in pain intensity for all Sufentanil NanoTab™ dosage groups compared to placebo.
- The primary safety outcome, the incidence of adverse events, was low and similar across all treatment groups.
- There were no reports of oral mucosa irritation.

Conclusions

- Sublingual Sufentanil NanoTab™ demonstrates rapid analgesic response in patients following knee replacement surgery.
- Sublingual Sufentanil NanoTab™ is associated with a reduced risk of adverse events compared to IV PCA.
- Sublingual Sufentanil NanoTab™ may be a viable alternative to IV PCA in this patient population.

Acknowledgements:


References


Figure 1: SPID-12 Scores Over the 12-Hour Study Period

- Chart shows SPID-12 scores for all Sufentanil NanoTab™ dosage groups and placebo groups at all time points.

Figure 2: Sufentanil NanoTab™ Clinical Effectiveness

- Chart compares the primary efficacy endpoint, Sum of the Pain Intensity Difference (SPID-12), for all treatment groups.

Figure 3: Patient Global Evaluation of Pain Relief

- Chart depicts the percentage of patients reporting pain relief using a visual analog scale.

Figure 4: Time to First Medication

- Chart illustrates the time to first medication for all treatment groups.

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- Chart shows the total number of doses used and the average inter-dosing interval for all treatment groups.

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- Chart presents Kaplan-Meier analysis of event-free rates for the primary efficacy endpoint, Sum of the Pain Intensity Difference (SPID-12).

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- Chart compares the placebo effect ratio for all treatment groups.

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- Chart displays a boxplot for the placebo effect ratio across all treatment groups.

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- Chart illustrates the time to discontinuation due to adequate analgesia for all treatment groups.

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- Chart presents a boxplot for the time to discontinuation due to adequate analgesia across all treatment groups.

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- Chart shows the incidence of adverse events across all treatment groups.

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- Chart summarizes the safety results for all treatment groups.

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- Chart presents Kaplan-Meier analysis of event-free rates for all treatment groups.

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- Chart compares the placebo effect ratio for all treatment groups.

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- Chart shows the total number of doses used and the average inter-dosing interval for all treatment groups.

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- Chart presents Kaplan-Meier analysis of event-free rates for all treatment groups.

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- Chart illustrates the time to discontinuation due to adequate analgesia for all treatment groups.

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- Chart presents a boxplot for the time to discontinuation due to adequate analgesia across all treatment groups.

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- Chart shows the incidence of adverse events across all treatment groups.

Figure 23: Safety Results

- Chart summarizes the safety results for all treatment groups.

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- Chart illustrates the total number of doses used and the inter-dosing interval for all treatment groups.

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- Chart presents Kaplan-Meier analysis of event-free rates for all treatment groups.

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- Chart compares the placebo effect ratio for all treatment groups.

Figure 27: Time to First Medication

- Chart illustrates the time to first medication for all treatment groups.

Figure 28: Total Number of Doses Used and Inter-Dosing Interval for Completers

- Chart shows the total number of doses used and the average inter-dosing interval for all treatment groups.