Opioid withdrawal associated with NKTR-181 or placebo was assessed systematically captured, then reviewed and adjudicated by experts in which is a rigorous approach in which adverse events and drug account...

COWS is an 11-item investigator-administered scale to assess clinical effects In an enriched-enrollment, randomized-withdrawal study of opioid-naïve subjects with chronic low-back pain (SUMMIT-07), NKTR-181 administered at peak more than an hour later with a more gradual increase and decline than oral oxycodone (60 and 40 mg) consistent with its slower onsetting and offsetting effects In an enrichment trial, randomized-withdrawal-study of opioids with chronic low-back pain [SUMMIT-11] at 100 to a 400 mg dose has a greater analgesic effect with a higher risk of withdrawal.

In the study, opioid withdrawal was evaluated using the Clinical Opiate Withdrawal Scale (COWS) and the Subjective Opiate Withdrawal Scale (SOWS). Here we present measurements of withdrawal of NKTR-181 and placebo patients during the randomized treatment and tapering following period to the SUMMIT study.

**Methods**

The randomized, double-blind, randomized withdrawal study included a screening period, an open-label trial period, a 10-week double-blind taper period, and a 2-week safety follow-up period. All study participants were opioid naïve adult patients with chronic, nonmalignant pain of more than 12 months duration, for which non-opioid analgesics therapy was inadequate. All patients were taking no concomitant analgesic treatment. Subjects achieving withdrawal with naloxone were randomized into double-blind withdrawal with NKTR-181. Those who were randomized to placebo had their naloxone dose elevated at 30-rapid increments of 0 mg at the end of the day (not more than 300 mg for the first dose) for five days, and then daily by 30 mg (not more than 900 mg) for up to 14 days prior to the start of the study. Subjects with a COWS score of <5 of the start of the study did not receive any naloxone dose. Subjects were randomized into double-blind withdrawal with NKTR-181.

Opioid withdrawal associated with NKTR-181 or placebo was assessed by COWS and SOWS throughout the trial. These scales were originally developed at patients with chronic active substance abuse with opioids. The COWS is a 16-item observer-administered instrument. It is a widely accepted and validated tool for the evaluation of opioid induced withdrawal symptoms. It is based on 10-point scale ranging from 0 (normal) to 9 (severe) at 16 items, and comprises of items across four domains: autonomic (0–9), mood (0–9), motor (0–9), and sensorial (0–9). The SOWS is a 32-item self-administered questionnaire. It is based on a 0–4 rating scale ranging from no withdrawal (0) to severe withdrawal (4). Both scales are administered at baseline, at randomization, and during the tapering period.

**Results**

COWS and SOWS scores were obtained at pre-specified time points or following early discontinuation. During randomized treatment, COWS scores were obtained at the end of the safety follow-up period only for subjects who did not enter a long-term withdrawal-study. During randomization, COWS scores were obtained at day 1, day 4, day 7, and day 10 for 3 days of treatment-discontinuing and daily during the tapering period. COWS and SOWS scores were mildly to moderate withdrawal symptoms.

**Conclusion**

More than 300 mg acetaminophen for breakthrough pain (1 tablet every 6 hours). During and after the randomization period, MADDERS identified 9/309 (2.9%) subjects and the ensuing follow-up period. These results show that reducing the rate of CNS entry does not predispose no moderate or severe cases reported based on COWS and SOWS scores, during randomized treatment, clinical symptoms of withdrawal were rare, with no moderate or severe cases reported based on COWS and SOWS scores. During randomized treatment, clinical symptoms of withdrawal were rare, with no moderate or severe cases reported based on COWS and SOWS scores.

**References**


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A recent phase 3 trial of an oral extended-release opioid with a 12-hour duration of action for chronic low back pain has been studied. Several studies have reported on the efficacy and safety of this novel opioid.