Objective: To evaluate the analgesic efficacy, safety, and tolerability of NKTR-181 administered at 100 to 400 mg twice daily in patients with moderate to severe chronic low-back pain.

Method: A double-blind, placebo-controlled, 12-week randomized-withdrawal study in patients enrolled in an open-label titration period, and to include a 7-day washout period before randomization. Patients were randomized in a 1:1 ratio to double-blind treatment with NKTR-181 or placebo. Sleep quality was evaluated using the Medical Outcomes Study (MOS) Sleep Scale–Revised. Assessments of key secondary endpoints included change from pre-treatment score at week 12 relative to the baseline pain score. Key secondary endpoints included the percentage of patients responding to rescue medication in NKTR-181 patients was less than placebo throughout the randomized treatment period.

Results: The percentage of patients characterized themselves as “very much improved” at week 12 (51% vs 35% for placebo, \(p=0.0019\)). Changes in MOS Sleep Scale scores among observed cases at week 12 are summarized in Table 2. The difference between treatment groups showed statistically significant improvement in the study’s primary endpoint, sleep disturbance (P<0.0001), sleep adequacy (P<0.001), and sleep quality (P<0.0001) for NKTR-181 compared with placebo. Scores for daytime sleepiness (somnolence) and sleep quantity were not statistically different between groups (P=0.23). The proportion of patients responding to rescue medication in NKTR-181 patients was less than placebo throughout the randomized treatment period.

Conclusions: This study demonstrated a strong efficacy and favorable safety/tolerability profile for NKTR-181, a novel opioid analgesic molecule in patients with moderate to severe chronic low-back pain. This population of patients with chronic low-back pain is underserved with effective treatment options, and NKTR-181 may present as a potential therapy to address the unmet need for a safer opioid analgesic for patients with chronic pain.

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