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EFFICACY AND SAFETY OF EN3231, AN NMDA-ENHANCED ANALGESIC: RESULTS OF A 3-MONTH RANDOMIZED, CONTROLLED TRIAL DEMONSTRATE FASTER RESOLUTION OF OPIOID-RELATED SIDE EFFECTS COMPARED TO MORPHINE ALONE

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The objectives of this study were to evaluate the average daily opioid dose requirement of the NMDA-enhanced analgesic EN3231 [a 1:1 (mg:mg) combination of morphine sulfate (MS) and dextromethorphan (DM)] compared to an opioid alone (MS), the degree of analgesia, and the incidence and severity of adverse events (AEs) over a 3-month treatment period.

This was a multiple-dose, randomized, 2-arm, double-blind, parallel-design trial. Patients with moderate-to-severe nociceptive chronic pain on stable doses of opioid analgesics (equivalent to 60 to 360 mg/day MS) were randomized to EN3231 (MS:DM, 15mg:15mg) PRN or MS 15mg PRN using stratification based on the MS-equivalent dose. Dosing began at 50% of the morphine-equivalent dose, and patients continually self-titrated to maintain the same degree of pain control over 90 days.

The primary outcome measure, change in daily morphine intake compared to baseline, showed no statistically significant difference between treatment groups. The average daily pain intensity, as expected, showed that patients maintained satisfactory pain control in both treatment groups throughout the 90-day treatment period.

Opioid-related side effects were assessed by patient daily self-report using an opioid Bothersome Scale measuring 9 symptoms. Kaplan-Meier survival analysis demonstrated that the time-to-resolution of gastrointestinal and central nervous system side effects was significantly sooner in patients receiving EN3231 compared to morphine alone ($p < 0.05$).

In conclusion, the results provide substantially new and clinically important data regarding the improved safety and tolerability of EN3231 compared to MS alone. While patients receiving EN3231 achieved equivalent pain control at equal doses vs. MS alone, EN3231 patients reported statistically significant and clinically meaningful reduction in time to complete resolution of common opioid-related side effects, including GI and CNS effects.

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