NALBUPHINE ER TABLETS IN HEMODIALYSIS PATIENTS WITH SEVERE UREMIC PRURITUS: MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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BACKGROUND

• A recently conducted study of 73,000 United States dialysis patients reported that 60% have pruritus and that 30% are moderately to extremely bothered by it1.
• Uremic pruritus is associated with significant decreases in quality of life (QoL), sleep, and greater use of IV antibiotics, ESA, and iron2.
• The pathogenesis of uremic pruritus may involve endogenous κ/µ opioid ligand ratio imbalance2,3.
• Nalbuphine ER tablets (NAL) are a κ-opioid agonist/µ-opioid antagonist being developed for chronic pruritic conditions.

METHODS

• In this multicenter, randomized, double-blind trial 373 hemodialysis patients were randomized (1:1:1) to NAL 60 mg (n=128) or 120 mg (n=120) or placebo (n=125) BID and treated for 8 weeks. Background antipruritic medications were allowed.
• The primary entry criteria were a mean numerical rating scale score (NRS) ≥4.5 (0 [no itch] -10 [worst possible itching]) with at least 2 of 6 scores >5 and a Patient-Assessed Disease Severity of B or C (sometimes or often bothered by scratch marks, and problems sleeping because of itching).

RESULTS (Severe Subgroup)

• A recently conducted study of 73,000 United States dialysis patients reported that 60% have pruritus and that 30% are moderately to extremely bothered by it1.

• Demographics, dialysis adequacy, phosphorus, PTH, and antihistamine use were balanced (Table 1). The mean duration of itching was 3.2 years.

• The study overall met its primary endpoint: The NRS in the NAL 120 mg group declined by 49%, from 6.9 (1.5) to 3.5 (2.1), p = 0.017 vs. placebo. The effects were significant within 1 week following titration and durable over 8 weeks.
• Among a subgroup of 183 patients with severe pruritus (baseline NRS ≥7.0), examined post-hoc, itching intensity in those randomized to NAL 120, decreased by 55% (from severe to mild, mean NRS 8.2 to 4.5 ) (Figures 1 and 2) and sleep disruption (Itch MOS, Figure 3) due to itching improved significantly (Figure 4).
• Itching-related Quality of Life (Skindex-10) improved, but not significantly (NAL120 vs. placebo, p = 0.114).

• The trial met its primary endpoint, demonstrating a significant reduction in itch intensity in the NAL120 group vs. placebo in hemodialysis patients with moderate and severe uremic pruritus receiving background antipruritic drugs such as antihistamines and corticosteroids.

• Among the subgroup of patients with severe uremic pruritus (NRS ≥7.0) at baseline receiving NAL 120, itching intensity and sleep disruption decreased significantly.
• This largest-to-date randomized trial in uremic pruritus demonstrated the efficacy of Nalbuphine ER tablets for one of the most distressing complications of end-stage renal disease.

REFERENCES

2. Kumagai In Itch Basic Mechanisms and Therapy 2004
3. Wang Int J Dermatology 2010