A Multicenter, Phase 2/3 Randomized, Double-Blind, Placebo-Controlled Trial Of Nalubiphine HCI ER Tablets for the Treatment of Uremic Pruritus: Baseline Population Characteristics

Vandana S. Mathur, MD FASN 1, Jayant Kumar, MD 2, Paul W. Crawford, MD 3, Howard Hait, MS 4, Thomas Sciascia, MD 4

1 Mathur Consulting, Woodsdale, CA, 2 Renal Medicine Associates, Albuquerque, NM, 3 Associates in Nephrology, South Carolina, 4 Trevi Therapeutics, New Haven, CT

BACKGROUND

- Moderate and severe uremic pruritus affects 15-40% of hemodialysis patients (HDPS) and is associated with poor quality of life, sleep disruption, and mood disturbances.
- Uremic pruritus is mainly characterized by the sensation of itchiness in the absence of any visible skin changes.
- Nalbuphine, a kappa opioid agonist and mu opioid antagonist, is being developed for treatment of uremic pruritus.
- Nalbuphine has been available in a parenteral formulation for analgesic use in the US and Europe for over 20 years and would be used under the same conditions and contraindications.
- The plasma half-life of injectable nalbuphine is 2 hours vs. 9 hours for the extended release (ER) formulation contained in this study.
- Nalbuphine is not a scheduled drug.

METHODS

Study Design (Figure 1)
- Multicenter, multinational, double-blind, placebo-controlled trial
- Study Population:
  - HDPS with moderate or severe pruritus
  - Worst Itching Numerical Rating Scale (NRS) itch intensity mean of 6
- Treatment Groups (Randomized 1:1:1)
  - Placebo
  - NAL 60 mg BID
  - NAL 120 mg BID
- Study Duration:
  - Treatment duration of 8 weeks, followed by a 2 week washout
- Secondary Efficacy Endpoints (validated measures in the dialysis population)
  - Patient reported outcomes measures across 4 quartiles of the baseline Worst Itching Numerical Rating Scale
  - Skindex 10 (measure of itch related quality of life (Type C) (most afflicted) (%)
  - Hospital Anxiety and Depression Scale (HADS)
  - Itch Basic Mechanisms and Therapy

RESULTS

- Approximately half the study population had “moderate pruritus” (Quartiles 1 and 2) and the other half had “severe pruritus” (Quartiles 3 and 4) (Figure 1)
- The proportion of patients with impaired quality of life (Skindex 10) including sleep, mood, and daily life of injectable nalbuphine is 2 hours vs. 9 hours for the extended release (ER) formulation contained in this study.
- Nalbuphine is not a scheduled drug.

- This analysis is limited to the study population, which included only moderate and severe pruritus.
- Factors traditionally hypothesized to be relevant in the pathogenesis of uremic pruritus (i.e. PTH, serum phosphate, under nutrition) were unassociated with itching intensity. This finding is consistent with the emerging concept that once incited, uremic pruritus is self perpetuating due to central nervous system sensitization, such that nor- mally non pruritic stimuli are perceived as itching.
- This finding is consistent with the emerging concept that once incited, uremic pruritus is self perpetuating due to central nervous system sensitization, such that nor- mally non pruritic stimuli are perceived as itching.
- These finding is consistent with the emerging concept that once incited, uremic pruritus is self perpetuating due to central nervous system sensitization, such that nor- mally non pruritic stimuli are perceived as itching.
- These finding is consistent with the emerging concept that once incited, uremic pruritus is self perpetuating due to central nervous system sensitization, such that nor- mally non pruritic stimuli are perceived as itching.
- These finding is consistent with the emerging concept that once incited, uremic pruritus is self perpetuating due to central nervous system sensitization, such that nor- mally non pruritic stimuli are perceived as itching.
- These finding is consistent with the emerging concept that once incited, uremic pruritus is self perpetuating due to central nervous system sensitization, such that nor- mally non pruritic stimuli are perceived as itching.
- These finding is consistent with the emerging concept that once incited, uremic pruritus is self perpetuating due to central nervous system sensitization, such that nor-

CONCLUSIONS AND DISCUSSIONS

This study demonstrates the association between the severity of itching in dialysis pa-

Financial Support: Trevi Therapeutics, Inc.