INTRODUCTION

• Prurigo nodularis (PN) is a relatively rare, intensely pruritic dermatologic disease that has developed from itching and scratching, with a high associated quality-of-life impact.1
• The current guidelines for treating PN are based on empirical observations and single, randomized, controlled trials.2,3,4
• Therapies such as calcineurin inhibitors, topical steroids, and systemic antihistamines have limited data to support their use.
• The synthetic opioid nalbuphine, a dual-acting a antagonist and k agonist, has shown efficacy in morphine-induced pruritus and uremic pruritis,5,6 but an evaluation of the efficacy and safety of nalbuphine in PN is currently lacking.

OBJECTIVE

To evaluate the efficacy and safety of oral nalbuphine extended release (NAL-ER) tablets in a phase 2, multicenter, randomized, double-blind, placebo-controlled trial with an open-label extension phase.

METHODS

• Patients with moderate-to-severe PN (pruritus duration ≥ 6 weeks) were randomized 1:1 to receive either NAL-ER 81 mg or 162 mg tablets twice-daily (b.i.d.), or placebo for 8 weeks of stable dosing following a 2-week titration period (for dose-escalation from 30 mg once-daily to the assigned target dose).
• Itch scores based on Worst Itch (WI) and average Itch Numerical Rating Scale (NRS) with 24-hour recall were collected daily by an electronic diary (DIARYpro).7
• The primary efficacy endpoint was the proportion of patients with a ≥ 30% reduction in 7-day mean WI-NRS from baseline to Week 10/last observation.

RESULTS

• Of 62 treated patients, 50 completed 10 weeks of treatment. The primary efficacy endpoint of percentage of responders with ≥ 30% reduction from baseline in 7-day WI intensity was not significant for the primary modified intent-to-treat analysis but was significant for NAL-ER 162 mg (66.7%) compared with placebo (40.0%; p = 0.062) among completers (Table 1).

RESULTS, continued

• Treatment-emergent adverse events (TEAEs) occurred predominantly during the titration period in both studies. During double-blind, stable-dose treatment that followed titration, TEAE incidence was similar for both active treatment arms and placebo (Table 2).
• Common TEAEs were nausea, dizziness, headache, and fatigue; the majority of these events were also considered treatment related in all 3 arms (Table 2).
• In the extension study, 34 patients reported 154 TEAEs, including 26 patients with ≥ 1 drug-related TEAE. TEAEs included nausea (n = 9; 25.0%), and dizziness and fatigue (n = 8 for each; 22.9%).

CONCLUSION

• The findings of this study indicate that in patients with PN, NAL-ER tablets, at a dose of 162 mg b.i.d., appear to have a measurable antipruritic effect for patients who successfully maintain the initial therapy for at least 10 weeks.
• The significantly greater response rate for NAL-ER 162 mg patients who completed the full 10 weeks of double-blind treatment compared with placebo is consistent with a clinical benefit that requires compliance with the designated dosing schedule and duration.
• Further evaluation of NAL-ER, including further elucidation of its underlying mechanism of action, is thus warranted in this difficult-to-treat disease, with a larger phase 2b/3 clinical trial currently evaluating the 162 mg b.i.d. dose.

CONFLICTS OF INTEREST

• IFW is an investigator in clinical trials for Kiniksa, Menlo Therapeutics, and Trevi Therapeutics. TRS is an employee of Trevi Therapeutics. SST is an investigator for Dermasecare, Galderma, Kiniksa, Menlo Therapeutics, Novartis, Sanofi, and Vanda Therapeutics; a consultant and/or advisory board member for Almirall, Bayer, Benerofard, Bellus Health, Bionorica, Cara Therapeutics, Celgene, Cis, DoBiopharma, Galderma, Kiniksa, Lilly, Menlo Therapeutics, Novartis, Pfizer, Sanofi, and Trevi Therapeutics.

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