Dupilumab improves itch and skin lesions in North American patients with prurigo nodularis: a subset analysis of the pooled results from two phase 3 trials (LIBERTY-PN PRIME and PRIME2)

Sarina B. Elmariah¹, Nicholas Mollanazar², H. Chi-ho Hong³, Kirsten Walker⁵, Daniel C. Butler⁷, Amy Praestgaard⁸, Joseph Zahn⁹, Simmi Wiggins¹⁰

¹University of California San Francisco, San Francisco, CA, USA; ²University of Pennsylvania, Philadelphia, PA, USA; ³University of British Columbia, Vancouver, BC, Canada; ⁴Probity Medical Research, Waterloo, ON, Canada; ⁵University of Saskatchewan College of Medicine, Saskatoon, SK, Canada; ⁶Probity Medical Research, Waterloo, ON, Canada; ⁷University of Arizona, Tucson, AZ, USA; ⁸Sanofi, Cambridge, MA, USA; ⁹Regeneron Pharmaceuticals Inc., Tarrytown, NY, USA; ¹⁰Sanofi, Reading, UK.

Introduction/Background: Prurigo nodularis (PN) is a chronic inflammatory skin disease characterized by pruritic papulonodular lesions that substantially affect quality of life. Dupilumab is the first systemic treatment approved by the US Food and Drug Administration for the treatment of PN.

Objectives: The aim of this post hoc subgroup analysis was to assess the efficacy and safety of dupilumab in North American patients with PN.

Methods: LIBERTY-PN PRIME and PRIME2 were randomized, double-blind, multi-center, parallel-group, 24-week, phase 3 trials in adults with PN with ≥20 nodules and severe itch, inadequately controlled with topical prescription therapies or for whom these therapies were inadvisable. This pooled subgroup analysis of LIBERTY-PN PRIME/PRIME2 (NCT04183335/NCT04202679) included adults with moderate-to-severe PN receiving 300 mg dupilumab (n = 153) or matched placebo (n = 158) every 2 weeks for 24 weeks. Approximately 20% and 16% of enrolled patients were based in North America in the PRIME and PRIME2 trials, respectively. This analysis included the proportion of patients in the North American subpopulation who achieved (i) ≥4-point improvement in the Worst Itch Numerical Rating Scale (WI-NRS); (ii) Investigator’s Global Assessment for PN stage of disease (IGA PN-S) score of 0 (no nodules) or 1 (≤5 nodules); (iii) both (i) and (ii); (iv) 9-point improvement in the
Dermatology Life Quality Index (DLQI); (v) 3-point improvement in the Sleep Numerical Rating Score (NRS); (vi) 4-point improvement in Skin Pain NRS. Reported P values calculated using Chi-square or Fisher’s exact tests are nominal and not adjusted for multiplicity. Treatment-emergent adverse effects (TEAE) and severe adverse effects (SAE) were assessed.

**Results:** Baseline disease characteristics of the North American subpopulation were consistent with the overall population, except for a longer duration of disease (North American subpopulation, mean [SD] years: dupilumab 7.2 [9.97] years; placebo 7.5 [9.72] years. Overall population: dupilumab 5.68 [7.21] years; placebo 5.44 [6.60] years).

At Week 12, a numerically greater proportion of dupilumab-treated patients in the North American subpopulation achieved ≥4-point improvement in the WI-NRS (dupilumab vs placebo: 41.4% vs 21.9%; \( P = 0.1 \)), and IGA PN-S score 0/1 (41.4% vs 28.1%; \( P = 0.28 \)). By Week 24, the proportion of dupilumab-treated patients who achieved these endpoints was significantly greater than the proportion of patients who were given placebo (WI-NRS: 62.1% vs 21.9%; \( P = 0.0014 \). IGA PN-S 0/1: 55.2% vs 21.9%; \( P = 0.007 \)). The proportion of patients who achieved both ≥4-point improvement in the WI-NRS and IGA PN-S score 0/1 was numerically greater at Week 12 (20.7% vs 12.5%; \( P = 0.5 \)) and significantly greater at Week 24 (44.9% vs 12.5%; \( P = 0.009 \)).

Patients in the dupilumab group were significantly more likely to achieve a ≥9-point improvement in DLQI, vs placebo (Week 12: 65.5% vs 21.9%; \( P = 0.0006 \). Week 24: 65.5% vs 25%; \( P = 0.0015 \)). Patients who received dupilumab were significantly more likely to achieve a 3-point improvement in the Sleep NRS (Week 12: 34.5% vs 9.4%; \( P = 0.027 \). Week 24: 48.3% vs 3.1%; \( P < 0.0001 \)). The proportion of dupilumab-treated patients who achieved a 4-point improvement in the Skin Pain NRS was numerically greater at Week 12 (41.4% vs 18.8%; \( P = 0.053 \)) and significantly greater at Week 24 (58.6% vs 21.9%; \( P = 0.003 \)) compared with placebo. Incidences of TEAE and SAE in the North American subpopulation were consistent with the overall population.
**Conclusions:** Dupilumab treatment led to improvements in itch, skin lesions, and health-related quality-of-life, in North American patients with PN. Overall safety was generally consistent with the known safety profile of dupilumab.

**Keywords:** prurigo nodularis, North America, dupilumab, itch, lesions.

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