Dupilumab Significantly Improves Itch and Skin Lesions in Patients with Prurigo Nodularis: Pooled Results from Two Phase 3 Trials (LiBERTY-PN PRIME and PRIME2)

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Introduction/Background: Prurigo nodularis (PN), a chronic inflammatory and pruritic skin condition with severely itchy skin nodules, substantially affects quality of life, and is often inadequately controlled with topical medications. Recently, the US Food and Drug Administration approved dupilumab as the first systemic therapy for PN. Two randomized clinical trials with similar design, LiBERTY-PN PRIME (NCT04183335) and PRIME2 (NCT04202679), demonstrated the efficacy and safety of dupilumab in adults with PN inadequately controlled with topical medications or for whom those were inadvisable.

Objective: To report the efficacy of dupilumab on pruritus and skin lesions in PN, as well as its safety, by analyzing pooled data from PRIME and PRIME2 trials, given their similar trial design.

Methods: PRIME and PRIME2 were multicenter, randomized, placebo-controlled, double-blinded, phase 3 trials, which comprised a 2–4-week screening, 24-week treatment, and 12-week follow-up
period. Itch severity was measured by Worst Itch Numerical Rating Scale (WI-NRS), ranging from 0 (no itch) to 10 (worst itch imaginable). Severity of skin lesions was assessed using Investigator’s Global Assessment for PN-Stage (IGA PN-S), as score 0 (no nodules), 1 (1–5 nodules), 2 (6–19 nodules), 3 (20–99 nodules), or 4 (over 100 nodules). To be eligible for enrollment patients had WI-NRS ≥ 7, and IGA PN-S score 3 or 4. Patients received subcutaneous dupilumab 300 mg (loading dose, 600 mg) or matched placebo every two weeks for 24 weeks. Efficacy endpoints were: proportion of patients with WI-NRS score reduction of ≥ 4 points, proportion of patients who achieved IGA PN-S score of 0 or 1, and proportion of patients who achieved concomitantly WI-NRS reduction of ≥ 4 points and IGA PN-S score of 0 or 1, at Week 12 and at Week 24.

**Results:** At baseline, demographic and disease characteristics were balanced between the PRIME and PRIME2 pooled dupilumab (n = 153), and pooled placebo groups (n = 158). All but 1 patient had used prior topical medications for PN, and 66.2% had used off-label systemic medications. Despite prior therapies, at baseline, the overall mean (standard deviation) WI-NRS score was 8.5 (1.0); 66.3% of patients had 20–99 nodules, and 33.7% had over 100 nodules. At Week 12, the ≥ 4-point reduction in WI-NRS in the dupilumab group was achieved by 62 patients (40.5%), and at Week 24, by 90 (58.8%), compared with 30 patients (19.0%) in the placebo group at each time point (P < 0.0001 for both). An IGA PN-S score of 0 or 1 was achieved by 44 (28.8%) patients in the dupilumab group vs 19 (12.0%) in the placebo group at Week 12 (P = 0.0002), and respectively by 71 (46.4%) vs 27 (17.1%) patients at Week 24 (P < 0.0001). The concomitant reduction in WI-NRS by ≥ 4 points and IGA PN-S score of 0 or 1 was achieved by 28 (18.3%) patients in the dupilumab group vs 11 (7.0%) in the placebo group at Week 12 (P = 0.0021), and respectively by 54 (35.3%) vs 14 (8.9%) patients at Week 24 (P < 0.0001). The rate of treatment-emergent adverse events was 59.9% with dupilumab and 51.0% with placebo. The most common adverse events were headache (5.3% vs 5.7%), neurodermatitis (2.0% vs 5.7%), skin infections (3.9% vs 7.6%), and injection-site reactions (3.9% vs 5.7%) in dupilumab vs placebo groups.
**Conclusion**: Dupilumab demonstrated clinically meaningful and statistically significant improvements in itch and skin lesions vs placebo in patients with PN, confirming the findings from individual PRIME and PRIME2 studies. The safety profile of dupilumab was consistent with the known safety profile in its approved indications.

**Keywords**: prurigo nodularis, dupilumab, WI-NRS, IGA PN-S, adults

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