Efficacy and Safety of Switching from Dupilumab to Upadacitinib in Moderate-to-Severe Atopic Dermatitis: Results from an Open-Label Extension Trial

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Introduction: Upadacitinib (UPA) is a selective oral Janus kinase (JAK) inhibitor with greater inhibitory potency for JAK1 than JAK2, JAK3, and tyrosine kinase 2. Phase 2 and 3 studies demonstrated that once daily UPA 15 mg or 30 mg is effective and well-tolerated in patients with moderate-to-severe atopic dermatitis (AD). In the phase 3b Heads Up clinical trial, UPA 30 mg demonstrated superior efficacy versus dupilumab (DUPI) for the primary and all secondary endpoints in adults with moderate-to-severe AD. Here, we evaluated the efficacy and safety of UPA using interim data from the open-label extension (OLE) study that followed Heads Up (M19-850, NCT04195698).

Methods: Efficacy and safety of open-label UPA 30 mg was evaluated in patients who were initially randomized to either UPA 30 mg orally once daily or DUPI 300 mg subcutaneously every two weeks (after initial loading dose), completed the 24-week Heads Up study, and were candidates for long-term UPA therapy. Regardless of response to treatment in Heads Up, all patients received open-label UPA 30 mg orally once daily upon entry to the OLE; there was no washout period, with the last dose of DUPI administered at Week 22 in Heads Up. Efficacy was assessed as proportions of patients achieving 75%, 90%, or 100% improvement in Eczema Area and Severity Index (EASI 75/90/100) as well as improvement in Worst Pruritus Numerical Rating Scale ≥4 (WP-NRS Improvement ≥4) upon entry and after 16 weeks into M19-850, using an observed cases (OC) analysis. Safety was assessed as treatment-emergent adverse events (AEs) for all patients receiving ≥1 dose of study drug.

Results: A total of 245 patients initially randomized to DUPI and 239 patients initially randomized to UPA who completed Heads Up were subsequently enrolled in the OLE and treated with open-label UPA 30 mg. At the end of Heads Up (Week 24), 85.7%, 66.4%, 16.0%, and 63.4% of DUPI-treated patients achieved EASI 75, EASI 90, EASI 100, and WP-NRS Improvement ≥4, respectively. After 16 weeks of UPA treatment (Week 40), 96.6% achieved EASI 75, 87.7% achieved EASI 90, 42.4% achieved EASI 100, and 78.7% achieved WP-NRS Improvement ≥4 (**Figure 1**). Among patients who did not achieve EASI 75 on DUPI at Week 24 in Heads Up, 87.5% achieved EASI 75, 68.8% achieved EASI 90, and 21.9% achieved EASI 100 after 16 weeks on UPA. Similarly, among patients who did not achieve WP-NRS Improvement ≥4 at Week 24 with DUPI, 57.7% achieved WP-NRS Improvement ≥4 after 16 weeks on UPA. Among patients initially randomized to UPA who continued on open-label UPA, proportions of patients achieving EASI 75, EASI 90, EASI 100 and WP-NRS Improvement ≥4 at the end of Heads Up were maintained through Week 16 of the OLE. The safety profile of UPA 30 mg remained unchanged with continued treatment. Exposure-adjusted rates of serious AEs, AEs leading to discontinuation, and AEs of special interest reported with UPA were generally lower or similar compared to those observed in the parent study; no new safety risks were observed.

Conclusions: At Week 40, both continued use of UPA as well as switching from DUPI to UPA at Week 24 were well-tolerated and resulted in improved efficacy with higher rates of skin clearance and itch improvement when compared to Week 24 response rates.

Figure 1: Proportions of Patients Achieving Efficacy Endpoints Over Time (OC)

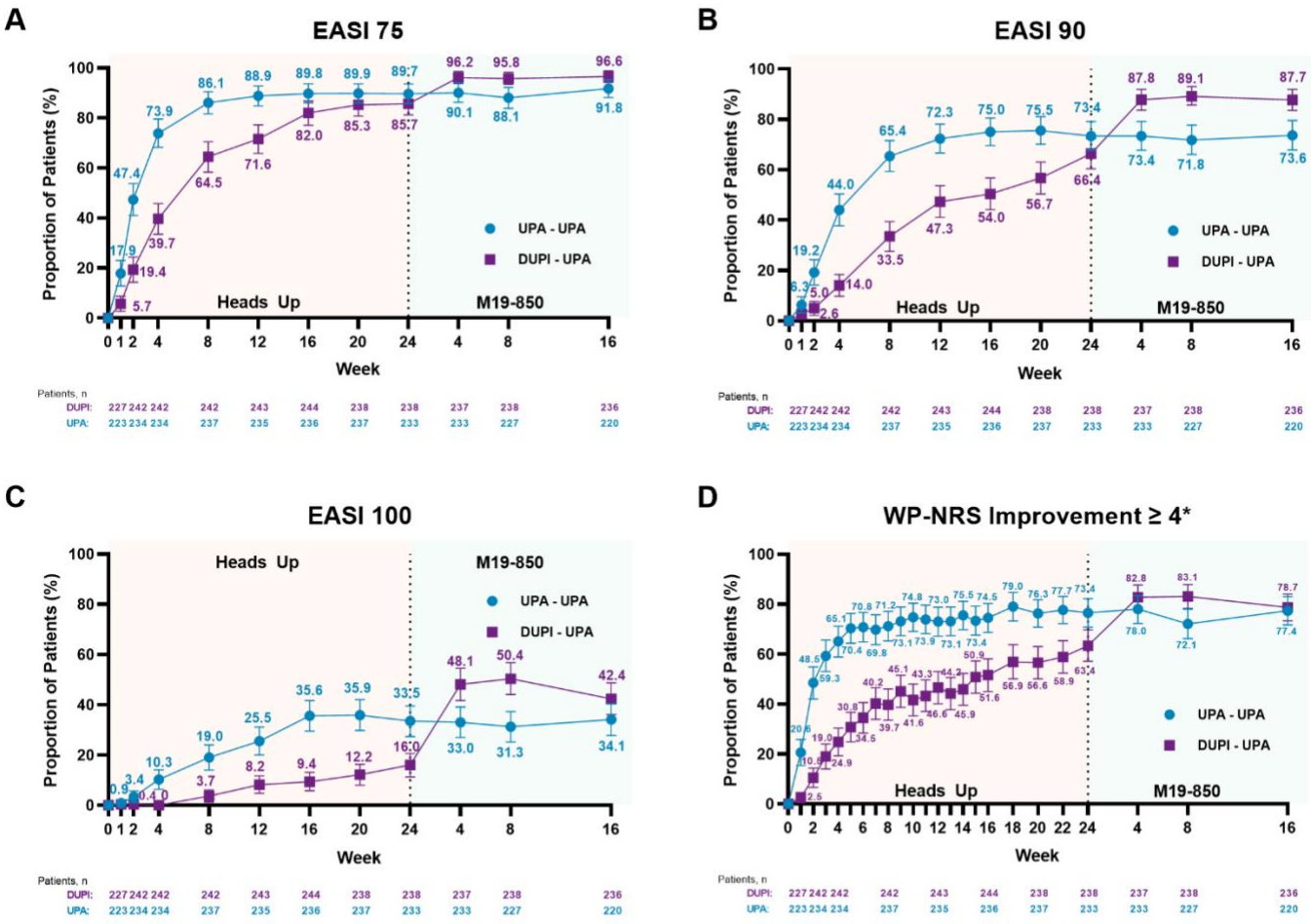

Figure 1. Proportions of patients initially randomized to upadacitinib (blue) or dupilumab (purple) and enrolled in OLE study achieving (A) EASI 75, (B) EASI 90, (C) EASI 100, and (D) WP-NRS Improvement ≥4.
*Assessed in patients with WP-NRS ≥4 at baseline
OC, observed cases imputation method; UPA, upadacitinib; DUPI, dupilumab; EASI, Eczema Area and Severity Index; WP-NRS, Worst Pruritus-Numerical Rating Scale; OLE, open-label extension