Efficacy of Upadacitinib for Moderate-to-Severe Atopic Dermatitis: Analysis of Time Spent in Skin Clearance Response States from the Measure Up 1, Measure Up 2, and Heads Up Studies

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Introduction/Background: Atopic dermatitis (AD) is a debilitating chronic inflammatory skin disease with fluctuating disease severity that requires long-term control. Patients report that complete or almost complete skin clearance is highly important as a treatment goal. Upadacitinib is a selective oral Janus kinase (JAK) inhibitor with greater inhibitory potency for JAK1 vs JAK2, JAK3, and tyrosine kinase 2.

Objectives: In this post-hoc analysis of the upadacitinib phase 3/3b studies, we analyzed the time patients spent in skin clearance response states over 16 weeks with upadacitinib 15 mg (UPA 15) and 30 mg (UPA 30) compared to placebo and dupilumab.

Methods: Data were from phase 3/3b multicenter, randomized, double-blinded studies comparing the safety and efficacy of upadacitinib to either placebo (Measure Up 1 and Measure Up 2) or dupilumab (Heads Up) in patients with moderate-to-severe AD. In the Measure Up 1 and Measure Up 2 studies, adults and adolescents were randomized to receive UPA 15, UPA 30, or placebo once daily for 16 weeks. In the Heads Up study, adults were randomized to receive UPA 30 once daily or dupilumab 300 mg every 2 weeks beginning at week 2 following

an initial loading dose of 600 mg. The days patients spent in skin clearance response states based on Eczema Area Severity Index (EASI) improvements ≥75%/90%/100% (EASI 75/90/100) from baseline were assessed. Missing data at study visits were imputed using non-responder imputation. Response states between study visits were interpolated using last observation carried forward.

Results: Integrated data from Measure Up 1 and Measure Up 2 included 1683 adults and adolescents randomized to UPA 15 (N=557), UPA 30 (N=567), or placebo (N=559); 44.0% were female, and 48.8% had previously received systemic therapy. In the Heads Up study, 692 adults were randomized to UPA 30 (N=348) or dupilumab (N=344); 45.5% were female, and 51.0% had previously received systemic therapy. Patients in Measure Up 1 and 2 taking UPA 15 or UPA 30 cumulatively spent a greater proportion of days in EASI 75 (UPA 15: 54.2%, UPA 30: 64.6%, Placebo: 10.2%), EASI 90 (UPA 15: 32.0%, UPA 30: 44.0%, Placebo: 3.2%), and EASI 100 (UPA 15: 7.5%, UPA 30: 13.5%, Placebo: 0.6%) response states compared to placebo over 16 weeks. In the Heads Up study, patients taking UPA 30 vs dupilumab cumulatively spent a greater proportion of days in EASI 75 (58.9% vs 36.9%), EASI 90 (42.1% vs 19.1%), and EASI 100 (11.8% vs 3.3%) response states over 16 weeks.

Conclusions: Treatment of moderate-to-severe AD with UPA 15 or UPA 30 resulted in a greater proportion of days spent with higher levels of skin clearance (EASI 75/90/100) compared to placebo over 16 weeks, mirroring findings from the Heads Up study comparing UPA 30 to dupilumab. Increases in time spent with high levels of skin clearance with upadacitinib treatment may reflect improved long-term disease control and translate into more time spent experiencing a better quality of life that is less burdened by AD.

Keywords (5): upadacitinib, dupilumab, atopic dermatitis, skin clearance, EASI

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BM Calimlim, Y Liu, and **A Platt** are full-time employees of AbbVie Inc and may hold AbbVie stock and/or stock options.

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