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Efficacy and Safety of Upadacitinib Through 140 Weeks in Adolescents and Adults with Moderate-to-Severe Atopic Dermatitis: Phase 3 Randomized Clinical Trial Results

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Introduction & Objectives: Upadacitinib (UPA) is an oral Janus kinase 1 (JAK1) inhibitor approved in multiple countries for the treatment of adolescents and adults with moderate-to-severe atopic dermatitis (AD). Here, we present the efficacy and safety of UPA administered over 140 weeks in an ongoing randomized, double-blinded, multicenter phase 3 study (Measure Up 1, NCT03569293).

Materials & Methods: Patients (12–75 years) with moderate-to-severe AD were randomized 1:1:1 to receive UPA 15 mg (UPA15), UPA 30 mg (UPA30), or placebo (PBO) once daily at baseline. At week 16, PBO-treated patients were re-randomized 1:1 to receive UPA15 (PBO/UPA15) or UPA30 (PBO/UPA30) once daily. Co-primary endpoints were the proportion of patients achieving ≥75% reduction in EASI (EASI 75) from baseline and vIGA-AD of clear (0) or almost clear (1) with ≥2 grades of reduction from baseline (vIGA-AD 0/1) at week 16. A meaningful improvement in itch, defined as a ≥4-point reduction in Worst Pruritus Numeric Rating Scale (ΔWP-NRS≥4), was assessed among patients with baseline WP-NRS≥4. All efficacy endpoints were summarized using the Observed Cases (OC) approach, and no missing data imputation was applied. Safety was assessed by monitoring of serious adverse events (SAEs), treatment-emergent adverse events (TEAEs), and treatment-emergent adverse events of special interest (AESI), which were analysed as exposure-adjusted rates per 100 patient-years (PY).

Results: Efficacy results were sustained up to week 140 since week 16. Proportions of patients in the UPA15 (205), UPA30 (206), PBO/UPA15 (91), and PBO/UPA30 (94) groups achieving EASI 75 at week 140 were 88.8% (182), 90.3% (186), 83.5% (76), and 89.4% (84), respectively, and for vIGA-AD 0/1 was 63.4% (130), 65.5% (135), 60.4% (55), and 75.5% (71), respectively. Proportions of patients achieving an improvement (reduction) in WP-NRS≥4 from baseline at week 140 were 68.0% (136), 70.5% (146), 71.3% (62), and 81.3% (74) respectively. Overall, the rates of AESIs were similar across treatment groups (Table 1), which aligned with prior reports at earlier time points. Both UPA15 and UPA30 were well-tolerated in all patients, and no new safety signals were observed compared to the known safety profile of UPA. Data from two additional pivotal studies will be available at the time

of presentation.

Conclusion: In this interim analysis, sustained skin clearance and itch and a consistent safety profile were observed with UPA 15 mg and UPA 30 mg across 140 weeks in adolescent and adult patients with moderate-to-severe AD.

Table 1. Treatment-Emergent Adverse Events (TEAEs) During Administration of Upadacitinib Through Week 140 for Patients Receiving UPA 15 mg or UPA 30 mg in Measure Up 1.

	UPA15 (N=432)	UPA30 (N= 432)	Total (N=864)
Events (events/100 PY)	**PY=1238.2**	**PY= 1270.6**	**PY= 2508.9**
AEs n (%)			
Any TEAE	2522 (203.7)	3197 (251.6)	5719 (228.0)
Severe AEs	137 (11.1)	205 (16.1)	342 (13.6)
Serious AEs	67 (5.4)	101 (7.9)	168 (6.7)
AEs leading to discontinuation of study drug	40 (3.2)	58 (4.6)	98 (3.9)
Deaths	0	2 (0.2)	2 (<0.1)
AESIs			
Serious infections	24 (1.9)	43 (3.4)	67 (2.7)
Opportunistic infection excluding tuberculosis and herpes zoster	1 (<0.1)	3 (0.2)	4 (0.2)
Herpes zoster	1 (<0.1)	4 (0.3)	5 (0.2)
Active tuberculosis	1 (<0.1)	0	1 (<0.1)
Non-melanoma skin cancer (NMSC)	1 (<0.1)	0	1 (<0.1)
Malignancy other than NMSC	4 (0.3)	6 (0.5)	10 (0.4)
Lymphoma	0	0	0
Hepatic disorder	0	1 (<0.1)	1 (<0.1)
Adjudicated gastrointestinal perforation	0	0	0
Anemia	0	0	0
Neutropenia	0	0	0
Lymphopenia	0	0	0
CPK elevation	1 (<0.1)	0	1 (<0.1)
Renal dysfunction	0	1 (<0.1)	1 (<0.1)
Adjudicated MACE	2 (0.2)	0	2 (<0.1)
Adjudicated VTE	2 (0.2)	1 (<0.1)	3 (0.1)

PY, patient year; AE, adverse event; TEAE, treatment-emergent adverse event; AESI, adverse event of special interest; NMSC, non-melanoma skin cancer; CPK, creatine phosphokinase; MACE, major adverse cardiovascular event; VTE, venous thromboembolic event; UPA upadacitinib; TCS, topical corticosteroid. Data include all patients who had at least one dose of UPA.