Improvement in Itch, Symptoms, and Quality of Life With Upadacitinib Through Week 16 in Adults and Adolescents With Atopic Dermatitis: Results From Phase 3 Studies (Measure Up 1, Measure Up 2, and AD Up)

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OBJECTIVE

To assess the effect of once daily oral upadacitinib (UPA)with or without topical corticosteroids on quality of life (QoL) in adults and adolescents with moderate-to-severe atopic dermatitis (AD)

CONCLUSIONS

With oral UPA, rapid and sustained meaningful improvement (as early as week 2) in itch, skin pain, sleep, and QoL was observed consistently in both adults and adolescents with moderate-to-severe AD

In adults and adolescents, both UPA 15 mg and UPA 30 mg were effective in improving symptoms and QoL, with UPA 30 mg yielding numerically greater response rates

These results support the effectiveness of UPA, alone or in combination with topical corticosteroids, in improving disease-specific symptoms and QoL for patients with moderate-to-severe AD

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BACKGROUND

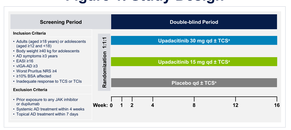
- Atopic dermatitis (AD) is a chronic, itchy, inflammatory skin disease affecting up to 20% of children and 10% of adults in high-income countries[1]
- AD negatively impacts patient quality of life (QoL) and may lead to sleep disturbance, depression, and anxiety[1]
- Efficacy and safety within 16 weeks with upadacitinib (UPA), an oral Janus kinase inhibitor, alone or in combination with topical corticosteroids (TCS), has been demonstrated in adults and adolescents enrolled in phase 3 trials[2,3]
- Patient-reported outcomes (PROs) on itch, symptoms, and QoL captured during the phase 3 trials may elucidate further benefit with UPA treatment in adults and adolescents with AD

METHODS

Study Design and Treatment

- Data from the 16-week double-blind period of 3 randomized, placebo (PBO)-controlled, multicenter, phase 3 clinical trials were used, including Measure Up 1 (NCT03569293), Measure Up 2 (NCT03607422), and AD Up (NCT03568318) **(Figure 1)**

Figure 1. Study Design



AD, atopic dermatitis; EASI, Eczema Area and Severity Index; BSA, body surface area; JAK, Janus kinase; NRS, numerical rating scale; qd, once daily; TCI, topical calcineurin inhibitor; TCS, topical corticosteroids; UPA, upadacitinib; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis.
[a]Patients in the Measure Up 1 and Measure Up 2 studies received UPA monotherapy, while patients in the AD Up study received UPA with concomitant TCS.

Patient-reported Outcome Assessments

- Assessed in adults (≥18 years) and adolescents (≥12 and <18 years) throughout the duration of the studies
- Evaluated as the proportion of patients achieving a predefined minimal clinically important difference from baseline (pre-specified endpoints) and as the proportion of patients achieving a minimal severity score (post hoc analyses)

	PRO Assessment		Clinically Meaningful Improvement (reduction)	Minimal Severity Score
	Itch	Worst Pruritus Numerical Rating Scale	≥4	0 or 1
	Skin Pain and Other Symptoms	Patient-Oriented Eczema Measure ADerm-SS Skin Pain ADerm-SS 7-item Total Symptom Score	≥4 ≥4 ≥28	0–2 0 or 1 0–11
	Sleep	ADerm-IS Sleep	≥12	0–3
	Quality of Life	ADerm-IS Emotional State ADerm-IS Daily Activities Dermatology Life Quality Index	≥11 ≥14 ≥4	0–2 0–2 0 or 1

ADerm-IS, Atopic Dermatitis Impact Scale; ADerm-SS, Atopic Dermatitis Symptom Scale.

RESULTS

Patients

- 2584 patients (2240 adults and 344 adolescents) were analyzed across the 3 trials **(Tables 1** and **2)**
- Baseline demographics and disease characteristics were generally balanced between UPA and PBO groups

Key Findings

- As early as week 2, significantly more adults treated with UPA achieved clinically meaningful improvement in itch, skin pain and other symptoms, sleep, and other QoL aspects compared with adults receiving PBO at week 16 (nominal *P* <.001 for all comparisons) **(Figure 2)**
- Comparable trends of significant improvement with UPA vs PBO were observed in adolescents at weeks 2 and 16 (nominal *P* <.05) **(Figure 3)**
- In addition, treatment with UPA led to higher response rates for achievement of minimal severity scores (eg, WP-NRS 0/1, DLQI 0/1) in PROs compared with patients receiving PBO at weeks 2 and 16 **(Figures 4** and **5)**
- In general, for both adults and adolescents, more patients treated with UPA 30 mg achieved clinically meaningful improvement across the PROs than did patients treated with UPA 15 mg
- Addition of TCS (AD Up study) to UPA 15-mg or UPA 30-mg treatment did not lead to an appreciable increase in the proportion of adults or adolescents achieving improvement in PROs when compared with UPA treatment alone (Measure Up 1 and Measure Up 2 studies)

RESULTS CONTINUED

Table 1. Baseline Demographics and Disease Characteristics

	Measure Up 1 Study			Measure Up 2 Study			AD Up Study		
Characteristic	PBO n = 281	UPA 15 mg n = 281	UPA 30 mg n = 285	PBO n = 278	UPA 15 mg n = 276	UPA 30 mg n = 282	PBO + TCS n = 304	UPA 15 mg + TCS n = 300	UPA 30 mg + TCS n = 297
Sex, n (%)									
Female	137 (48.8)	124 (44.1)	130 (45.6)	124 (44.6)	121 (43.8)	120 (42.6)	126 (41.4)	121 (40.3)	107 (36.0)
Male	144 (51.2)	157 (55.9)	155 (54.4)	154 (55.4)	155 (56.2)	162 (57.4)	178 (58.6)	179 (59.7)	190 (64.0)
Age, years, mean (SD)	34.4 (15.5)	34.1 (15.7)	33.6 (15.8)	33.4 (14.8)	33.3 (15.7)	34.1 (16.0)	34.3 (15.1)	32.5 (14.0)	35.5 (15.8)
Age group, n (%)									
<18 years	40 (14.2)	42 (14.9)	42 (14.7)	36 (12.9)	33 (12.0)	35 (12.4)	40 (13.2)	39 (13.0)	37 (12.5)
≥18 years	241 (85.8)	239 (85.1)	243 (85.3)	242 (87.1)	243 (88.0)	247 (87.6)	264 (86.8)	261 (87.0)	260 (87.5)
EASI score, mean (SD)	28.8 (12.6)	30.6 (12.8)	29.0 (11.1)	29.1 (12.1)	28.6 (11.7)	29.7 (12.2)	30.3 (13.0)	29.2 (11.8)	29.7 (11.8)
Patient-reported Outcomes, mean (SD)									
Weekly WP-NRS	7.3 (1.7)	7.2 (1.6)	7.3 (1.5)	7.3 (1.6)	7.2 (1.6)	7.3 (1.6)	7.1 (1.6)	7.1 (1.8)	7.4 (1.6)
ADerm-SS Skin Pain	6.5 (2.4)	6.2 (2.3)	6.5 (2.1)	6.5 (2.2)	6.4 (2.1)	6.4 (2.3)	6.3 (2.2)	6.3 (2.3)	6.5 (2.4)
ADerm-SS TSS-7	46.1 (14.5)	45.7 (14.0)	46.3 (13.4)	47.2 (13.6)	46.8 (13.2)	46.3 (13.8)	45.9 (13.5)	46.0 (14.6)	47.4 (13.9)
POEM Total Score	21.5 (5.4)	21.2 (4.8)	21.4 (5.1)	21.9 (5.2)	21.2 (5.1)	21.8 (4.8)	21.1 (5.1)	21.0 (5.0)	21.5 (5.3)
ADerm-IS Sleep	18.7 (7.5)	18.0 (7.5)	18.1 (7.6)	19.5 (7.5)	18.3 (7.3)	18.8 (7.7)	17.8 (7.6)	18.2 (7.8)	19.2 (7.4)
ADerm-IS Daily Activities	22.6 (10.6)	22.7 (11.0)	22.5 (11.1)	24.2 (10.6)	23.5 (9.9)	23.0 (10.0)	22.9 (10.5)	23.2 (10.9)	23.9 (10.5)
ADerm-IS Emotional State	20.0 (8.3)	20.2 (8.0)	20.1 (8.4)	20.6 (8.0)	20.6 (7.8)	20.1 (8.2)	20.1 (7.8)	19.6 (8.2)	19.9 (8.2)
DLQI[a]	17.0 (6.9) n = 252	16.2 (7.0) n = 259	16.4 (7.0) n = 261	17.1 (7.2) n = 257	16.9 (7.0) n = 253	16.7 (6.9) n = 256	16.3 (7.0) n = 276	16.4 (7.2) n = 276	17.1 (7.0) n = 273
CDLQI[b]	13.0 (6.8) n = 25	13.9 (5.9) n = 20	14.4 (6.0) n = 20	14.5 (6.1) n = 14	14.1 (6.3) n = 18	14.2 (5.0) n = 13	14.3 (6.1) n = 25	13.4 (4.8) n = 22	11.6 (6.9) n = 21

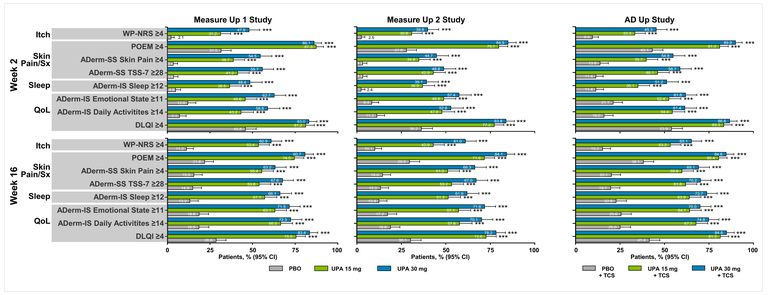
ADerm-IS, Atopic Dermatitis Impact Scale; ADerm-SS, Atopic Dermatitis Symptom Scale; CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; PBO, placebo; POEM, Patient-Oriented Eczema Measure; TSS-7, 7-item total symptom score; UPA, upadacitinib; WP-NRS, Worst Pruritus Numeric Rating Scale.
[a]DLQI was administered to patients who were aged ≥16 years at the time of the screening visit.
[b]CDLQI was administered to patients who were aged <16 years at the time of the screening visit.

Table 2. Demographics and Baseline Characteristics for Adolescents

	Measure Up 1 Study			Measure Up 2 Study			AD Up Study		
Characteristic	PBO n = 61	UPA 15 mg n = 64	UPA 30 mg n = 64	PBO n = 60	UPA 15 mg n = 58	UPA 30 mg n = 62	PBO n = 63	UPA 15 mg n = 60	UPA 30 mg n = 60
Sex, n (%)									
Female	33 (54.1)	34 (53.1)	36 (56.3)	35 (58.3)	38 (65.5)	26 (41.9)	36 (57.1)	27 (45.0)	25 (41.7)
Male	28 (45.9)	30 (46.9)	28 (43.8)	25 (41.7)	20 (34.5)	36 (58.1)	27 (42.9)	33 (55.0)	35 (58.3)
Age, years, mean (SD)	15.1 (1.7)	15.5 (2.0)	15.7 (1.6)	15.5 (1.7)	15.2 (1.8)	15.8 (1.7)	15.1 (1.9)	15.4 (1.7)	15.3 (1.9)
Age group, n (%)									
12–14	23 (37.7)	22 (34.4)	15 (23.4)	18 (30.0)	23 (39.7)	15 (24.2)	23 (36.5)	14 (23.3)	21 (35.0)
15–17	38 (62.3)	42 (65.6)	49 (76.6)	42 (70.0)	35 (60.3)	47 (75.8)	40 (63.5)	46 (76.7)	39 (65.0)
EASI, mean (SD)	29.7 (14.1)	30.7 (12.8)	27.8 (10.6)	30.1 (13.3)	28.0 (12.2)	31.2 (14.0)	30.3 (12.1)	29.6 (11.7)	28.7 (10.1)
Patient-reported Outcomes									
Weekly Worst Pruritus NRS	7.2 (1.8)	7.2 (1.6)	7.4 (1.6)	7.3 (1.6)	7.1 (1.8)	6.9 (1.7)	7.3 (1.7)	7.0 (1.9)	6.9 (1.9)
ADerm-SS Skin Pain	5.8 (2.9)	6.4 (2.3)	6.8 (2.0)	6.4 (2.5)	6.5 (2.2)	6.2 (2.2)	6.6 (2.4)	6.4 (2.3)	6.8 (2.1)
ADerm-SS TSS-7	45.7 (15.5)	45.3 (15.2)	47.6 (13.5)	47.1 (14.6)	45.5 (13.6)	44.6 (13.8)	46.9 (14.3)	46.8 (14.1)	46.4 (14.4)
POEM Total Score	20.1 (5.6)	20.6 (4.9)	21.2 (4.0)	20.1 (5.5)	19.3 (5.7)	19.5 (5.3)	20.3 (5.5)	19.9 (5.5)	18.5 (5.9)
ADerm-IS Sleep	18.3 (7.8)	17.9 (8.0)	17.7 (7.9)	16.2 (8.6)	16.2 (8.3)	16.6 (7.8)	18.2 (7.5)	17.7 (7.8)	16.7 (8.8)
ADerm-IS Daily Activities	22.1 (11.3)	20.9 (11.4)	22.4 (11.1)	21.8 (11.3)	20.4 (11.0)	21.3 (9.5)	22.9 (11.1)	22.4 (10.0)	20.9 (11.7)
ADerm-IS Emotional State	19.1 (8.8)	19.1 (8.9)	19.5 (8.1)	18.6 (8.5)	19.3 (8.7)	18.5 (8.6)	19.7 (8.6)	19.7 (7.8)	17.6 (9.7)
DLQI[a]	14.9 (7.2) (n = 22)	14.5 (6.6) (n = 30)	15.7 (6.7) (n = 33)	13.7 (7.1) (n = 26)	14.2 (7.1) (n = 23)	14.3 (7.1) (n = 32)	12.8 (5.8) (n = 24)	14.0 (6.2) (n = 25)	13.4 (5.8) (n = 20)
CDLQI[b]	12.6 (6.3) (n = 38)	14.3 (6.0) (n = 33)	13.7 (5.7) (n = 31)	13.8 (6.2) (n = 32)	14.2 (5.5) (n = 35)	14.7 (5.6) (n = 25)	14.5 (6.6) (n = 38)	14.7 (5.7) (n = 35)	13.1 (7.0) (n = 39)

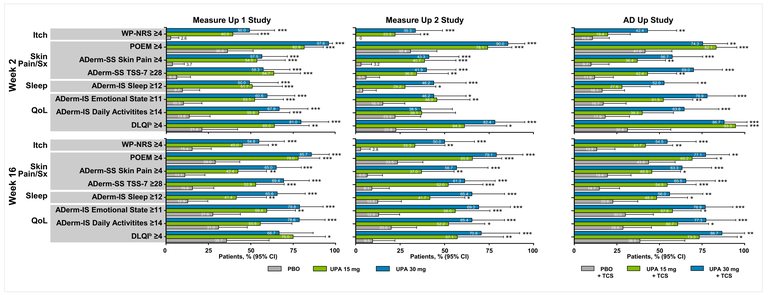
ADerm-IS, Atopic Dermatitis Impact Scale; ADerm-SS, Atopic Dermatitis Symptom Scale; CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; PBO, placebo; POEM, Patient-Oriented Eczema Measure; TCS, topical corticosteroids; TSS-7, 7-item total symptom score; UPA, upadacitinib; WP-NRS, Worst Pruritus Numeric Rating Scale.
[a]DLQI was administered to patients who were aged ≥16 years at the time of the screening visit.
[b]CDLQI was administered to patients who were aged <16 years at the time of the screening visit.

Figure 2. Proportion of Adults With Moderate-to-Severe AD Achieving a Clinically Meaningful Improvement (Reduction)[a] in Patient-reported Symptoms and Quality of Life Measures With Upadacitinib



ADerm-IS, Atopic Dermatitis Impact Scale; ADerm-SS, Atopic Dermatitis Symptom Scale; DLQI, Dermatology Life Quality Index; PBO, placebo; POEM, Patient-Oriented Eczema Measure; PRO, patient-reported outcome; QoL, quality of life; Sx, symptoms; TCS, topical corticosteroids; TSS-7, SS 7-item total symptom score; UPA, upadacitinib; WP-NRS, Worst Pruritus Numerical Rating Scale.
Based on nominal *P* value of ***P <.001 vs PBO.
For categorical variables, missing data were imputed based on nonresponder imputation incorporating multiple imputation for missing data due to COVID-19. *P* values were calculated according to the Cochran-Mantel-Haenszel test adjusted for strata based on age (adolescent vs adult) for the comparison of treatment groups.
[a]Reported as achievement of minimal clinically important difference (reduction) in score for each PRO.

Figure 3. Proportion of Adolescents With Moderate-to-Severe AD Achieving a Clinically Meaningful Improvement (Reduction)[a] in Patient-reported Symptom and Quality of Life Measures With Upadacitinib



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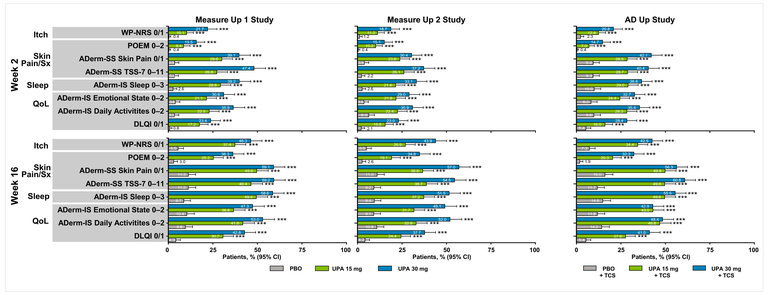
Based on nominal *P* values of *P <.05, **P <.01, ***P <.001 vs PBO.
For categorical variables, missing data were imputed based on nonresponder imputation incorporating multiple imputation for missing data due to COVID-19. *P* values were calculated according to the Cochran-Mantel-Haenszel test adjusted for strata based on age (adolescent vs adult) for the comparison of treatment groups.
[a]Reported as achievement of minimal clinically important difference (reduction) in score for each PRO.
[b]CDLQI data represented are from adolescent patients aged ≥16 years.

Figure 4. Proportion of Adults With Moderate-to-Severe AD Achieving a Minimal Severity Score[a] With Upadacitinib Across Patient-reported Symptom and Quality of Life Measures



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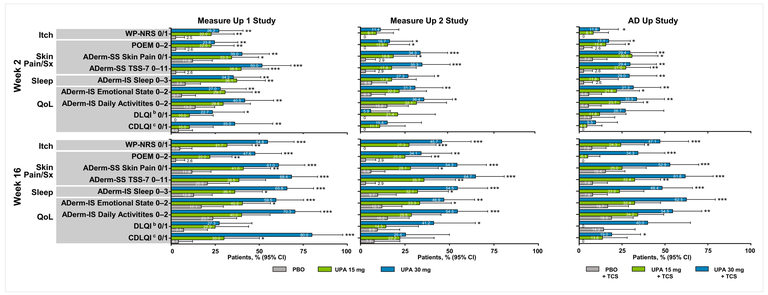
[a]Reported as achievement of a minimal severity score for each PRO.

Figure 5. Proportion of Adolescents With Moderate-to-Severe AD Achieving a Minimal Severity Score[a] With Upadacitinib Across Patient-reported Symptom and Quality of Life Measures



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[a]Reported as achievement of a minimal severity score for each PRO.
[b]DLQI data represented are from adolescent patients aged ≥16 years.
[c]CDLQI data represented are from adolescent patients aged <16 years.