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

Andrew Blauvelt[1], Barry Ladizinski[2], Vimal H Prajapati[3], Vivian Laquer[4], Alison Fischer[5], Samantha Eisman[6], Tianshuang Wu[2], Namita Vigna[2], Henrique D Teixeira[2], John Liu[2], Kilian Eyerich[7]

[1]Oregon Medical Research Center, Portland, Oregon, United States; [2]AbbVie Inc., North Chicago, Illinois, United States; [3]Division of Dermatology, Department of Medicine, University of Calgary, Calgary, Alberta, Canada; Section of Community Pediatrics, Department of Pediatrics, University of Calgary, Calgary; Section of Pediatric Rheumatology, Department of Pediatrics, University of Calgary, Calgary; Skin Health & Wellness Centre, Calgary; Dermatology Research Institute, Calgary; Probity Medical Research, Calgary, Alberta, Canada; [4]First OC Dermatology, Fountain Valley, California, United States; [5]Southside Dermatology, Tulsa; Oklahoma State University Center for Health Sciences, Tulsa, Oklahoma, United States; [6]Sinclair Dermatology, East Melbourne, Victoria, Australia; [7]Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden; Department of Dermatology and Allergy, Technical University of Munich, Germany

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BACKGROUND

- Upadacitinib is an oral, once daily, Janus kinase (JAK) inhibitor with greater inhibitory potency for JAK1 than JAK2, JAK3, and tyrosine kinase 2 approved by the European Commission for the treatment of adults and adolescents with moderate-to-severe atopic dermatitis (AD) and is under review with the FDA
- The Heads Up study was a 24-week Head-to-Head Phase 3b, multicenter, randomized, double-blinded, double-dummy, active controlled study comparing the safety and efficacy of upadacitinib 30 mg to dupilumab in adults with moderate-to-severe AD
- In Heads Up, upadacitinib achieved superiority vs dupilumab for primary and all ranked secondary endpoints, including early improvements in itch and skin clearance; there were no new safety signals reported for either upadacitinib or dupilumab

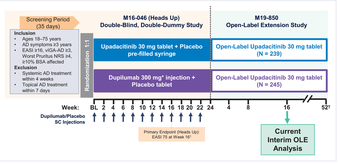
OBJECTIVE

- Evaluate the efficacy and Safety of Switching from Dupilumab to Upadacitinib or Continuous Upadacitinib in Moderate-to-Severe Atopic Dermatitis during the open-label extension (OLE) trial that followed Heads Up (M19-850, NCT04195698)

METHODS

- Open-label extension of the head-to-head, Phase 3b, multicenter, randomized, double-blinded, double-dummy, active-controlled study assessing the long-term safety and efficacy of upadacitinib in adults with moderate-to-severe AD

Figure 1. Heads Up Study Design and Open-Label Extension



*Dupilumab 300 mg SC injection administered every other week starting at the Week 2 visit and until the Week 22 visit, after an initial dose of 600 mg at the baseline visit.
†132 weeks in some countries.
AD, atopic dermatitis; BL, baseline; BSA, body surface area; EASI, Eczema Area and Severity Index; NRS, Numerical Rating Scale; OLE, open-label extension; vIGA-AD, validated Investigators Global Assessment for Atopic Dermatitis.

RESULTS

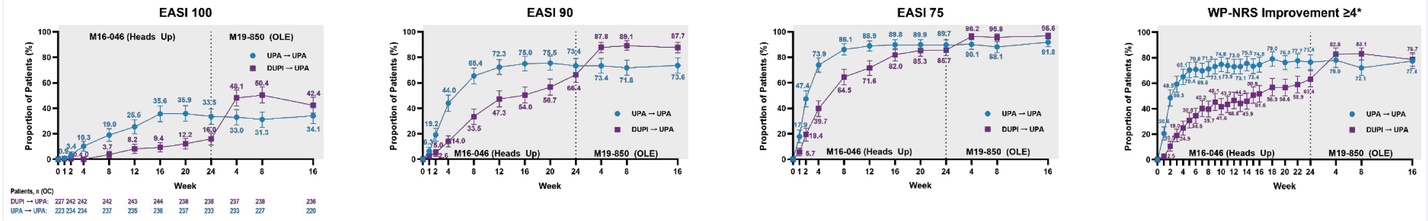
Table 1. Heads Up Patient Demographics & Baseline Disease Characteristics Among Those Patients Who Entered OLE

Demographics and Baseline Characteristics, mean (SD) or n (%)		DUPI → UPA (N = 245)	UPA → UPA (N = 239)
Sex, n (%)			
Female		105 (42.9)	107 (44.8)
Male		140 (57.1)	132 (55.2)
Age (years), mean (SD)		35.6 (13.2)	36.4 (14.6)
Age group, n (%)			
< 40 years		169 (69.0)	156 (65.3)
≥ 40 to < 65 years		68 (27.8	72 (30.1)
≥ 65 years		8 (3.3)	11 (4.6)
Disease duration since diagnosis (years), mean (SD)		24.9 (13.6)	23.8 (14.9)
Weight (kg), mean (SD)		75.3 (18.8)	78.8 (21.7)
EASI, mean (SD)	M16-046	28.8 (11.1)	30.5 (12.3)
	M19-850	3.3 (4.1)	2.6 (4.3)
BSA in percentage, mean (SD)	M16-046	45.1 (22.2)	47.2 (23.4)
	M19-850	7.13 (10.0)	5.3 (9.1)
vIGA-AD, n (%)	M16-046		
3: Moderate		120 (49.0)	120 (50.2)
4: Severe		125 (51.0)	119 (49.8)
Worst Pruritus NRS (weekly average)	M16-046	7.6 (1.6)	7.4 (1.6)
	M19-850	3.0 (2.4)	2.2 (2.6)

DUPI, dupilumab; BMI, body mass index; BSA, body surface area; EASI, Eczema Area and Severity Index; NRS, numerical rating scale; UPA, upadacitinib; vIGA-AD, variable Investigators Global Assessment for Atopic Dermatitis.

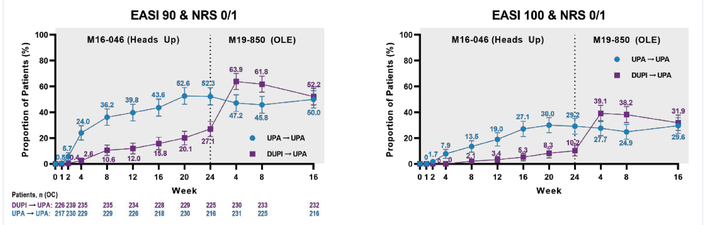
RESULTS (CONTINUED)

Figure 2. Achievement of EASI 100, 90, 75, and NRS ≥ 4 Through Week 40 Among Those Subjects Who Entered OLE (ITT Population, OC)



*Assessed in patients with WP-NRS ≥4 at baseline; Error bars indicate 95% confidence interval.
DUPI, dupilumab; EASI, Eczema Area and Severity Index; ITT, intent-to-treat population; UPA, upadacitinib; WP-NRS, Worst Pruritus-Numerical Rating Scale.

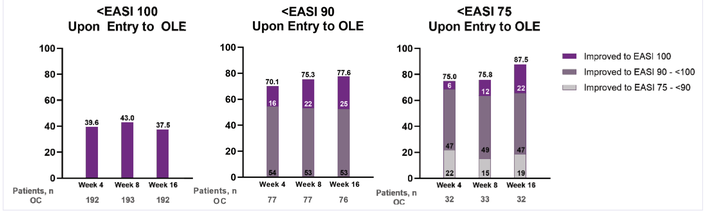
Figure 3. Patients Simultaneously Achieving EASI 90 or EASI 100 AND NRS 0/1 Through Week 40 Among Those Patients Who Entered OLE (ITT Population, OC)



Error bars indicate 95% confidence interval.
DUPI, dupilumab; EASI, Eczema Area and Severity Index; ITT, intent-to-treat population; OC, observed case analysis; UPA, upadacitinib; WP-NRS, Worst Pruritus-Numerical Rating Scale.

Figure 4. Improvement in Clinical Response After Switching From Dupilumab to Upadacitinib (ITT Population, OC)

M19-850 (OLE) EASI responses in patients who received dupilumab in Heads Up



EASI, Eczema Area and Severity Index; ITT, intent-to-treat population; OC, observed case analysis.

- Among patients who did not achieve WP-NRS Improvement ≥4 at Week 24 with dupilumab, 57.7% achieved WP-NRS Improvement ≥4 after 16 weeks of upadacitinib treatment
- Among patients receiving continuous upadacitinib, 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

Table 2. Heads Up Patient Demographics & Baseline Disease Characteristics Among Those Patients Who Entered OLE

Treatment-Emergent Adverse Events (TEAEs)[a], Events (E/100PY)	DUPI → UPA (N = 245) [PY = 141.7]	UPA → UPA (N = 239) [PY = 242.3]	Total (N = 484) [PY = 383.9]
Adverse event (AE)	446 (314.8)	1082 (446.6)	1528 (398.0)
AE with reasonable possibility of being drug-related[a]	175 (123.5)	402 (165.9)	577 (150.3)
Severe AE	10 (7.1)	39 (16.1)	49 (12.8)
Serious AE (SAE)	4 (2.8)	16 (6.6)	20 (5.2)
SAE with reasonable possibility of being drug-related[b]	2 (1.4)	4 (1.7)	6 (1.6)
AE leading to discontinuation of study drug	2 (1.4)	15 (6.2)	17 (4.4)
AE leading to death[c]	0	1 (0.4)	1 (0.3)

[a]TEAEs are defined as any adverse events that begin or worsen in severity after initiation of upadacitinib during study M16-046 or study M19-850 through 30 days following the last dose of upadacitinib.
[b]As assessed by investigator.
[c]Bone tuberculosis in a 69-year-old female patient with no significant risk factors other than a history of missionary work.
DUPI, dupilumab; PY, patient years; UPA, upadacitinib.

Table 3. Treatment-Emergent Adverse Events of Special Interest Through Week 40 Among Those Patients Who Entered OLE

TEAEs of Special Interest, Events (E/100PY)	DUPI → UPA (N = 245) [PY = 141.7]	UPA → UPA (N = 239) [PY = 242.3]	Total (N = 484) [PY = 383.9]
Serious infections	1 (0.7)	6 (2.5)	7 (1.8)
Opportunistic infections (excl. TB and herpes zoster)	2 (1.4)	4 (1.7)	6 (1.6)
Malignancy	0	0	0
Lymphoma	0	0	0
Hepatic disorder	10 (7.1)	14 (5.8)	24 (6.3)
Adjudicated gastrointestinal perforations	0	0	0
Anemia	2 (1.4)	8 (3.3)	10 (2.6)
Neutropenia	7 (4.9)	7 (2.9)	14 (3.6)
Lymphopenia	0	3 (1.2)	3 (0.8)
Herpes zoster	10 (7.1)	15 (6.2)	25 (6.5)
Creatine phosphokinase (CPK) elevation	23 (16.2)	46 (19.0)	69 (18.0)
Renal dysfunction	0	0	0
Active tuberculosis (TB)	0	1 (0.4)	1 (0.3)
Adjudicated MACE	0	0	0
Adjudicated VTE	0	0	0

DUPI, dupilumab; MACE, major adjudicated cardiovascular event; TB, tuberculosis; UPA, upadacitinib; VTE; venous thromboembolic event.

CONCLUSIONS

- Patients who switched from dupilumab to Open-Label upadacitinib showed improvements in EASI response and WP-NRS at Week 16 and as early as Week 4 post switch, including multi-dimensional improvements with stringent endpoints
- Patients who continued use of upadacitinib 30 mg maintained skin and itch response through 40 weeks
- Switching from dupilumab to upadacitinib resulted in increased rates of efficacy and achievement of higher efficacy thresholds
- The safety profile of upadacitinib 30 mg with continued treatment through 40 weeks and in subjects switching from dupilumab to upadacitinib, was consistent with the safety profile of upadacitinib observed in the Phase 3 pivotal AD studies, Measure Up 1, Measure Up 2, and AD Up; no new safety risks were observed

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DISCLOSURES

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