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ORIGINAL RESEARCH

Achieving Optimal Treatment Targets and Minimal Disease Activity with Upadacitinib for Moderate-to-Severe Atopic Dermatitis: Integrated Analysis of Phase 3 Studies (Measure Up 1 and 2)

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ABSTRACT

Introduction: The Aiming High in Eczema/Atopic Dermatitis (AHEAD) guidelines recommend achieving minimal disease activity (MDA) in atopic dermatitis (AD), defined as simultaneous achievement of optimal treatment targets for at least one clinician- and one patient-reported outcome (ClinRO + PRO). We assessed the effect of upadacitinib on achieving optimal ClinROs, optimal PROs, and MDA in Measure Up 1 (NCT03569293) and Measure Up 2 (NCT3607422) studies for patients with moderate to severe AD.

Methods: Patients were randomized to receive upadacitinib (15 mg or 30 mg) or placebo. Achievement of ≥ 1 optimal target in ClinROs, ≥ 1 optimal target in PROs, and MDA (≥ 1 optimal ClinROs and ≥ 1 optimal PROs) were reported at weeks 16 (upadacitinib vs placebo) and 52 (upadacitinib only). MDAs in selected combinations were also assessed at weeks 16 and 52. A total of 1683 and 1124 patients were included in the week 16 and 52 analysis, respectively.

Results: At week 16, a significantly higher proportion of patients receiving upadacitinib (15 mg: 42.5%, 30 mg: 55.9%) compared with placebo (6.4%) achieved MDA. At week 52, 57.4% and 69.9% of patients receiving 15 mg

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and 30 mg of upadacitinib achieved MDA, respectively. Specifically, patients receiving upadacitinib attained higher rates of ≥ 90% reduction from baseline in Eczema Area and Severity Index (EASI 90) + Worst Pruritus-Numerical Rating Scale (WP-NRS) 0/1 at week 16 (15 mg: 25.3%, 30 mg: 39.4% vs placebo: 1.8%) and maintained at week 52 (15 mg: 38.1%, 30 mg: 46.9%).

Conclusion: Treatment with upadacitinib achieved both ClinRO and PRO optimal treatment targets as well as MDA and may optimize overall disease management in patients with moderate-to-severe AD.

PLAIN LANGUAGE SUMMARY

Patients with atopic dermatitis (AD) often suffer from skin symptoms such as itch, pain, and rash. These symptoms affect the patient's sleep, mental health, and quality of life. Optimal treatment goals for AD have been established for skin severity assessments made by the doctor (ClinRO) and symptom and quality of life assessments made by the patient (PRO). Patients are said to have achieved minimal disease activity (MDA) when they achieve an optimal ClinRO treatment goal and an optimal PRO treatment goals. In this article, we report the results from two clinical trials (Measure Up 1 and 2) where patients received either upadacitinib (15 mg or 30 mg) or placebo for treatment of their AD. After 16 weeks, patients who took upadacitinib were more likely to achieve optimal ClinRO or PRO treatment goals and MDA compared to patients receiving placebo. Most patients receiving upadacitinib achieved optimal ClinRO or PRO treatment goals and MDA after 52 weeks of treatment. This study found that patients with AD experienced high levels of both skin improvement and symptom relief after 16 and 52 weeks of upadacitinib treatment.

Keywords: Atopic dermatitis; Minimal disease activity; Quality of life; Clinician reported outcome; Patient reported outcome; Upadacitinib

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Key Summary Points

Why carry out this study?

Recent expert consensus recommendations in atopic dermatitis (AD) have established optimal targets for clinician- (ClinRO) and patient-reported outcomes (PRO), with achievement of both defined as minimal disease activity (MDA).

We assess the effect of treatment with upadacitinib on achieving MDA and optimal ClinRO and PRO targets in adults and adolescents with moderate-to-severe AD.

What was learned from the study?

At week 16, a significantly higher portion of patients receiving 15 mg or 30 mg of upadacitinib achieved MDA as well as at least one optimal ClinRO or PRO target.

At week 52, more than half of patients achieved at least one optimal ClinRO, PRO, or both (MDA) with upadacitinib.

Treatment with upadacitinib demonstrated achievement of MDA and optimal ClinRO or PRO targets and may optimize overall disease management in patients with moderate-to-severe AD.

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disease often characterized by intense itch and eczematous skin lesions [1]. Patients with AD often suffer from a high physical disease burden affecting health-related quality of life (HRQoL) [2].

As disease management of AD is evolving with more advanced therapies becoming available, optimal treatment targets in AD are also evolving. While partial skin clearance, such as a ≥ 75% reduction in the Eczema Area and Severity Index (EASI 75), is often used as a clinical trial endpoint, studies have shown that reaching a higher threshold such as EASI 90 or EASI 100 (near-complete or complete skin clearance) is associated with greater improvement in patients' quality of life than EASI 75 [3]. Furthermore, studies indicate that achieving the stringent itch relief threshold of little-to-no itch (i.e., Worst Pruritus-Numerical Rating Scale [WP-NRS] 0/1) is related to better HRQoL such as sleep improvement compared with partial itch reduction (i.e., improvement in WP-NRS) [4, 5].

The recently established Aiming High in Eczema/Atopic Dermatitis (AHEAD) recommendations have highlighted the need to incorporate the patient voice into disease management [6]. Specifically, a new approach combining treat-to-target principles with shared decision-making was established by aiming for optimal treatment targets in both clinician-reported outcomes (ClinROs), such as skin clearance, and patient-reported outcomes (PROs), such as itch [2]. Additionally, if these treatment targets are not met within 3–6 months, treatment modification or escalation should be considered. Minimal Disease Activity (MDA) is defined, in this context, as simultaneous achievement of at least one optimal target in a ClinRO and at least one optimal target in a PRO [2]. The AHEAD recommendations also state that clinicians and patients should aim for long-term disease control, minimal flares, and achievement of MDA.

Upadacitinib is a selective oral Janus kinase inhibitor approved for the treatment of AD in adolescents and adults that has previously demonstrated improved skin clearance, itch, and other patient-reported quality of life measures [7–9]. Here, we assess the achievement of MDA in patients receiving upadacitinib compared with placebo in the phase 3 clinical trials Measure Up 1 and 2.

METHODS

This post-hoc analysis was conducted using the on-going phase 3, multicenter, randomized clinical trials Measure Up 1 [NCT03569293] and Measure Up 2 [NCT03607422] over the double-blind and blinded extension periods till week 52. Complete methodology for these studies was

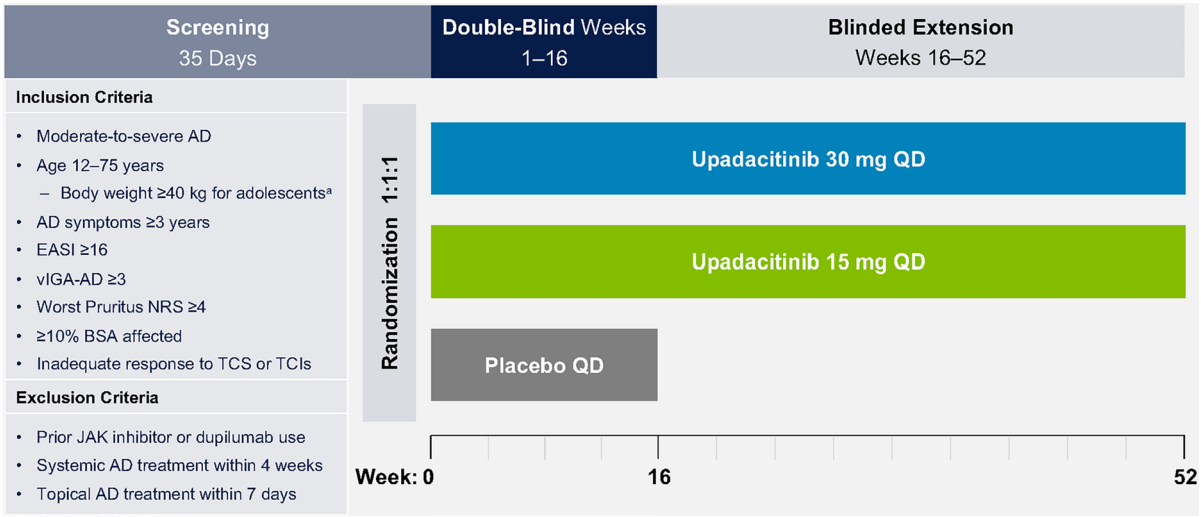


Fig. 1 Study design of Measure Up 1 and 2. [a]Aged < 18 years. *AD* atopic dermatitis, *EASI* Eczema Area and Severity Index, *BSA* body surface area, *JAK* Janus kinase, *NRS* numeric rating scale, *QD* once daily, *TCI* topical calcineurin inhibitor, *TCS* topical corticosteroids, *vIGA-AD* Validated Investigator Global Assessment for Atopic Dermatitis. Previously published in Silverberg et al. Disease activity among patients with moderate-to-severe atopic dermatitis: results from phase 3 studies (Measure Up 1 and Measure Up 2) presented at AAD 2024

previously reported [8, 10]. The original studies that collected the data analyzed within this article were approved by the institutional review board (IRB) and conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from participants. Briefly, adolescent and adult patients were originally randomized 1:1:1 to receive daily oral upadacitinib at either 15 mg or 30 mg, or placebo for the first 16 weeks (Fig. 1). Beginning at week 4, rescue treatment could be provided at the discretion of the investigator. After 16 weeks, the placebo group was re-randomized 1:1 to receive daily oral 15 mg or 30 mg upadacitinib during the blinded extension period. This analysis reports results for patients originally randomized to upadacitinib through week 52.

Measurements of ClinROs assessed in the trials include EASI, SCORing Atopic Dermatitis (SCORAD), Investigators' Global Assessment (IGA), and affected body surface area (BSA). Measurements of PRO include itch as assessed by WP-NRS; skin appearance/condition as assessed by Patient Oriented Eczema Measure (POEM); impact on quality of life as assessed by Dermatology Life Quality Index (DLQI) and skin pain as assessed by Atopic Dermatitis Symptom Scale (ADerm-SS) skin pain item reported on an 11-point numerical rating scale; sleep disturbance as assessed using Atopic Dermatitis Impact Scale (ADerm-IS) sleep impact item reported on an 11-point numerical rating scale; and mental health assessed by HADS-Anxiety (HADS-A) and HADS-Depression (HADS-D). Achievement of optimal ClinROs and PROs was assessed at weeks 16 and 52 (Table 1).

Achievement of ≥ 1 ClinRO optimal target and ≥ 1 PRO optimal target and simultaneously attaining ≥ 1 ClinRO optimal target and ≥ 1 PRO optimal target were assessed at weeks 16 and 52. Achievement of MDA in specific ClinRO/PRO combinations was also assessed. Due to the high number of combination possibilities for all ClinROs and PROs for MDA achievement, PROs used in the specific combinations were selected from the Harmonising Outcome Measures for Eczema group recommendations, that is: WP-NRS, POEM, and DLQI [11]. Therefore, MDA combinations between the three optimal ClinRO treatment targets (EASI 90,

Table 1 MDA Treatment targets for clinician- and patient-reported outcomes

Measurement	Optimal target
Clinician-reported outcomes	
EASI response	Improvement ≥ 90%
EASI category	≤ 3
SCORAD response	Improvement ≥ 75%
SCORAD category	≤ 10
IGA and BSA	IGA 0/1 and BSA ≤ 2%
Patient-reported outcomes	
Itch (WP-NRS)	≤ 1
Skin pain (Pain NRS)[a]	≤ 1
Skin condition (POEM)	≤ 2
Sleep disturbance (Sleep NRS)[b]	≤ 1
Impact on daily activities (DLQI/CDLQI)	0/1
Mental health (HADS-A and HADS-D)	Both < 8

AD atopic dermatitis, *ADerm-IS* Atopic Dermatitis Impact Scale, *ADerm-SS* Atopic Dermatitis Symptom Scale, *BSA* body surface area, *CDLQI* Children's Dermatology Life Quality Index, *DLQI* Dermatology Life Quality Index, *EASI* Eczema Area and Severity Index, *HADS* Hospital Anxiety and Depression Scale, *HADS-A* HADS-anxiety, *HADS-D* HADS-depression, *IDQOL* Infants' Dermatitis Quality of Life, *IGA* Investigators' Global Assessment, *NRS* numeric rating scale, *POEM* Patient-Oriented Eczema Measure, *SCORAD* Scoring Atopic Dermatitis, *WP-NRS* Worst Pruritus Numerical Rating Scale

[a]ADerm-SS item on skin pain ("During the past 24 hours, how bad was your worst skin pain due to AD?") was used and reported on an 11-point scale, with higher numbers representing worse outcomes

[b]ADerm-IS item on sleep disturbance ("During your sleep hours, how much did your AD impact your sleep?") was used and reported on an 11-point scale, with higher numbers representing worse outcomes

SCORAD 75, and IGA 0/1 + BSA ≤ 2%) and three optimal PRO treatment targets (WP-NRS 0/1, POEM ≤ 2, and DLQI 0/1) were assessed.

Results at week 16 were reported using non-responder imputation with no special data handling for missing data due to COVID-19 (NRI-NC). *P*values were calculated according to the Cochran-Mantel-Haenszel tests adjusted for strata (study, baseline vIGA-AD categories, and age [adolescent vs. adult]) for comparison of the treatment groups at week 16. Observed case analysis was conducted for results at week 52 in addition to NRI-NC.

RESULTS

Patients

A total of 1683 patients were included in the week 16 analysis (placebo = 559, upadacitinib 15 mg = 557, upadacitinib 30 mg = 567). The week 52 analysis included 1124 patients who were originally randomized to upadacitinib at baseline (upadacitinib 15 mg = 557, upadacitinib 30 mg = 567). Baseline demographics for these studies were previously reported, and patient characteristics were generally balanced between treatment groups [9].

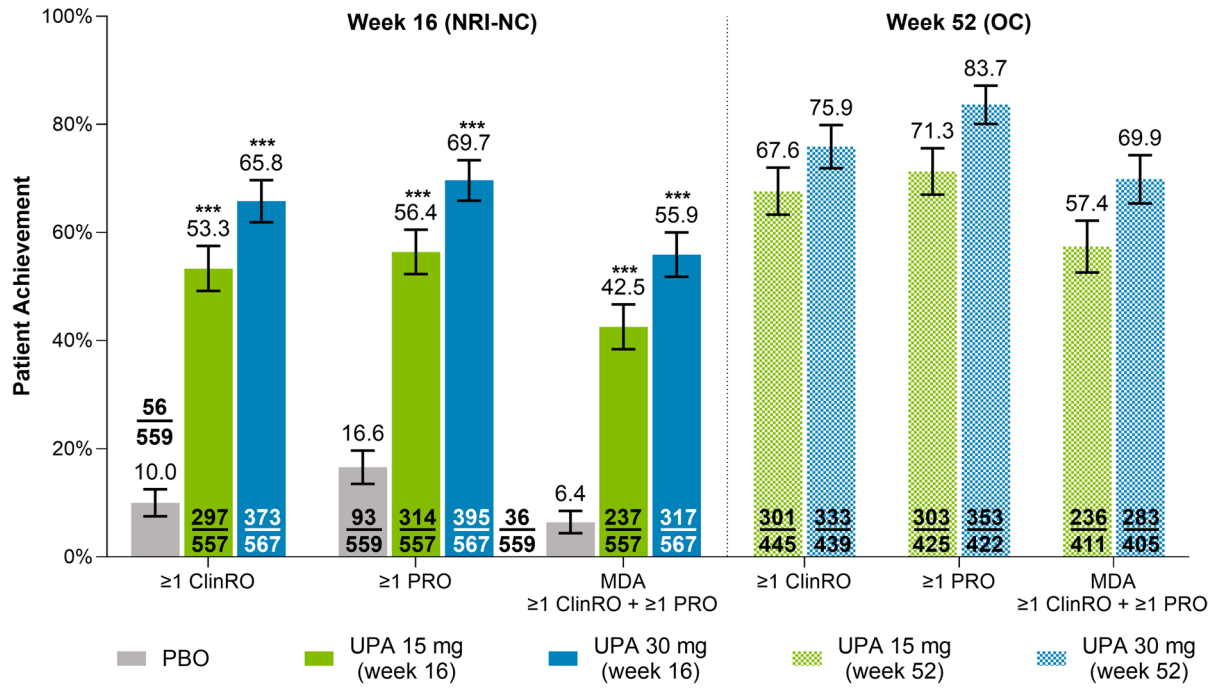


Fig. 2 Achievement of optimal targets for at least one ClinRO, one PRO, and MDA. ***$P < 0.001$ vs placebo. Error bars represent 95% CI. *ClinRO*, clinician-reported outcome; *MDA* minimal disease activity, *NRI-NC* non-responder imputation with no special data handling for missing data due to COVID-19, *OC* observed cases, *PBO* placebo, *PRO* patient-reported outcome, *UPA* upadacitinib

Achievement of MDA Treatment Targets

At week 16, a significantly higher proportion of patients receiving upadacitinib 15 mg or 30 mg achieved at least one ClinRO or at least one PRO compared with those receiving placebo (Fig. 2). For patients receiving 15 mg of upadacitinib, 53.5% achieved at least one ClinRO and 56.4% achieved at least one PRO compared with 10.0% and 16.6%, respectively, of patients receiving a placebo ($P < 0.001$). Similarly, 65.8% of patients receiving 30 mg of upadacitinib achieved at least one ClinRO and 69.7% of patients achieved at least one PRO ($p < 0.001$ vs placebo; Fig. 2). MDA, defined as achieving at least one ClinRO and at least one PRO simultaneously, was achieved by 42.5% and 55.9% of patients receiving upadacitinib 15 mg and 30 mg, respectively, compared with 6.4% of patients receiving a placebo ($p < 0.001$ vs placebo; Fig. 2).

These results were maintained through week 52 (Fig. 2, Supplemental Fig. 1). At week 52 for patients receiving upadacitinib 15 mg, 67.6% achieved at least one ClinRO, 71.3% achieved at least one PRO, and 57.4% achieved MDA (Fig. 2). For patients receiving 30 mg of upadacitinib, 75.9% achieved at least one ClinRO, 83.7% achieved at least one PRO, and 69.9% achieved MDA (Fig. 2). A similar trend was observed in week 52 data reported using NRI-NC (Supplemental Fig. 1).

Achievement of MDA in Specific ClinRO and PROs

At week 16, across all MDA combinations assessed, a significantly higher proportion of patients receiving upadacitinib 15 mg or 30 mg, compared with placebo, achieved MDA (all $P < 0.001$; Fig. 3). Achievement rates were numerically higher across all combinations for

patients receiving upadacitinib 30 mg (26.5% to 39.4%) compared with those receiving upadacitinib 15 mg (15.0% to 25.3%) at week 16 (Fig. 3).

At week 52, these achievement rates were generally similar or improved from their week 16 assessments (Fig. 3, Supplemental Fig. 2). Similar to results at week 16, a numerically higher proportion of patients receiving upadacitinib 30 mg (31.3% to 46.9%), compared with those receiving upadacitinib 15 mg (25.2% to 38.1%), achieved the optimal treatment target combinations (Fig. 3).

DISCUSSION

The results from this analysis show that a significantly higher proportion of patients treated with upadacitinib (15 mg or 30 mg) achieved at least one optimal ClinRO or PRO treatment target compared with patients receiving placebo. Additionally, a significantly higher proportion of patients receiving upadacitinib achieved MDA compared with those receiving placebo. These effects were maintained at week 52 and for all MDA combinations investigated including EASI 90 and WP-NRS 0/1.

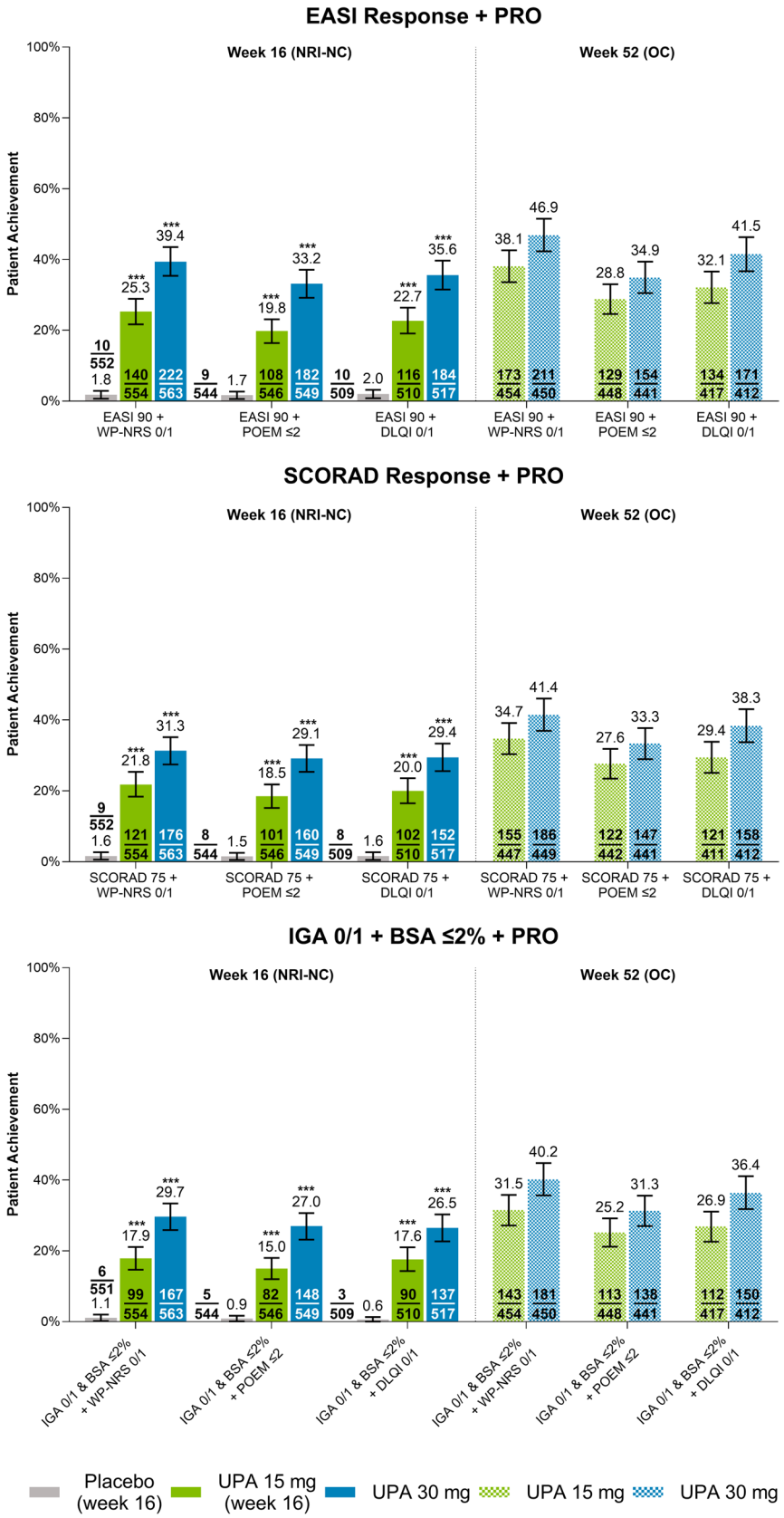
MDA in AD is a novel concept introduced recently by the AHEAD recommendations based on qualitative patient research [6] and consensus among international dermatology experts [2]. The AHEAD recommendations aim to provide a framework to optimize disease management and improve the standard of care in AD [2]. Lower efficacy targets, such as EASI 50, were often considered acceptable in the past because of limited therapies that could not achieve higher efficacy [9, 12, 13]. However, with the availability of more effective targeted therapies, such as upadacitinib, aiming for higher treatment targets becomes possible to optimize patient outcomes.

Studies have shown that achieving more stringent clinical treatment targets is associated with increased patient outcomes including sleep, itch, pain, and emotional state, including anxiety and depression [4, 5, 14]. Patients who achieved EASI 90 (optimal treatment target) reported greater improvements in daily activities, function, and treatment satisfaction than patients achieving EASI 75 (moderate treatment target) [3, 4]. More importantly, for those who achieved MDA in near-complete clear skin clearance and little-to-no itch simultaneously (EASI 90 and WP-NRS 0/1), HRWoL improvement was higher compared with those who achieved EASI 90 alone or those who achieved WP-NRS 0/1 alone [4].

Due to the extensive impact of AD on the patient's daily life, the patient's voice is critical in the shared decision-making processes related to AD treatment. In a study by de Wijs et al., patients reported that physicians sometimes underestimated both their physical and emotional wellbeing and felt the need for increased recognition of the overall impact of their disease [15]. Patients specifically mentioned the need for their physicians to particularly acknowledge feelings such as shame, loneliness, stress, and fear and behaviors such as social avoidance and poor sleep, which are captured as part of MDA [15]. Patients also felt that they should have an important role in determining the impact of AD on their lives, noting the value of including not only physician but also patient assessment in the disease management of AD [15].

By combining patient and physician assessments, MDA represents a more holistic view on patients' overall disease management. In addition to the current study findings, upadacitinib has demonstrated superiority versus dupilumab in achieving EASI 90+WP-NRS 0/1 [7, 16]. In the HEADS UP study, more patients receiving upadacitinib 30 mg achieved near-complete clear skin clearance (EASI 90) and little-to-no itch (WP-NRS 0/1) than with dupilumab at week 16 (32.7% vs 12.6%) [17]. In the LEVEL UP trial, more than twice as many patients who started with upadacitinib 15 mg achieved the same outcome (EASI 90 and WP-NRS 0/1) compared with dupilumab (19.9% vs 8.9%) at week 16. Upadacitinib is effective in attaining optimal treatment targets and enables patients to achieve MDA as measured by EASI 90 and WP-NRS 0/1.

A strength of this study is that it provides a large sample size from two pooled phase 3 clinical trials and provides support for including MDA endpoints in future clinical trials to provide a more holistic perspective to patients and physicians regarding the efficacy of different


EASI Response + PRO
Week 16 (NRI-NC)
Week 52 (OC)
Patient Achievement
100%
80%
60%
40%
20%
0%
10/552 1.8
140/554 25.3 ***
222/563 39.4 ***
9/544 1.7
108/546 19.8 ***
182/549 33.2 ***
10/509 2.0
116/510 22.7 ***
184/517 35.6 ***
173/454 38.1
211/450 46.9
129/448 28.8
154/441 34.9
134/417 32.1
171/412 41.5
EASI 90 + WP-NRS 0/1
EASI 90 + POEM ≤2
EASI 90 + DLQI 0/1
EASI 90 + WP-NRS 0/1
EASI 90 + POEM ≤2
EASI 90 + DLQI 0/1
SCORAD Response + PRO
Week 16 (NRI-NC)
Week 52 (OC)
Patient Achievement
9/552 1.6
121/554 21.8 ***
176/563 31.3 ***
8/544 1.5
101/546 18.5 ***
160/549 29.1 ***
8/509 1.6
102/510 20.0 ***
152/517 29.4 ***
155/447 34.7
186/449 41.4
122/442 27.6
147/441 33.3
121/411 29.4
158/412 38.3
SCORAD 75 + WP-NRS 0/1
SCORAD 75 + POEM ≤2
SCORAD 75 + DLQI 0/1
SCORAD 75 + WP-NRS 0/1
SCORAD 75 + POEM ≤2
SCORAD 75 + DLQI 0/1
IGA 0/1 + BSA ≤2% + PRO
Week 16 (NRI-NC)
Week 52 (OC)
Patient Achievement
6/551 1.1
99/554 17.9 ***
167/563 29.7 ***
5/544 0.9
82/546 15.0 ***
148/549 27.0 ***
3/509 0.6
90/510 17.6 ***
137/517 26.5 ***
143/454 31.5
181/450 40.2
113/448 25.2
138/441 31.3
112/417 26.9
150/412 36.4
IGA 0/1 & BSA ≤2% + WP-NRS 0/1
IGA 0/1 & BSA ≤2% + POEM ≤2
IGA 0/1 & BSA ≤2% + DLQI 0/1
IGA 0/1 & BSA ≤2% + WP-NRS 0/1
IGA 0/1 & BSA ≤2% + POEM ≤2
IGA 0/1 & BSA ≤2% + DLQI 0/1
Placebo (week 16)
UPA 15 mg (week 16)
UPA 30 mg
UPA 15 mg
UPA 30 mg

◂**Fig. 3** MDA achievement with selected ClinRO and PRO optimal treatment targets. ***$P < 0.001$ vs placebo. Error bars represent 95% CI. IGA/BSA optimal treatment target IGA 0/1 and BSA ≤ 2%. *BSA* affected body surface area, *DLQI* Dermatology Life Quality Index, *EASI 90* ≥ 90% improvement from baseline in the Eczema Area and Severity Index, *IGA* Investigator Global Assessment, *NRI-NC* non-responder imputation with no special data handling for missing data due to COVID-19, *OC* observed cases, *PBO* placebo, *POEM* patient-oriented eczema measure, *SCORAD 75* ≥ 90% improvement from baseline in scoring atopic dermatitis score, *UPA* upadacitinib, *WP-NRS* worst pruritus numerical rating scale

treatment options. However, while this article presents MDA achievement with upadacitinib, it is a post hoc analysis of a randomized clinical trial, thereby making it infeasible to integrate the shared decision-making component of the AHEAD recommendations. Additionally, due to the lack of placebo treatment at week 52, statistical testing is not feasible for week 52 data. Safety was not assessed as part of this analysis but was previously reported [8, 10]. This is the first study to our knowledge to evaluate MDA achievement with upadacitinib, and additional future work can assess the achievements of MDA in patients treated with upadacitinib in a real-world setting.

CONCLUSION

At week 16, a significantly higher proportion of patients with AD treated with either 15 mg or 30 mg of upadacitinib achieved MDA at week 16 compared with patients receiving placebo. A high proportion of MDA achievement was maintained at week 52. Thus, treatment with upadacitinib demonstrated achievement of both ClinRO and PRO optimal treatment targets as well as MDA and may optimize overall disease management in patients with moderate-to-severe AD.

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Data Availability. AbbVie is committed to responsible data sharing regarding the clinical trials we sponsor. This includes access to anonymized, individual, and trial-level data (analysis data sets), as well as other information (eg, protocols, clinical study reports, or analysis plans), as long as the trials are not part of an ongoing or planned regulatory submission. This includes requests for clinical trial data for unlicensed products and indications. These clinical trial data can be requested by any qualified researchers who engage in rigorous, independent, scientific research, and will be provided following review and approval of a research proposal, Statistical Analysis Plan (SAP), and execution of a Data Sharing Agreement (DSA).

Data requests can be submitted at any time after approval in the US and Europe and after acceptance of this manuscript for publication. The data will be accessible for 12 months, with possible extensions considered. For more information on the process or to submit a request, visit the following link: https://vivli.org/ourmember/abbvie/ then select "Home".

Declarations

Conflict of interest. Jonathan Silverberg has received honoraria as a consultant and/or advisory board member for AbbVie, Aldena, Aldena, Amgen, AObiome, Apollo, Arcutis, Arena, Asana, Aslan, Attovia, Bodewell, Boehringer-Ingelheim, Bristell-Meyers Squibb, Cara, Castle Biosciences, Celgene, Connect Biopharma, Corevitas, Dermavant, Eli Lilly, FIDE, Galderma, GlaxoSmithKline, Incyte, Inmagene, Invea, Kiniksa, Leo Pharma, Merck, Nektar, Novartis, Optum, Pfizer, RAPT, Recludix, Regeneron, Sandoz, Sanofi-Genzyme, Shaperon, TARGET-RWE, Teva, Triveni, Union, UpToDate; speaker for AbbVie, Arcutis, Dermavant, Eli Lilly, Galderma, Leo Pharma, Pfizer, Regeneron, Sanofi-Genzyme; institution received grants from Galderma, Incyte, Pfizer. Valeria Aoki has served as an investigator in clinical trials (Sanofi, Amgen, Abbvie) and consultant/advisory board: Eli Lilly, Galderma, Abbvie. Yousef Binamer has received speaker honoraria for serving as a consultant for, and travel support from AbbVie, Eli Lilly, Janssen, Kyowa Kirin, NewBridge, Novartis, and Sanofi, and received research grants from Novartis and Sanofi. Brad Glick is an advisory board member, consultant, speaker and/or investigator for and received honoraria or grants from Amgen, AbbVie, AstraZeneca, Almirall, Acrutis, Bausch Health/Valeant, OrthoDermatologics, Boehringer Ingelheim, Bristol-Myers Squibb, Brickell Biotech, Cara Therapeutics, ChemoCentryx, Dermavant, Dermira, Eli Lilly, EPI/Novan Pharmaceuticals, Incyte, Janssen Pharmaceuticals, LEO Pharma, Galderma, Nimbus Lakshmi, Inc, Novartis Pharmaceutical Corporation, Sun Pharma, Pfizer, Sanofi, Regeneron, UCB Biopharmaceuticals and the CorEvitas AD, CorEvitas PSO and PROSE Registries. Dr. Glick is a shareholder of Top MD, LLC. Melinda Gooderham has been an investigator, speaker and/or advisor for: AbbVie, Acelyrin, Alumis, Amgen, Akros, Arcutis, Aristea, AnaptysBio, Apogee, Bausch Health, BMS, Boehringer Ingelheim, Cara, Dermira, Dermavant, Eli Lilly, Galderma, GSK, Incyte, InMagene, JAMP Pharma, Janssen, LEO Pharma, L'Oreal, MedImmune, Meiji, Moonlake, Nektar, Nimbus, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, Tarsus, Takeda, UCB, Union, Ventyx and Vyne. Norito Katoh has received honoraria as a speaker/consultant for Sanofi, Maruho, Abbvie, Eli Lilly Japan, Taiho Pharmaceutical, Pfizer, Mitsubishi Tanabe Pharma, Jansen Pharma, Kyowa Kirin, Celgene Japan, Torii Pharmaceutical, and Otsuka Pharmaceutical, and has received grants as an investigator from Mitsubishi Tanabe Pharma, Torii Pharmaceutical, Maruho, Sun Pharma, Boehringer Ingelheim Japan, Eisai, and Leo Pharma. Andrew Pink has acted as investigator, speaker, advisor, received educational support from, or received research support from AbbVie, Lilly, Pfizer, Sanofi, Leo, Galderma, Amgen, Novartis, J&J, BMS, BI, UCB, Almirall and Celgene. Petra Staubach-Renz has served as a speaker or advisor for AbbVie, Almirall, BMS, Boehringer Ingelheim, Janssen, Infectopharm, Leo, Lilly, Novartis, Pfizer, Sanofi, Galderma, Pierre Fabre, Klinge Pharma, Beiersdorf, L´Oreal, Galderma, Ichthyol, Incyte, Kalvista, Celltrion, Pharvaris, and Stadapharma. Andreas Wollenberg has served as an advisor or paid speaker for, or participated in clinical trials (with honoraria paid to the institution) sponsored by: AbbVie, Aileens, Almirall, Amgen, Apogee, Beiersdorf, Bioderma, Bioproject, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Chugai, DKSH, Eli Lilly, Galapagos, Galderma, Glenmark, GSK, Hans Karrer, Hexal, Incyte, Janssen-Cilag, Kyowa Kirin, Leo Pharma, L'Oreal, Maruho, MedImmune, MSD, Mylan, MSD, Nektar, Novartis, Pfizer, Pierre Fabre, Regeneron, Sandoz, Santen, Sanofi-Aventis and UCB. Brian Calimlim, Ayman Grada, Wan-Ju Lee, Chao Li, and Alvaro Moreira are full-time employees of AbbVie and may hold AbbVie stock or stock options.

Ethical Approval. The original studies that collected the data analyzed within this manuscript were approved by the IRB, were conducted in accordance with the Declaration of Helsinki, and informed consent was obtained for participants.

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