Achieving a Deep Response on Patient-Reported Outcomes with Upadacitinib in Patients with Moderate-to-Severe Atopic Dermatitis: Results from Three Phase 3 Trials

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OBJECTIVE

To compare the effects of upadacitinib vs placebo in achieving a deep response on patient-reported outcomes measures based on absolute threshold values

CONCLUSIONS

Patients receiving upadacitinib reported deep, clinically meaningful improvements after 16 weeks of treatment across multiple patient-reported outcome measures assessing AD symptoms and impact, including skin pain, sleep, physical and emotional function, and severity of disease

Overall, the consistency and reproducibility of the results across patient-reported outcomes support the benefits of upadacitinib treatment in reducing the symptoms of AD and improving the lives of affected patients

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INTRODUCTION

- Atopic dermatitis (AD) is a chronic inflammatory skin disease with signs and symptoms that can negatively affect patients' lives
- Several patient-reported outcome measures are used to assess the severity of AD signs and symptoms and the impact of AD on health-related quality of life (HRQoL)
- Upadacitinib is an oral Janus kinase (JAK) inhibitor with greater potency for JAK1 than JAK2, JAK3, or tyrosine kinase 2[1,2]
- Once-daily upadacitinib is associated with improvement in lesion severity and extent in patients with moderate-to-severe AD[3,4]

METHODS

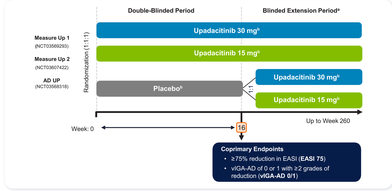
Patients

- Adolescents (aged 12–17 years) and adults (aged 18–75 years) with moderate-to-severe AD, defined as:
  - Eczema Area and Severity Index (EASI) ≥16
  - Validated Investigator Global Assessment for AD (vIGA-AD) ≥3
  - Rolling average of Worst Pruritus Numerical Rating Scale (NRS) score ≥4
  - ≥10% body surface area affected
- Candidate for systemic therapy
  - Showed inadequate response to topical AD treatments
  - Was using systemic treatment for AD
  - Confirmed topical treatments are otherwise medically inadvisable
- No systemic AD treatment within 4 weeks, topical AD treatment with 7 days, or prior exposure to any JAK inhibitor or dupilumab

Study Design and Treatment

- 3 pivotal, randomized, double-blind, placebo-controlled, multicenter phase 3 trials **(Figure 1)**

Figure 1. Study Design for Measure Up 1, Measure Up 2, and AD Up[3,4]



*The blinded extension period is ongoing. †AD Up trial tested study drug in combination with topical corticosteroids for all study arms.
EASI, Eczema Area and Severity Index; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis.

Patient-Reported Outcome Measures

- Patient-reported outcomes were assessed and their corresponding absolute threshold values[5,6] are shown in **Figure 2**

Figure 2. Patient-Reported Outcome Measures Assessing Severity and Impact of AD on Patients' Lives

Patient-Reported Outcomes (Week 2 and Week 16)		
ADerm-SS Skin Pain No/minimal skin pain: ≤1 on a scale of 0–10	**ADerm-IS Sleep** No/minimal impact: ≤3 on a scale of 0–30	**ADerm-IS Emotional State** No/minimal impact: ≤2 on a scale of 0–30
ADerm-SS 7-Item Total Symptom Score (TSS-7) No/minimal symptoms: ≤11 on a scale of 0–70	**ADerm-IS Daily Activities** No/minimal impact: ≤2 on a scale of 0–40	**POEM** "Clear or almost clear": ≤2 on a scale of 0–28

AD, atopic dermatitis; ADerm-SS, *AD Symptom Scale*; ADerm-IS, AD Impact Scale; POEM, Patient-Oriented Eczema Measure.

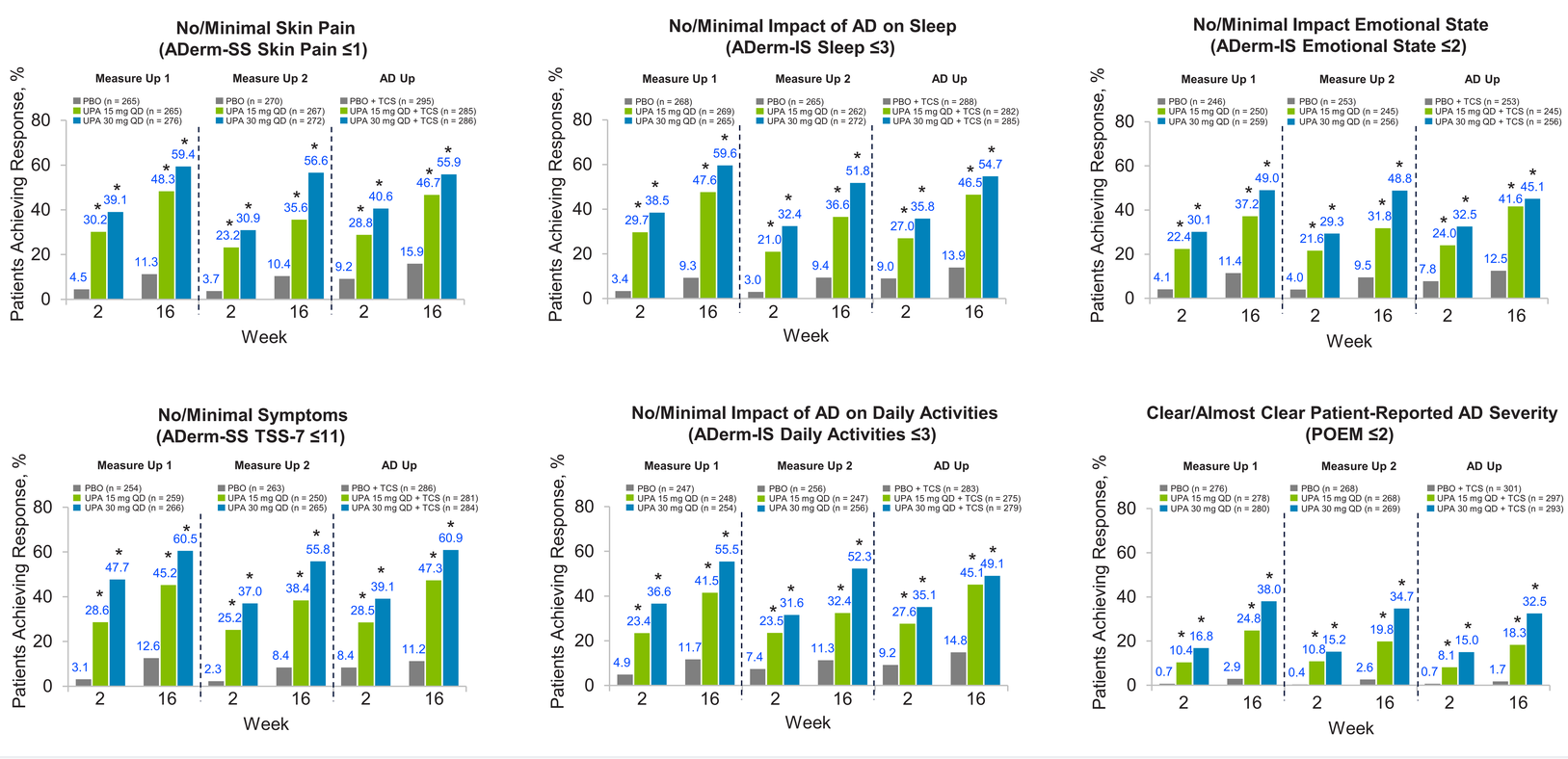
Statistical Analysis

- This was a post hoc analysis that used the intent-to-treat population from each study
- Nonresponder imputation incorporating multiple imputation to handle missing data due to COVID-19 (NRI-C) was used for nonresponder imputation only if there were no missing data due to COVID-19

RESULTS

- At Week 2, greater proportions of patients treated with upadacitinib 15 mg/30 mg vs placebo achieved scores corresponding to no/minimal skin pain and symptoms, as well as no/minimal impact on sleep, daily activities, or emotional state **(Figure 3)**
- At Week 2, greater proportion of patients treated with upadacitinib 15 mg/30 mg vs placebo achieved scores corresponding to clear/almost clear patient-reported disease
- At Week 16, differences between upadacitinib 15 mg/30 mg vs placebo were larger across all patient-reported outcomes

Figure 3. Proportions of Patients Achieving Scores Corresponding to No/Minimal Impact or Symptoms, or "Clear/Almost Clear" on Patient-Reported Outcome Measures at Week 2 and Week 16 of Upadacitinib Treatment (ITT Population, NRI-C)



*P < 001 compared with placebo. ADerm-SS, Atopic Dermatitis Symptom Scale; ADerm-IS, Atopic Dermatitis Impact Scale; ITT, intent to treat; NRI-C, nonresponder imputation incorporating multiple imputation to handle missing data due to COVID-19; PBO, placebo; POEM, Patient-Oriented Eczema Measure; QD, once daily; TCS, topical corticosteroids; UPA, upadacitinib.