Efficacy of Abrocitinib and Dupilumab in Patients With Moderate-to-Severe Atopic Dermatitis With Severe Itch at Baseline and in Subgroups by Baseline Thresholds of Severe Itch: A Post Hoc Analysis of the JADE COMPARE and JADE DARE Clinical Trials

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INTRODUCTION

- Itch associated with atopic dermatitis (AD) has a substantial impact on the patient's quality of life[1]
- Patients with moderate-to-severe AD often describe itch as their most burdensome symptom[2]
- Abrocitinib, an oral Janus kinase-1-selective inhibitor, provided significantly greater itch responses at week 2 of treatment compared with dupilumab, an injectable interleukin-4 receptor alpha inhibitor, in patients with moderate-to-severe AD who received background topical therapy in 2 randomized clinical trials[3,4]
- Efficacy of abrocitinib and dupilumab has not been investigated in patients with AD and severe itch

OBJECTIVE

- To evaluate the efficacy of abrocitinib and dupilumab in patients with moderate-to-severe AD and severe itch using various baseline thresholds of severe itch

METHODS

Study Design

- This post hoc analysis included data from patients with moderate-to-severe AD who received abrocitinib 200 mg QD or dupilumab 300 mg Q2W in combination with background topical therapy in the JADE COMPARE (NCT03720470) and JADE DARE (NCT04345367) phase 3 trials (**Supplementary Figure**)
- Patients from JADE COMPARE and JADE DARE who had severe itch at baseline (Peak Pruritus Numerical Rating Scale [PP-NRS, used with permission from Regeneron Pharmaceuticals, Inc., and Sanofi] score ≥7) were pooled for analysis

Analyses

- All patients having baseline PP-NRS ≥7, as well as individual subgroups with baseline PP-NRS scores of 7, 8, 9, and 10, were assessed at week 2 and week 16 for achievement of ≥4-point improvement in PP-NRS (PP-NRS4), PP-NRS score of 0 or 1 (itch-free state), and Dermatology Life Quality Index score of 0 or 1 (DLQI 0/1)
- Patient-Oriented Eczema Measure (POEM) score of ≤2 was assessed at week 16
- Missing data were handled using nonresponder imputation, whereby if a subject withdrew from the study, they were considered nonresponders after withdrawal

RESULTS

Patients and Baseline Disease Characteristics

- A total of 875 patients had severe itch at baseline (abrocitinib 200 mg, 453; dupilumab 300 mg, 422)
- Overall, patients had substantial itch (median PP-NRS: 8 [abrocitinib] and 8 [dupilumab]) and quality of life impairment (median DLQI: 16 [abrocitinib] and 16 [dupilumab]) at baseline
- Baseline disease characteristics for the overall pooled population and individual subgroups by baseline PP-NRS scores are shown in **Table 1**
  - Subgroups with baseline PP-NRS score of 9 or 10 were associated with greater baseline disease severity
  - Similarly, median DLQI scores at baseline were greater in subgroups with baseline PP-NRS scores of 9 or 10 than those with baseline PP-NRS scores of 7 or 8

Itch Response and Patient-Reported Outcomes by Baseline Itch Severity

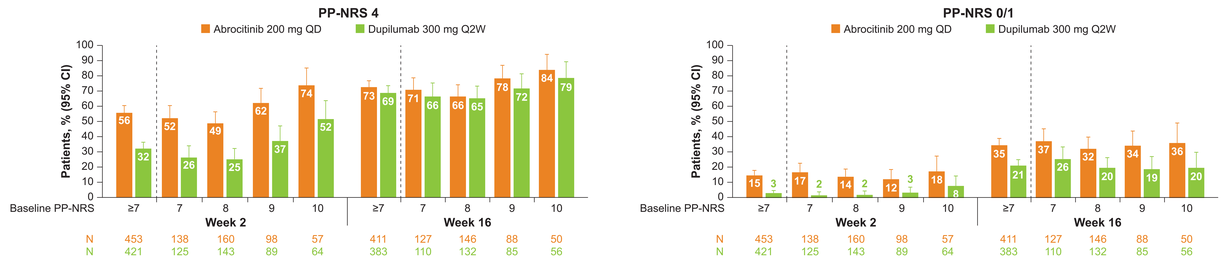
- The proportions of patients achieving PP-NRS4 and PP-NRS 0/1 at week 2 were greater with abrocitinib than with dupilumab in patients with severe itch, regardless of the baseline threshold; by week 16, the relative differences between treatment groups diminished for PP-NRS4 but were maintained for PP-NRS 0/1 (**Figure 1**)
- The proportions of patients achieving POEM ≤2 response at week 16 were greater with abrocitinib than dupilumab across all evaluated thresholds of severe itch (**Figure 2**)
- A greater proportion of patients achieved DLQI 0/1 response with abrocitinib than dupilumab at week 2 which was maintained at week 16 across all evaluated thresholds of severe itch (**Figure 2**)

Table 1. Baseline Disease Characteristics in the Overall Pooled Population and Individual Subgroups of Severe Itch

	Baseline PP-NRS ≥7		Baseline PP-NRS of 7		Baseline PP-NRS of 8		Baseline PP-NRS of 9		Baseline PP-NRS of 10	
	Abrocitinib 200 mg n=453	Dupilumab 300 mg n=422	Abrocitinib 200 mg n=138	Dupilumab 300 mg n=125	Abrocitinib 200 mg n=160	Dupilumab 300 mg n=143	Abrocitinib 200 mg n=98	Dupilumab 300 mg n=90	Abrocitinib 200 mg n=57	Dupilumab 300 mg n=64
IGA, n (%) 3 (Moderate) 4 (Severe)	 255 (56) 198 (44)	 243 (58) 179 (42)	 89 (64) 49 (36)	 78 (62) 47 (38)	 97 (61) 63 (39)	 95 (66) 48 (34)	 48 (49) 50 (51)	 42 (47) 48 (53)	 21 (37) 36 (63)	 28 (44) 36 (56)
EASI, median (IQR)	26 (20, 36)	26 (19, 37)	26 (19, 34)	26 (19, 35)	25 (20, 35)	23 (19, 36)	27 (21, 39)	28 (20, 38)	31 (22, 44)	28 (19, 41)
%BSA, median (IQR)	42 (28, 60)	40 (25, 59)	41 (27, 58)	38 (23, 53)	39 (26, 60)	38 (23, 58)	44 (31, 63)	45 (29, 67)	46 (30, 63)	47 (29, 72)
DLQI, median (IQR)	16 (11, 20)	16 (11, 20)	13 (9, 19)	13 (10, 18)	17 (12, 21)	16 (11, 22)	18 (13, 21)	16 (12, 19)	18 (14, 26)	20 (16, 24)
POEM, median (IQR)	22 (19, 26)	22 (19, 27)	20 (16, 24)	20 (18, 24)	22 (19, 26)	23 (20, 26)	23 (20, 26)	23 (19, 27)	25 (21, 28)	26 (21, 28)

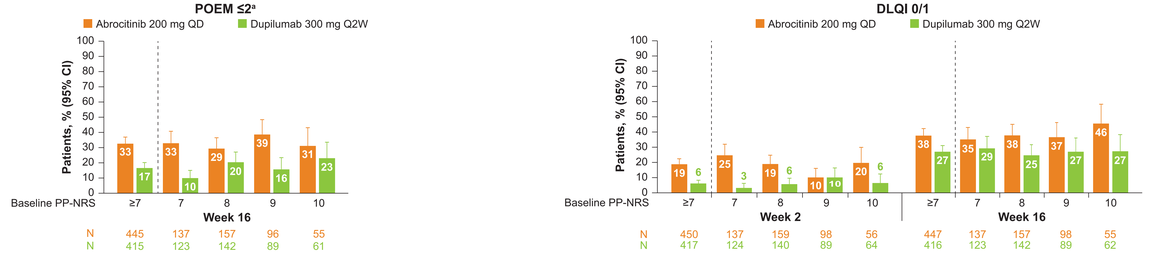
%BSA, percentage of body surface area; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; IQR, interquartile range; POEM, Patient-Oriented Eczema Measure; PP-NRS, Peak Pruritus Numerical Rating Scale.

Figure 1. Itch Response at Week 2 and Week 16 by Baseline Itch Severity



Q2W, once every 2 weeks; QD, once daily; PP-NRS, Peak Pruritus Numerical Rating Scale; PP-NRS4, ≥4-point improvement in PP-NRS; PP-NRS 0/1, PP-NRS score of 0 or 1.

Figure 2. Patient-Reported Outcomes at Week 2 and Week 16 by Baseline Itch Severity



DLQI, Dermatology Life Quality Index; DLQI 0/1, DLQI score of 0 or 1; Q2W, once every 2 weeks; QD, once daily; POEM, Patient-Oriented Eczema Measure.
[a]POEM was not collected at week 2 in JADE COMPARE or JADE DARE.

CONCLUSIONS

- Patients with moderate-to-severe AD who had a higher burden of itch at baseline reported a greater impairment in patient-reported measures of quality of life and disease severity
- Across various thresholds of severe itch, abrocitinib provided more rapid achievement of an itch-free state (defined as PP-NRS 0/1) and substantial quality of life improvements that were greater than dupilumab as early as the first assessment at week 2
- The difference between abrocitinib and dupilumab treatment groups largely diminished by week 16 for PP-NRS4 but was maintained for PP-NRS 0/1, POEM ≤2, and DLQI 0/1, suggesting a 4-point improvement in PP-NRS may not be sufficient for patients with severe itch at baseline
- Abrocitinib may be an appropriate treatment option for patients who have severe itch and are expecting to achieve an itch-free state

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