Abrocitinib in the Treatment of Moderate-to-Severe Atopic Dermatitis Refractory to Dupilumab Treatment: An Analysis of JADE-EXTEND, a Phase 3 Long-Term Extension Study

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BACKGROUND

- Dupilumab, an anti–interleukin 4 receptor alpha monoclonal antibody, is approved for the treatment of patients with atopic dermatitis (AD) who are candidates for systemic therapy[1]
- Patients with moderate-to-severe AD who do not respond to dupilumab have limited treatment options
- Abrocitinib is a Janus kinase 1 (JAK1) inhibitor that is under investigation for the treatment of moderate-to-severe AD[2,3]

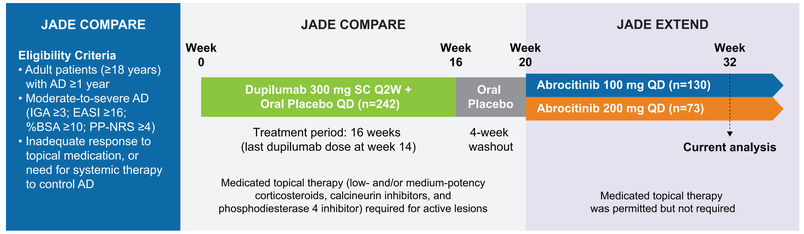
OBJECTIVE

- To assess the proportion of dupilumab nonresponder patients from JADE COMPARE who experienced clinically meaningful improvement in signs and symptoms of AD after switching to abrocitinib in JADE EXTEND

METHODS

- Phase 3 JADE COMPARE included adults with moderate-to-severe AD and inadequate response to topical medication or a need for systemic therapy to control AD
- This post hoc analysis focused on patients with moderate-to-severe AD who received dupilumab and concomitant topical therapy for 16 weeks in JADE COMPARE followed by entry into JADE EXTEND (**Figure 1**)
- Upon entering JADE EXTEND, patients were randomized to either abrocitinib 200 mg or 100 mg once daily
- In JADE EXTEND, medicated topical therapy was permitted but not required
- Patients who did not achieve an Investigator's Global Assessment (IGA) of 0 or 1 with ≥2-point improvement, ≥75% or ≥90% improvement in Eczema Area and Severity Index (EASI), 4-point improvement on the Peak Pruritus Numerical Rating Scale (PP-NRS), or PP-NRS score of 0 or 1 at week 16 with dupilumab were reassessed at week 32 with abrocitinib 200 mg or 100 mg
- Safety was assessed by monitoring treatment-emergent adverse events (TEAEs)

Figure 1. Study Design



AD, atopic dermatitis; %BSA, percentage of affected body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; PP-NRS, Peak Pruritus Numerical Rating Scale; Q2W, every 2 weeks; QD, once daily; SC, subcutaneous.

The PP-NRS is used with permission of Regeneron Pharmaceuticals, Inc., and Sanofi.

RESULTS

Patients

- Disease characteristics were well balanced across treatment arms at entry to JADE EXTEND (**Table 1**)
- Most patients had moderate AD per IGA: 64.4% of patients in the 200-mg arm and 66.9% in the 100-mg arm

Table 1. Baseline Characteristics (Safety Population)[a]

	Abrocitinib 100 mg QD n=130	Abrocitinib 200 mg QD n=73
Duration of AD, mean (SD), y	24.2 (15.0)	23.6 (15.6)
IGA, n (%)		
Moderate (3)	87 (66.9)	47 (64.4)
Severe (4)	43 (33.1)	26 (35.6)
%BSA, mean (SD)	45.4 (21.2)	47.9 (22.9)
EASI, mean (SD)	29.6 (11.2)	31.2 (12.4)
PP-NRS, mean (SD)	7.4 (1.7)	7.2 (1.6)

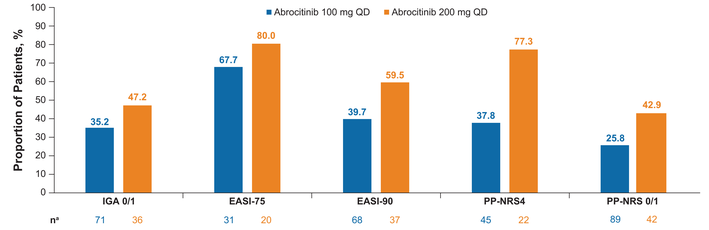
AD, atopic dermatitis; %BSA, percentage of affected body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; PP-NRS, Peak Pruritus Numerical Rating Scale; QD, once daily; SD, standard deviation.

[a]Safety population represents all patients who received prior dupilumab in JADE COMPARE and were randomly assigned to receive abrocitinib in JADE EXTEND.

Efficacy

- A substantial portion of dupilumab nonresponders achieved clinically meaningful efficacy responses after switching to abrocitinib (**Figure 2**)
- Among dupilumab IGA 0/1 nonresponders (based on failing to achieve an IGA of clear [0] or almost clear [1] and ≥2-grade improvement from baseline in JADE COMPARE), 47.2% of the abrocitinib 200-mg group and 35.2% of the abrocitinib 100-mg group achieved IGA 0/1 at week 12 of JADE EXTEND
- Among dupilumab EASI-75 nonresponders (based on failing to achieve at least a 75% improvement from baseline in EASI in JADE COMPARE), 80.0% of the abrocitinib 200-mg group and 67.7% of the abrocitinib 100-mg group achieved EASI-75 at week 12 of JADE EXTEND
- Among dupilumab EASI-90 nonresponders (based on failing to achieve at least a 90% improvement from baseline in EASI in JADE COMPARE), 59.5% of the abrocitinib 200-mg group and 39.7% of the abrocitinib 100-mg group achieved EASI-90 at week 12 of JADE EXTEND
- Among dupilumab PP-NRS4 nonresponders (based on failing to achieve at least a 4-point improvement from baseline in PP-NRS in JADE COMPARE), 77.3% of the abrocitinib 200-mg group and 37.8% of the abrocitinib 100-mg group achieved PP-NRS4 at week 12 of JADE EXTEND (representing a clinically meaningful improvement in itch)
- Among dupilumab PP-NRS 0/1 nonresponders (based on failing to achieve a PP-NRS score of 0 [representing no itch] or 1 [representing minimal itch] in JADE COMPARE), 42.9% of the abrocitinib 200-mg group and 25.8% of the abrocitinib 100-mg group achieved PP-NRS 0/1 at week 12 of JADE EXTEND

Figure 2. Abrocitinib Efficacy at Week 12 Among Dupilumab Nonresponders



EASI-75, ≥75% improvement from baseline in Eczema Area and Severity Index; EASI-90, ≥90% improvement from baseline in Eczema Area and Severity Index; IGA 0/1, Investigator's Global Assessment of clear (0) or almost clear (1) and ≥2-grade improvement from baseline; PP-NRS4, ≥4-point improvement from baseline in Peak Pruritus Numerical Rating Scale score; PP-NRS 0/1, Peak Pruritus Numerical Rating Scale score of 0 (no itch) or 1 (minimal itch); QD, once daily.

[a]Number of dupilumab nonresponders according to each efficacy endpoint at week 16 of JADE COMPARE.

Safety

- TEAEs were reported in 50.7% of patients in the abrocitinib 200-mg group and in 41.5% of patients in the abrocitinib 100-mg group (**Table 2**)
- The incidence of adverse events (AEs) that were serious, severe, or led to study discontinuation was <3%
- The most common AE in both abrocitinib treatment arms was nasopharyngitis, occurring in 11.0% of patients in the 200-mg group and 6.9% of patients in the 100-mg group

Table 2. Safety

	Abrocitinib 100 mg QD n=130	Abrocitinib 200 mg QD n=73
Patients who had ≥1 TEAE, n (%)	54 (41.5)	37 (50.7)
Serious	3 (2.3)	1 (1.4)
Severe	3 (2.3)	2 (2.7)
Leading to study discontinuation	1 (0.8)	1 (1.4)
TEAEs reported for ≥4 patients in any group, n (%)		
Nasopharyngitis	9 (6.9)	8 (11.0)
Nausea	0	6 (8.2)
Acne	3 (2.3)	5 (6.8)
Headache	1 (0.8)	5 (6.8)
Upper respiratory tract infection	6 (4.6)	2 (2.7)
Urinary tract infection	4 (3.1)	1 (1.4)

QD, once daily; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- In a substantial proportion of dupilumab nonresponders, clinically meaningful improvement in signs (IGA, EASI-75, EASI-90) and symptoms (PP-NRS4, PP-NRS 0/1) of moderate-to-severe AD was achieved after switching to abrocitinib
- The safety profile of abrocitinib in JADE EXTEND was consistent with previous studies; no new safety signals were observed at 12 weeks
- The efficacy and safety profile of oral abrocitinib 200 mg or 100 mg QD in this analysis supports the role of abrocitinib as treatment for patients with moderate-to-severe AD, regardless of prior experience with dupilumab

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DISCLOSURES

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