Consistent Efficacy Responses of Abrocitinib Monotherapy Across Phase 2/3 Randomized Controlled Clinical Trials: Results From JADE MONO-1, JADE MONO-2, and the Phase 2b Proof-of-Concept Trial

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BACKGROUND

- Atopic dermatitis (AD) is a chronic, relapsing, inflammatory skin condition characterized by itchy, dry skin[1]
- In current practice, systemic therapy is used after failure or excessive use of topical treatments to manage moderate-to-severe AD[1]
  - Current treatments may not adequately treat all patients with AD, and additional options, including treatments with oral administration, are needed[2]
- Abrocitinib is an oral once-daily Janus kinase 1 selective inhibitor under investigation for the treatment of moderate-to-severe AD
  - In a phase 2b study (NCT02780167), abrocitinib monotherapy was safe and effective in reducing signs and symptoms of AD[3]
  - In the phase 3 JADE MONO-1 (NCT03349060) and JADE MONO-2 (NCT03575871) studies, a significantly greater proportion of abrocitinib-treated (200 mg or 100 mg once daily) patients than placebo-treated patients achieved an Investigator's Global Assessment (IGA) score of 0/1, ≥75% improvement from baseline in Eczema Area and Severity Index (EASI-75), and ≥4-point improvement from baseline in Peak Pruritus Numerical Rating Scale (PP-NRS4; the PP-NRS is used with permission of Regeneron Pharmaceuticals, Inc., and Sanofi) responses ($P<0.05$)[4,5]
- We compare the results from the phase 2b, JADE MONO-1, and JADE MONO-2 trials, which were conducted to investigate the efficacy of once-daily abrocitinib 200 mg or 100 mg compared with placebo in adults with moderate-to-severe AD

OBJECTIVES

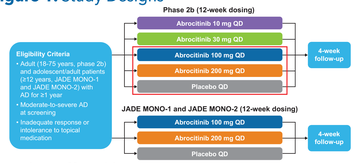
- To evaluate the consistency of efficacy and safety response across monotherapy trials and in the pooled population of the 3 monotherapy trials

METHODS

Study Overview

- The phase 2b study was a multicenter, randomized, double-blind, placebo-controlled trial[3] (**Figure 1**)
- JADE MONO-1 and JADE MONO-2 were identically designed multicenter, randomized, double-blind, placebo-controlled, monotherapy studies[4,5] (**Figure 1**)

Figure 1. Study Designs[a]



AD, atopic dermatitis; QD, once daily.
[a]Only data from abrocitinib 200 mg, abrocitinib 100 mg, and placebo were included in this pooled analysis.

Efficacy and Safety Endpoints

Efficacy

- The proportion of patients who had IGA 0/1 response (clear [0] or almost clear [1] with ≥2-grade improvement from baseline) at week 12 (primary endpoint in all 3 studies)
- The proportion of patients at week 12 who achieved EASI-75 for abrocitinib (200 mg or 100 mg) compared with placebo (JADE MONO-1/JADE MONO-2: coprimary endpoint, phase 2b: additional secondary endpoint)
- The proportion of patients who had ≥4-point improvement from baseline in itch score at week 12 (JADE MONO-1/ JADE MONO-2 [PP-NRS4]: key secondary endpoint; phase 2b [pruritus numerical rating scale]: additional secondary endpoint)

Safety

- Incidence of treatment-emergent adverse events (TEAEs), serious TEAEs, TEAEs leading to discontinuation, most frequently reported TEAEs, and death

Statistical Analysis

- Comparisons were based on the Fisher exact test for comparing 2 proportions
  - In the original studies, the familywise type 1 error rate for testing the coprimary and key secondary endpoints was strictly controlled at 5% using a sequential, Bonferroni-based procedure; testing of all other secondary endpoints was performed at the nominal 5% significance level and was not controlled for multiplicity
  - Efficacy was analyzed in the full analysis set, defined as all patients randomly assigned to receive treatment who received ≥1 dose of study medication

RESULTS

Demographics and Baseline Disease Characteristics

- Demographics and baseline disease characteristics were balanced across the phase 2b, JADE MONO-1, and JADE MONO-2 studies. Pooled demographics are presented (**Table 1**)

Table 1. Demographics and Baseline Disease Characteristics of Pooled Population

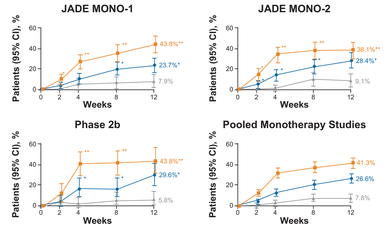
	Placebo n=210	Abrocitinib 100 mg n=369	Abrocitinib 200 mg n=363
Age, mean (SD), y	35 (15.0)	35.9 (15.8)	34.1 (16.4)
Male, n (%)	117 (55.7)	215 (58.3)	197 (54.3)
Race, n (%)			
White	141 (67.1)	253 (68.6)	231 (63.6)
Asian	39 (18.6)	80 (21.7)	85 (23.4)
Other	27 (13.0)	35 (9.5)	43 (11.9)
EASI, mean (SD)	27.6 (11.8)	29.4 (12.4)	29.0 (13.4)
IGA, n (%)			
Moderate (3)	132 (62.9)	228 (61.8)	231 (63.6)
Severe (4)	78 (37.1)	141 (38.2)	132 (36.4)
Itch score,[a] mean (SD)	7.0 (1.0)	7.1 (1.9)	7.0 (1.9)

IGA, Investigator's Global Assessment; NRS, numerical rating scale; PP-NRS, Peak Pruritus Numerical Rating Scale; EASI, Eczema Area and Severity Index.
[a]All 3 studies included the proportion of patients achieving ≥4-point improvement in itch. The PP-NRS4 (self-report of worst itch in the past 24 hours) was used to assess itch during screening and daily on days 1-15 and thereafter on study visit days for JADE MONO-1 and JADE MONO-2; pruritus NRS (self-report of itch in the past 24 hours) was used to assess itch daily on days 1-15 and thereafter on study visit days for the phase 2b study.

Efficacy: IGA, EASI-75, and Itch Responses at Week 12

- IGA 0/1 response rates were consistent across studies and were greater with abrocitinib 200 mg or 100 mg than with placebo starting at weeks 2-8 and continuing through week 12 (**Figure 2**)

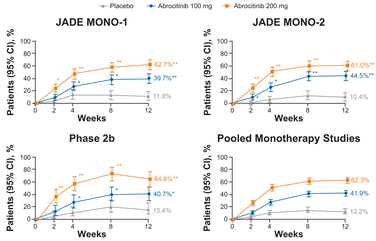
Figure 2. Percentage of Patients Who Achieved IGA 0/1 Response (clear [0] or almost clear [1] with ≥2-grade improvement)



IGA, Investigator's Global Assessment.
*$P<0.05$, **$P<0.0001$ compared with placebo. Conclusion of statistical significance was controlled for multiplicity only at week 12 for JADE MONO-1, JADE MONO-2, and the phase 2b study.

- EASI-75 response rates were consistent across studies and were greater with abrocitinib 200 mg or 100 mg than with placebo starting at weeks 2-4 and continuing through week 12 (**Figure 3**)

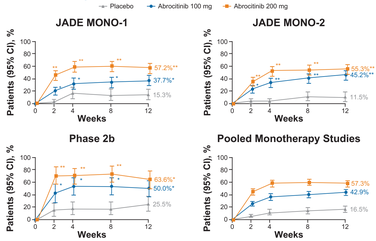
Figure 3. Percentage of Patients Who Achieved EASI-75



EASI, Eczema Area and Severity Index.
*$P<0.05$, **$P<0.0001$ compared with placebo. Conclusion of statistical significance was controlled for multiplicity only at week 12 for JADE MONO-1 and JADE MONO-2.

- The proportion of patients who had ≥4-point improvement in itch score was also consistently higher with abrocitinib 200 mg or 100 mg than with placebo across studies starting at week 2 and continuing through week 12 (**Figure 4**)

Figure 4. Percentage of Patients Who Achieved ≥4-Point Improvement in Itch Score[a]



NRS, numerical rating scale; PP-NRS, Peak Pruritus Numerical Rating Scale.
*$P<0.05$, **$P<0.0001$ compared with placebo. Conclusion of statistical significance was controlled for multiplicity only at weeks 2, 4, and 12 for JADE MONO-1 and JADE MONO-2.
[a]JADE MONO-1/JADE MONO-2: PP-NRS4; phase 2b study: pruritus NRS.

Safety Summary

- The safety profile of abrocitinib was similar across the 3 monotherapy studies (**Table 2**)
- Based on the pooled population, the most frequently reported TEAEs were nausea, nasopharyngitis, headache, upper respiratory tract infection, and dermatitis atopic; the TEAEs mostly were mild

Table 2. Safety Summary

	Phase 2b			JADE MONO-1			JADE MONO-2			Pooled Monotherapy Studies		
n (%)	Placebo n=56	Abrocitinib 100 mg n=56	Abrocitinib 200 mg n=55	Placebo n=77	Abrocitinib 100 mg n=156	Abrocitinib 200 mg n=154	Placebo n=78	Abrocitinib 100 mg n=158	Abrocitinib 200 mg n=155	Placebo n=211	Abrocitinib 100 mg n=370	Abrocitinib 200 mg n=364
TEAEs	32 (57.1)	43 (76.8)	41 (74.5)	44 (57.1)	108 (69.2)	120 (77.9)	42 (53.8)	99 (62.7)	102 (65.8)	118 (55.9)	250 (67.9)	263 (72.3)
Serious TEAEs	2 (3.6)	3 (5.4)	2 (3.6)	3 (3.9)	5 (3.2)	5 (3.2)	1 (1.3)	5 (3.2)	2 (1.3)	6 (2.8)	13 (3.5)	9 (2.5)
Severe TEAEs	3 (5.4)	9 (16.1)	4 (7.3)	9 (11.7)	8 (5.1)	5 (3.2)	5 (6.4)	7 (4.4)	6 (3.9)	17 (8.1)	24 (6.5)	15 (4.1)
TEAEs leading to discontinuation	9 (16.1)	12 (21.4)	8 (14.5)	7 (9.1)	9 (5.8)	9 (5.8)	10 (12.8)	6 (3.8)	5 (3.2)	26 (12.3)	27 (7.3)	22 (6.0)
Deaths, n (%)	0	0	0	0	0	0	0	1 (0.6)[b]	0	0	1 (0.3)[b]	0
Most frequently reported TEAEs (≥5% in any group in pooled monotherapy studies)												
Nausea	1 (1.8)	1 (1.8)	8 (14.5)	2 (2.6)	14 (9.0)	31 (20.1)	2 (2.6)	12 (7.6)	22 (14.2)	5 (2.4)	27 (7.3)	61 (16.8)
Nasopharyngitis	0	0	0	8 (10.4)	23 (14.7)	18 (11.7)	5 (6.4)	20 (12.7)	12 (7.7)	18 (8.5)	53 (14.3)	36 (9.9)
Headache	2 (3.6)	5 (8.9)	4 (7.3)	2 (2.6)	12 (7.7)	15 (9.7)	2 (2.6)	9 (5.7)	12 (7.7)	6 (2.8)	26 (7.0)	31 (8.5)
Upper respiratory tract infection	5 (8.9)	3 (5.4)	5 (9.1)	5 (6.5)	11 (7.1)	11 (7.1)	3 (3.8)	14 (8.9)	5 (3.2)	13 (6.2)	28 (7.6)	21 (5.8)
Dermatitis atopic	7 (12.5)	7 (12.5)	7 (12.7)	13 (16.9)	22 (14.1)	8 (5.2)	12 (15.4)	9 (5.7)	6 (3.9)	32 (15.2)	38 (10.3)	21 (5.8)

TEAE, treatment-emergent adverse event.
[b]Sudden cardiac death in a 73-year-old woman with history of aortic valve sclerosis and untreated hypertension during follow-up period; the event was considered not related to treatment.

CONCLUSIONS

- The efficacy and safety of abrocitinib monotherapy in patients with moderate-to-severe AD was consistent across the phase 2b and the phase 3 JADE MONO trials
- Across studies, the time to onset of IGA 0/1, EASI-75, and PP-NRS4 response was rapid, becoming apparent within the first 2-4 weeks of treatment in most cases
- At week 12, the 200-mg and 100-mg once-daily doses of abrocitinib were significantly more effective than placebo at relieving AD signs and symptoms in patients with moderate-to-severe AD
- The rate of AEs was higher with abrocitinib (200 mg or 100 mg) than with placebo
  - However, few patients in any treatment group experienced serious or severe AEs, and the AEs that most frequently occurred with abrocitinib (nausea) were mild

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