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

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Background: Abrocitinib, an oral once-daily Janus kinase 1 selective inhibitor under investigation for the treatment of moderate-to-severe atopic dermatitis (AD), was effective and safe in randomized, double-blind, phase 2b (Ph2b [NCT02780167]) and phase 3 monotherapy trials (JADE MONO-1 [NCT03349060] and JADE MONO-2 [NCT03575871]).

Objectives: To evaluate the consistency of efficacy and safety response across monotherapy trials and the pooled population of the 3 monotherapy trials.

Methods: Patients (phase 2b, 18-75 years of age; MONO-1 and MONO-2, ≥12 years of age) with moderate-to-severe AD were randomly assigned to receive once-daily abrocitinib monotherapy (MONO-1/MONO-2: 200 or 100 mg; phase 2b: 200, 100, 30, or 10 mg) or placebo for 12 weeks. Only data from patients treated with abrocitinib 200 mg, abrocitinib 100 mg, or placebo were included in this analysis. Endpoints were the proportion of patients who achieved Investigator's Global Assessment (IGA) response (clear [0] or almost clear [1] with ≥2-grade improvement from baseline) at week 12 (primary in all 3

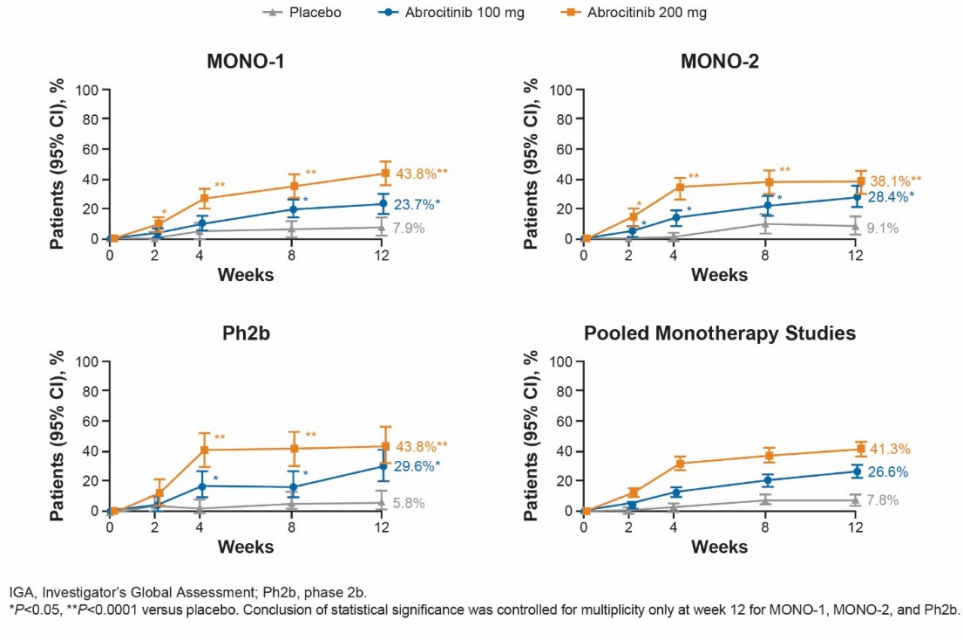
studies), ≥75% improvement from baseline in Eczema Area and Severity Index (EASI-75) at week 12 (MONO-1/MONO-2: coprimary, phase 2b: additional secondary), and/or ≥4-point improvement from baseline in itch score (MONO-1/MONO-2 [Peak Pruritus Numerical Rating Scale [PP-NRS]; used with permission of Regeneron Pharmaceuticals, Inc., and Sanofi]: key secondary; phase 2b [pruritus NRS]: additional secondary).

Results: Data from 364, 370, and 211 patients in the pooled monotherapy population who received abrocitinib 200 mg, abrocitinib 100 mg, or placebo, respectively, were used in this analysis. The IGA response rates (Figure 1) with abrocitinib (200 mg and 100 mg) were consistently higher than with placebo, starting at weeks 2-8 and continuing through week 12 across all studies. Similarly, EASI-75 response (Figure 2) with abrocitinib (200 mg and 100 mg) was consistently higher than with placebo, starting at weeks 2-4 and continuing through week 12 across all studies. The proportion of patients with ≥4-point improvement in itch score rates (Figure 3) 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. The safety profile (Table) of abrocitinib was also consistent across the 3 monotherapy studies. Based on the pooled population, the most frequently reported treatment-emergent adverse events were nausea, nasopharyngitis, headache, upper respiratory tract infection, and dermatitis atopic, and were mostly mild.

Conclusion: Abrocitinib was consistently safe and effective in improving the signs and symptoms of AD across phase 2b and phase 3 monotherapy trials in patients with moderate-to-severe AD.

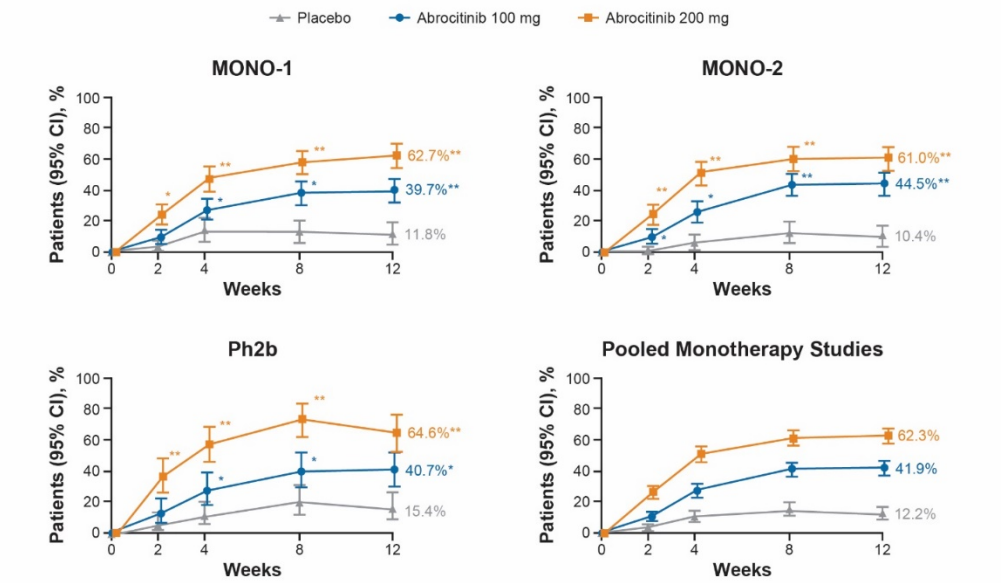
Figures and Tables:

Figure 1. Patients Achieving IGA Response (clear [0] or almost clear [1] with ≥2-grade improvement)



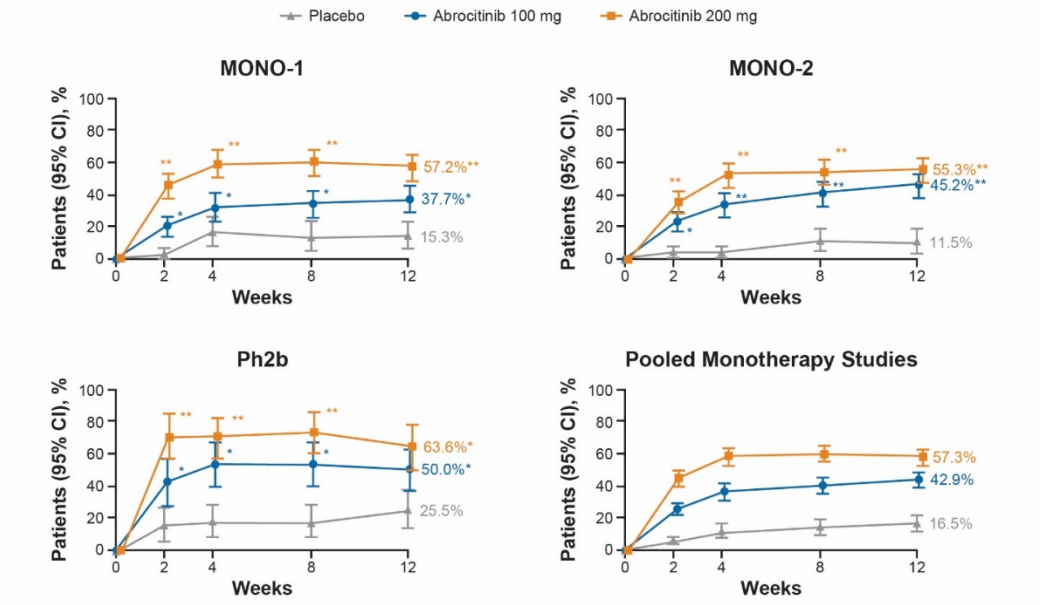
IGA, Investigator's Global Assessment; Ph2b, phase 2b.
*P<0.05, **P<0.0001 versus placebo. Conclusion of statistical significance was controlled for multiplicity only at week 12 for MONO-1, MONO-2, and Ph2b.

Figure 2. Patients Achieving ≥75% Improvement in EASI



EASI, Eczema Area and Severity Index; Ph2b, phase 2b.
*P<0.05, **P<0.0001 versus placebo. Conclusion of statistical significance was controlled for multiplicity only at week 12 for MONO-1 and MONO-2.

Figure 3. Patients achieving ≥4-Point Improvement in Itch Score[a]



Ph2b, phase 2b.
*P<0.05, **P<0.0001 versus placebo. Conclusion of statistical significance was controlled for multiplicity only at weeks 2, 4, and 12 for MONO-1 and MONO-2.
[a]MONO-1/MONO-2: Peak Pruritus Numerical Rating Scale; Ph2b: pruritus numeric rating scale.

Table. Adverse Event Summary

n (%)	MONO-1			MONO-2			Ph2b			Pooled Monotherapy Studies		
	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=56	Abrocitinib 100 mg N=56	Abrocitinib 200 mg N=55	Placebo N=211	Abrocitinib 100 mg N=370	Abrocitinib 200 mg N=364
TEAEs	44 (57.1)	108 (69.2)	120 (77.9)	42 (53.8)	99 (62.7)	102 (65.8)	32 (57.1)	43 (76.8)	41 (74.5)	118 (55.9)	250 (67.6)	263 (72.3)
Serious TEAEs	3 (3.9)	5 (3.2)	5 (3.2)	1 (1.3)	5 (3.2)	2 (1.3)	2 (3.6)	3 (5.4)	2 (3.6)	6 (2.8)	13 (3.5)	9 (2.5)
Severe TEAEs	9 (11.7)	8 (5.1)	5 (3.2)	5 (6.4)	7 (4.4)	6 (3.9)	3 (5.4)	9 (16.1)	4 (7.3)	17 (8.1)	24 (6.5)	15 (4.1)
TEAEs leading to study discontinuation	7 (9.1)	9 (5.8)	9 (5.8)	10 (12.8)	6 (3.8)	5 (3.2)	9 (16.1)	12 (21.4)	8 (14.5)	26 (12.3)	27 (7.3)	22 (6.0)
Deaths, n (%)	0	0	0	0	1 (0.6)[a]	0	0	0	0	0	1 (0.3)[a]	0
Most frequently reported TEAEs (≥5% in any group in pooled monotherapy studies)												
Nausea	2 (2.6)	14 (9.0)	31 (20.1)	2 (2.6)	12 (7.6)	22 (14.2)	1 (1.8)	1 (1.8)	8 (14.5)	5 (2.4)	27 (7.3)	61 (16.8)
Nasopharyngitis	8 (10.4)	23 (14.7)	18 (11.7)	5 (6.4)	20 (12.7)	12 (7.7)	0	0	0	18 (8.5)	53 (14.3)	36 (9.9)
Headache	2 (2.6)	12 (7.7)	15 (9.7)	2 (2.6)	9 (5.7)	12 (7.7)	2 (3.6)	5 (8.9)	4 (7.3)	6 (2.8)	26 (7.0)	31 (8.5)
Upper respiratory tract infection	5 (6.5)	11 (7.1)	11 (7.1)	3 (3.8)	14 (8.9)	5 (3.2)	5 (8.9)	3 (5.4)	5 (9.1)	13 (6.2)	28 (7.6)	21 (5.8)
Dermatitis atopic	13 (16.9)	22 (14.1)	8 (5.2)	12 (15.4)	9 (5.7)	6 (3.9)	7 (12.5)	7 (12.5)	7 (12.7)	32 (15.2)	38 (10.3)	21 (5.8)

TEAE, treatment-emergent adverse event.

[a]Sudden cardiac death in a 73-year-old woman during follow-up period (3 weeks after end of therapy with abrocitinib 100 mg); this patient had a history of aortic valve sclerosis and untreated hypertension; the event was considered not related to treatment by the investigator