Long-Term Efficacy and Safety of Abrocitinib in Patients With Moderate-to-Severe Atopic Dermatitis Who Had Failed or Were Intolerant to Oral Non-Steroidal Immunosuppressants: Pooled Analysis of JADE Clinical Trials

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Background: Systemic non-steroidal immunosuppressants (NSISS) are frequently used to treat moderate-to-severe atopic dermatitis (AD), but their long-term use is sometimes limited due to insufficient efficacy and/or toxicities and side effects. Abrocitinib, an oral Janus kinase 1 selective inhibitor, has been shown to be efficacious and well tolerated as monotherapy or in combination with topical therapy in patients with moderate-to-severe AD. The impact of failure or intolerance to previous treatment with NSISS on the efficacy and safety of abrocitinib remains to be determined.

Objective: To assess the long-term efficacy and safety of abrocitinib in patients who had failed or were intolerant to prior oral NSISS compared with those without prior use of any systemic therapy (i.e., received prior topical treatments only) in a pooled post hoc analysis of phase 3 clinical trials.

Methods: Data were pooled for analysis from trials with abrocitinib 100 mg or 200 mg administered orally once daily as monotherapy (phase 3 JADE MONO-1 [NCT03349060] and MONO-2 [NCT03575871]; patients ≥12 years of age), or in combination with topical therapy (patients ≥18 years of age from phase 3 JADE COMPARE [NCT03720470] who were subsequently enrolled in JADE EXTEND [NCT03422822]). Patients were stratified into subgroups who had failed or were intolerant to ≥1 prior NSISS and those who were naïve to any prior systemic therapy. Efficacy was assessed at baseline through week 48 after treatment by achievement of an Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear)

and ≥2 points improvement from baseline, ≥75% improvement in Eczema Area and Severity Index (EASI-75), and ≥4 points improvement in Peak Pruritus Numerical Rating Scale (PP-NRS4). Adverse events (AEs) were assessed through week 48.

Results: Patients who had failed or were intolerant to prior NSISS had more severe disease at baseline (IGA score of 4: 100 mg, 48.7%; 200 mg, 60.2%) than those who were systemic therapy-naïve (100 mg, 28.8%; 200 mg, 32.7%). Abrocitinib-treated patients experienced rapid achievement of IGA score 0/1, and EASI-75 and PP-NRS4 response within 2 weeks of treatment (**Table**). The proportion of patients with improvements continued to increase through week 12 in a dose-dependent manner in both subgroups. These improvements were sustained through week 48: IGA score of 0/1 was achieved in 30.0% (95% CI: 19.3, 40.7) and 51.6% (39.2, 64.1) of patients with abrocitinib 100 mg and 200 mg, respectively, in the prior NSISS group, and in 45.2% (38.7, 51.8) and 55.3% (48.6, 62.1) of patients in the systemic therapy-naïve group. EASI-75 response rates were 62.0% (50.7, 73.3) with abrocitinib 100 mg, and 80.6% (70.8, 90.5) with abrocitinib 200 mg in the prior NSISS group, and 72.5% (66.7, 78.4) and 82.2% (77.0, 87.4) in the systemic therapy-naïve group. PP-NRS4 response rates were 54.9% (43.4, 66.5) with abrocitinib 100 mg, and 73.3% (62.1, 84.5) with abrocitinib 200 mg in prior NSISS group, and 50.5% (43.8, 57.2) and 67.6% (61.3, 74.0) in the systemic therapy-naïve group. The incidence of AEs was 65.2% and 71.8% with abrocitinib 100 mg and 200 mg, respectively, in the prior NSISS group, and 59.6% and 67.0% in the systemic therapy-naïve group, with no new safety signals through week 48.

Conclusion: Abrocitinib as monotherapy or in combination with topical therapy demonstrated rapid skin clearance and itch relief which was sustained through 48 weeks in patients with moderate-to-severe AD who were naïve to any prior systemic therapy, as well as those who had failed or were intolerant to prior oral NSISS. The safety profile of abrocitinib was similar in both subgroups, and consistent with the overall population. These results support the use of abrocitinib both as a systemic first-line treatment and in patients in whom oral NSISS have failed or were intolerant.

Table. Abrocitinib Efficacy in Patients Who Failed or Were Intolerant to Prior NSISS and Those Who Were Naïve to Any Prior Systemic Therapy (Full Analysis Set[a])

	Week	Failure and/or Intolerance to ≥1 Prior NSISS		Naïve to Any Prior Systemic Therapy[b]	
		Abrocitinib 100 mg ± TCS	Abrocitinib 200 mg ± TCS	Abrocitinib 100 mg ± TCS	Abrocitinib 200 mg ± TCS
IGA score of 0/1, n/N (%) (95% CI)	2	10/111 (9.0) (3.7-14.3)	12/102 (11.8) (5.5-18.0)	62/390 (15.9) (12.3-19.5)	72/374 (19.3) (15.3-23.2)
	12	29/114 (25.4) (17.4-33.4)	47/101 (46.5) (36.8-56.3)	164/390 (42.1) (37.2-47.0)	185/372 (49.7) (44.7-54.8)
	48	21/70 (30.0) (19.3-40.7)	32/62 (51.6) (39.2-64.1)	100/221 (45.2) (38.7-51.8)	114/206 (55.3) (48.6-62.1)
EASI-75, n/N (%) (95% CI)	2	19/110 (17.3) (10.2-24.3)	29/102 (28.4) (19.7-37.2)	114/391 (29.2) (24.7-33.7)	139/374 (37.2) (32.3-42.1)
	12	57/114 (50.0) (40.8-59.2)	69/101 (68.3) (59.2-77.4)	252/391 (64.5) (59.7-69.2)	279/372 (75.0) (70.6-79.4)
	48	44/71 (62.0) (50.7-73.3)	50/62 (80.6) (70.8-90.5)	161/222 (72.5) (66.7-78.4)	171/208 (82.2) (77.0-87.4)
PP-NRS4, n/N (%) (95% CI)	2	26/113 (23.0) (15.2-30.8)	51/99 (51.5) (41.7-61.4)	120/384 (31.3) (26.6-35.9)	163/367 (44.4) (39.3-49.5)
	12	49/106 (46.2) (36.7-55.7)	64/97 (66.0) (56.6-75.4)	185/361 (51.2) (46.1-56.4)	221/347 (63.7) (58.6-68.7)
	48	39/71 (54.9) (43.4-66.5)	44/60 (73.3) (62.1-84.5)	108/214 (50.5) (43.8-57.2)	140/207 (67.6) (61.3-74.0)

[a]Patients who withdrew from the study were counted as non-responders; [b]Patients received prior topical therapies only

EASI-75, ≥75% improvement in Eczema Area and Severity Index; IGA 0/1, Investigator's Global Assessment score of 0 (clear) or 1 (almost clear); NSISS, non-steroidal immunosuppressants; PP-NRS4, ≥4 points improvement in Peak Pruritus Numerical Rating Scale; TCS, topical corticosteroids.