Predictors of Maintenance of Response in Patients With Moderate-to-Severe Atopic Dermatitis After Oral Janus Kinase 1 Selective Inhibitor Abrocitinib Interruption

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[a]At the time of this study

BACKGROUND

- Abrocitinib is an oral once-daily Janus kinase 1 selective inhibitor under investigation for the treatment of atopic dermatitis (AD)
- In a phase 2b study (NCT02780167), abrocitinib 200 mg or 100 mg produced clinically meaningful proportions of Investigator's Global Assessment (IGA) responders (clear [0] or almost clear [1] with ≥2-grade improvement), ≥90% improvement in Eczema Area and Severity Index (EASI-90) responders, and ≥4-point improvement in pruritus numeric rating scale (pruritus NRS4) responders at week 12[1]

OBJECTIVE

- To ascertain whether patients with moderate-to-severe AD who achieved response with abrocitinib maintained response after abrocitinib interruption
- To determine the predictors for maintenance of response after abrocitinib interruption

METHODS

- In this double-blind, dose-ranging, phase 2b study of abrocitinib, patients aged 18-75 years with moderate-to-severe AD (defined as IGA ≥3, EASI ≥12, and percentage of body surface area [%BSA] affected ≥10) for >1 year who had inadequate response or intolerance to topical medication or needed systemic therapy to control AD were randomly assigned 1:1:1:1:1 to receive abrocitinib 200 mg, 100 mg, 30 mg, 10 mg, or placebo for 12 weeks, followed by a 4-week treatment-free period
- In this post hoc analysis, patients who achieved ≥50% improvement in EASI (EASI-50), ≥75% improvement in EASI (EASI-75), IGA, EASI-90, and/or pruritus NRS4 response at week 12 were analyzed

RESULTS

- Overall, 263 patients received abrocitinib 200 mg (N=54), 100 mg (N=55), 30 mg (N=50), 10 mg (N=49), or placebo (N=55) and were included in this analysis (**Table 1**)

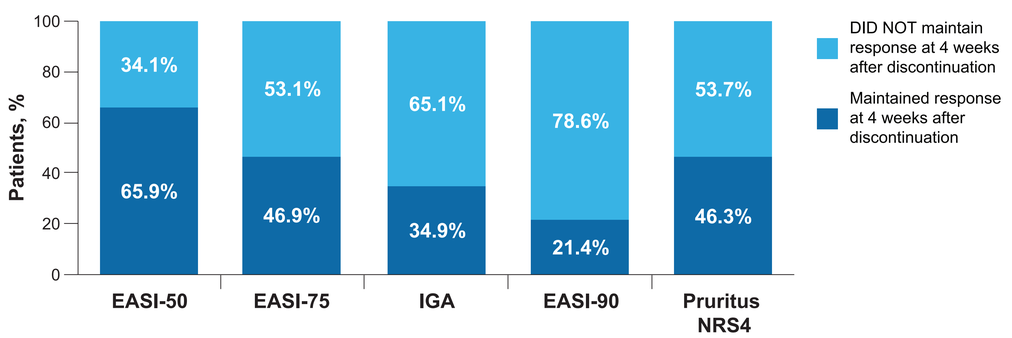
Table 1. Demographics and Baseline Disease Characteristics

	Total N=263
Age, mean (SD), y	40.6 (16.0)
Female, n (%)	140 (53.2)
Disease duration, mean (SD), y	26.5 (17.5)
IGA, n (%) Moderate (3) Severe (4)	 152 (57.8) 111 (42.2)
EASI, mean (SD)	25.4 (12.5)
Pruritus NRS, mean (SD)	7.4 (2.1)
%BSA, mean (SD)	39.7 (22.4)

%BSA, percentage of body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NRS, numeric rating scale.

- Proportions of patients who maintained response were greater when response thresholds were lower (ie, EASI-50) (**Figure 1**)
- Patients who maintained IGA response tended to be older, have lower baseline EASI score, have moderate disease at baseline (per IGA), and have lower baseline %BSA involvement (**Table 2**)
- Patients who maintained EASI response tended to have lower baseline EASI score and lower baseline %BSA involvement (**Table 2**)
- Patients who maintained pruritus NRS4 response tended to have a higher baseline pruritus NRS score (**Table 2**)
- After discontinuation, pruritus reappearance might be the most sensitive sign of relapse (**Figure 2**)
- Disease rebound was rare across all treatment arms, with relatively few patients with EASI scores >25% or >50% greater than baseline (**Table 3**)

Figure 1. Proportion of Week-12 Responders Who Maintained or Did Not Maintain Response at 4 Weeks After Discontinuation



IGA, Investigator's Global Assessment; EASI-50, ≥50% improvement in Eczema Area and Severity Index; EASI-75, ≥75% improvement in Eczema Area and Severity Index; EASI-90, ≥90% improvement in Eczema Area and Severity Index; Pruritus NRS4, ≥4-point improvement in pruritus numeric rating scale.
IGA response defined as clear (0) or almost clear (1) with ≥2-grade improvement.

Table 2. Demographics and Baseline Disease Characteristics of Week-12 Responders Who Maintained or Did Not Maintain Response at 4 Weeks After Discontinuation

	EASI-50		EASI-75		IGA		EASI-90		Pruritus NRS4	
	Maintained N=58	Did NOT Maintain N=30	Maintained N=30	Did NOT Maintain N=34	Maintained N=15	Did NOT Maintain N=28	Maintained N=9	Did NOT Maintain N=33	Maintained N=31	Did NOT Maintain N=36
Age, mean (SD), y	40.2 (17.4)	41.3 (14.8)	41.0 (17.2)	39.3 (16.5)	47.6 (16.5)	36.6 (15.7)	49.8 (16.9)	41.5 (16.9)	41.7 (15.5)	42.5 (18.1)
Female, n (%)	29 (50.0)	13 (43.3)	17 (56.7)	17 (50.0)	8 (53.3)	17 (60.7)	4 (44.4)	19 (57.6)	20 (64.5)	20 (55.6)
Disease duration, mean (SD), y	23.4 (17.5)	23.6 (18.8)	25.6 (19.3)	21.4 (16.1)	23.9 (18.8)	23.3 (18.5)	24.0 (21.7)	26.4 (19.2)	27.4 (20.6)	21.7 (15.1)
IGA, n (%) Moderate (3) Severe (4)	 41 (70.7) 17 (29.3)	 15 (50.0) 15 (50.0)	 21 (70.0) 9 (30.0)	 21 (61.8) 13 (38.2)	 13 (86.7) 2 (13.3)	 16 (57.1) 12 (42.9)	 6 (66.7) 3 (33.3)	 21 (63.6) 12 (36.4)	 19 (61.3) 12 (38.7)	 23 (63.9) 13 (36.1)
EASI, mean (SD)	22.0 (11.1)	27.2 (11.5)	19.1 (6.8)	24.7 (10.8)	18.2 (7.1)	22.4 (9.1)	20.0 (8.4)	22.9 (19.2)	21.8 (9.5)	22.7 (9.5)
Pruritus NRS, mean (SD)	6.9 (2.4)	6.7 (2.3)	7.0 (2.3)	6.6 (2.6)	6.7 (2.7)	7.3 (2.1)	6.8 (2.1)	7.2 (2.4)	8.4 (1.2)	7.5 (1.7)
%BSA, mean (SD)	33.8 (21.0)	39.2 (22.0)	29.2 (18.8)	35.8 (18.6)	28.4 (18.1)	34.1 (20.0)	29.7 (19.4)	35.0 (19.6)	35.1 (21.2)	35.7 (19.7)
EASI-50 response at week 2, n (%)	38 (65.5)	15 (50.0)	21 (70.0)	24 (70.6)	11 (73.3)	22 (78.6)	8 (88.9)	24 (72.7)	18 (58.1)	20 (55.6)

%BSA, percentage of body surface area; IGA, Investigator's Global Assessment; EASI, Eczema Area and Severity Index; EASI-50, ≥50% improvement in Eczema Area and Severity Index; EASI-75, ≥75% improvement in Eczema Area and Severity Index; EASI-90, ≥90% improvement in Eczema Area and Severity Index; Pruritus NRS4, ≥4-point improvement in pruritus numeric rating scale.
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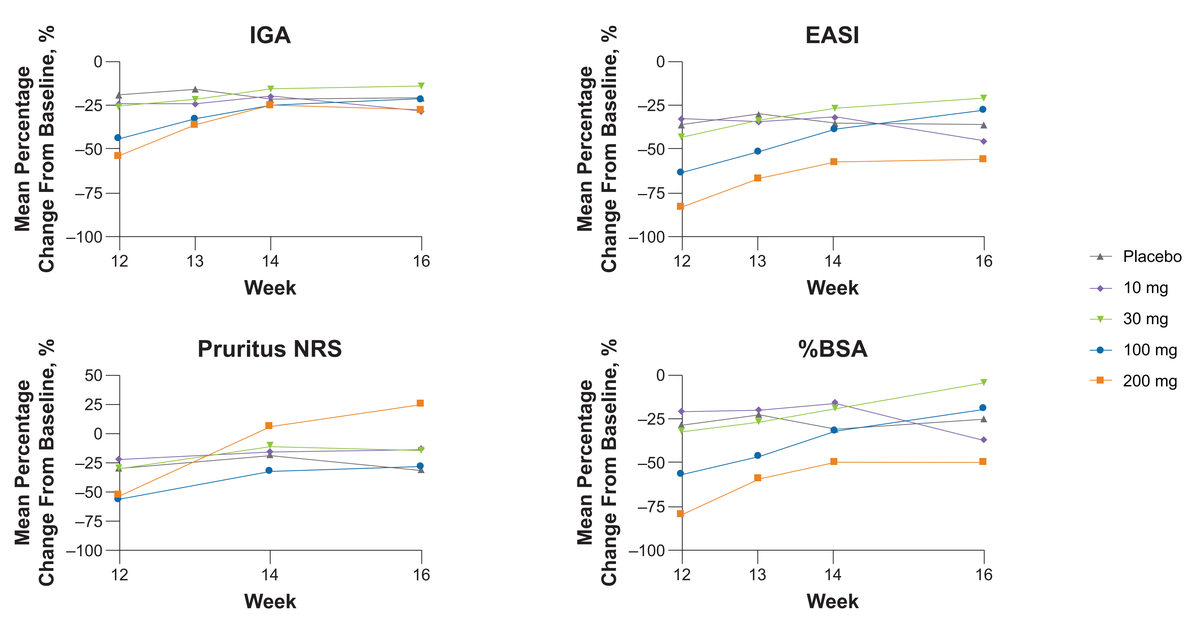
Figure 2. Outcomes Over the 4 Weeks After Discontinuation



%BSA, percentage of body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NRS, numeric rating scale.

Table 3. Patients With EASI Greater Than Baseline at 4 Weeks After Discontinuation

n (%)	Placebo	Abrocitinib 10 mg	Abrocitinib 30 mg	Abrocitinib 100 mg	Abrocitinib 200 mg
EASI >25% greater than baseline	2 (7.1)	3 (11.5)	4 (14.8)	7 (19.4)	1 (2.6)
EASI >50% greater than baseline	1 (3.6)	0	1 (3.7)	2 (5.6)	0

EASI, Eczema Area and Severity Index.

CONCLUSIONS

- The proportion of patients who lost response after 4 weeks was inversely related to the rigor of the endpoint; less than one-quarter of patients maintained EASI-90 or IGA response
- Patients who maintained response tended to have less severe disease at baseline
- Pruritus seems to be the most sensitive outcome for disease recurrence
- Disease rebounds (ie, EASI that is >50% greater than baseline) are infrequently observed

REFERENCE

1. Gooderham MJ et al. *JAMA Dermatol.* Published online ahead of print October 2, 2019. doi: 10.1001/jamadermatol.2019.2855.

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