Supplementary Information

Early itch response with abrocitinib is associated with later efficacy outcomes in patients with moderate-to-severe atopic dermatitis: subgroup analysis of the randomized phase III JADE COMPARE trial

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Appendix S1

Supporting Methods

In order to be more rigorous about the onset of relief of severity of pruritus, a step-down approach with the PP-NRS4 endpoint from week 2 to earlier time points will be utilized as an additional family of hypothesis tests once statistical significance is demonstrated at week 2. Rejection of each hypothesis of no difference in PP-NRS4 at week 2 will enable further assessing at earlier time points. Specifically, further hypotheses of no difference in PP-NRS4 will be assessed along the following four sequences:

- If hypothesis of no difference in PP-NRS4 at week 2 between abrocitinib 200 mg QD and placebo is rejected in sequence A, compare abrocitinib 200 mg QD vs placebo at day 15, day 14, day 13, day 12, … day 2, in that order. Any hypotheses after the last time point (or day) for which the comparison of abrocitinib 200 mg QD vs placebo is significant will not be considered statistically significant.

- If hypothesis of no difference in PP-NRS4 at week 2 between abrocitinib 100 mg QD and placebo is rejected in sequence A, compare abrocitinib 100 mg QD vs placebo at day 15, day 14, day 13, day 12, … day 2, in that order. In this sequence, any hypotheses after the last time point (or day) for which both comparisons (200 mg QD vs placebo and 100 mg QD vs placebo) are significant will not be considered statistically significant.

- If hypothesis of no difference in PP-NRS4 at week 2 between abrocitinib 200 mg QD and dupilumab is rejected in sequence A, compare abrocitinib 200 mg QD vs dupilumab at day 15, day 14, day 13, day 12, … day 2, in that order. For this sequence, any hypotheses after the last time point (or day) for which both comparisons (abrocitinib 200 mg QD vs placebo and abrocitinib 200 mg QD vs dupilumab) are significant will not be considered statistically significant.

- If hypothesis of no difference in PP-NRS4 at week 2 between abrocitinib 100 mg QD and dupilumab is rejected in sequence A, compare abrocitinib 100 mg QD vs dupilumab at day 15, day 14, day 13, day 12, …, day 2, in that order. For this sequence, any hypotheses after the last time point (or day) for which all four comparisons (abrocitinib 200 mg QD vs placebo, abrocitinib 200 mg QD vs dupilumab, abrocitinib 100 mg QD vs placebo and abrocitinib 100 mg QD vs dupilumab) are significant will not be considered significant.

All hypotheses in each of the four sequences will be assessed at the 5% level of significance. Although this testing procedure will not protect the type-I error for the family of all possible comparisons, it will provide type-I error protection for the family of PP-NRS4 time points within each treatment group and treatment groups within each time point.

Table S1. Baseline demographics and disease characteristics

	Placebo (*n* = 131)	**Abrocitinib 100 mg QD (*n* = 238)**	**Abrocitinib 200 mg QD (*n* = 226)**	**Dupilumab 300 mg Q2W (*n* = 242)**
Age, mean (SD), y	37.4 (15.2)	37.3 (14.8)	38.8 (14.5)	37.1 (14.6)
Female, *n* (%)	54 (41.2)	118 (49.6)	122 (54.0)	134 (55.4)
Duration of AD, mean (SD), y	21.4 (14.4)	22.7 (16.3)	23.4 (15.6)	22.8 (14.8)
IGA[a], n (%)				
Moderate (IGA score = 3)	88 (67.2)	153 (64.3)	138 (61.1)	162 (66.9)
Severe (IGA score = 4)	43 (32.8)	85 (35.7)	88 (38.9)	80 (33.1)
EASI[b], mean (SD)	31.0 (12.6)	30.3 (13.5)	32.1 (13.1)	30.4 (12.0)
DLQI[c], mean (SD)	15.2 (6.0)	15.5 (6.4)	16.3 (6.6)	15.6 (6.6)
PP-NRS[d], mean (SD)	7.1 (1.8)	7.1 (1.7)	7.6 (1.5)	7.3 (1.7)

DLQI Dermatology Life Quality Index, *EASI* Eczema Area and Severity Index, *IGA* Investigator's Global Assessment, *PP-NRS* Peak Pruritus Numerical Rating Scale, *Q2W* once every 2 weeks, *QD* once daily

[a]IGA is measured on a 5-point scale which ranges from clear (0) to severe (4); [b]EASI ranges from 0 to 72, with higher scores indicating more severe disease; [c]DLQI ranges from 0 to 30, with higher scores representing worst health-related quality of life; [d]PP-NRS scores represent maximum itch severity in the previous 24 hours and range from 0 to 10, with higher scores representing more severe itch.

Table S2. Chi-squared test cross tabulation of week 2 PP-NRS4 subgroup vs week 12 IGA score and EASI percentage change from baseline categories

Treatment	Interaction	Chi-square value	*P*-value
Placebo	Week 2 PP-NRS4 × Week 12 IGA	8.662	0.070
	Week 2 PP-NRS4 × Week 12 EASI	0.565	0.904
Abrocitinib 100 mg QD	Week 2 PP-NRS4 × Week 12 IGA	14.419	**0.006**
	Week 2 PP-NRS4 × Week 12 EASI	10.473	**0.015**
Abrocitinib 200 mg QD	Week 2 PP-NRS4 × Week 12 IGA	14.655	**0.006**
	Week 2 PP-NRS4 × Week 12 EASI	11.238	**0.011**
Dupilumab 300 mg Q2W	Week 2 PP-NRS4 × Week 12 IGA	0.993	0.911
	Week 2 PP-NRS4 × Week 12 EASI	2.295	0.513

EASI Eczema Area and Severity Index, *IGA* Investigator's Global Assessment, *PP-NRS4* ≥ 4-point improvement from baseline in Peak Pruritus Numerical Rating Scale, *QD* once daily, *Q2W* once every 2 weeks

Bolded nominal *p*-values represent statistically significant associations ($p \leq 0.05$).

EASI percentage change from baseline category (< 50%, ≥ 50% to < 75%, ≥ 75% to < 90%, ≥ 90% improvement from baseline)

Table S3. Predictive value of week 2 change from baseline in PP-NRS for week 12 IGA 0/1, EASI-75, EASI-90, and DLQI 0/1 responses

Treatment	Week 12 response	Predictability[a]
Placebo	IGA 0/1	52.0%
	EASI-75	51.6%
	EASI-90	53.9%
	DLQI 0/1	77.4%
Abrocitinib 100 mg QD	IGA 0/1	68.8%
	EASI-75	60.2%
	EASI-90	66.0%
	DLQI 0/1	66.3%
Abrocitinib 200 mg QD	IGA 0/1	66.8%
	EASI-75	65.7%
	EASI-90	66.3%
	DLQI 0/1	69.4%
Dupilumab 300 mg Q2W	IGA 0/1	52.1%
	EASI-75	60.0%
	EASI-90	53.9%
	DLQI 0/1	58.0%

DLQI 0/1 Dermatology Life Quality Index of 0 or 1, *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-NRS* Peak Pruritus Numerical Rating Scale, *QD* once daily, *Q2W* once every 2 weeks

[a]Predictability measured by area under the receiver operating characteristic curve.