Rapid and Sustained Improvement in Skin Pain With Abrocitinib in Adult and Adolescent Patients With Moderate-to-Severe Atopic Dermatitis

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Background: Skin pain is a clinically meaningful yet poorly understood symptom in atopic dermatitis (AD), and is associated with itch, sleep difficulties, and quality of life impairment. The efficacy and safety of abrocitinib, an oral Janus kinase 1 selective inhibitor, has been established in patients with moderate-to-severe AD in phase 2b and phase 3 clinical trials.

Objective: To examine the efficacy of abrocitinib on skin pain in patients with moderate-to-severe AD in a post hoc analysis of 5 studies from the abrocitinib JADE clinical program.

Methods: Data were analyzed from trials with abrocitinib 200 mg or 100 mg administered as monotherapy (pooled phase 2b [NCT02780167], and phase 3 JADE MONO-1 [NCT03349060] and MONO-2 [NCT03575871]; patients ≥12 years of age), or in combination with topical therapy (phase 3 JADE COMPARE [NCT03720470; patients ≥18 years of age] and JADE TEEN [NCT03796676; patients 12-17 years of age]). Patients received abrocitinib 200 mg or abrocitinib 100 mg orally once daily or placebo. The JADE COMPARE study also included an active-control arm (dupilumab 300 mg administered subcutaneously every other week). Patients rated their skin pain over the past 24 hours from 0 (no symptoms) to 10 (extreme symptoms) using the Pruritus and Symptom Assessment for Atopic Dermatitis (PSAAD) instrument. Least squares mean (LSM) change from baseline in the skin pain score (PSAAD item #2) was recorded over the duration of the studies.

Results: At baseline, mean PSAAD item #2 score was 5.6 (SD, 2.5) in patients in the pooled monotherapy trials, 5.6 (2.6) in JADE COMPARE, and 5.0 (2.6) in the JADE TEEN trial (**Table**). Abrocitinib improved skin pain scores as early as week 1 in a dose-dependent manner across

all studies. At week 1, LSM change (95% CI) from baseline in pain score was greater in patients receiving abrocitinib 200 mg and 100 mg versus placebo (monotherapy: -1.5 [-1.7 to -1.4] and -1.1 [-1.2 to -0.9] vs -0.1 [-0.3 to 0.2]; COMPARE: -1.7 [-1.9 to -1.5] and -1.3 [-1.6 to -1.1] vs -0.8 [-1.2 to -0.5]]; TEEN: -1.3 [-1.6 to -1.0] and -1.1 [-1.4 to -0.8] vs -0.4 [-0.7 to -0.1]). This improvement was sustained through week 12 of treatment (monotherapy: -3.5 [-3.8 to -3.2] and -2.6 [-2.9 to -2.4] vs -1.0 [-1.4 to -0.6]; COMPARE: -4.0 [-4.3 to -3.7] and -3.1 [-3.4 to -2.8] vs -1.8 [-2.2 to -1.4]; TEEN: -3.6 [-4.1 to -3.2] and -3.0 [-3.5 to -2.6] vs -2.1 [-2.6 to -1.7]).

Conclusion: Abrocitinib as monotherapy or in combination with topical therapy provided rapid and sustained improvement in skin pain in adult and adolescent patients with moderate-to-severe AD.

Table. Baseline Characteristics of Patients in JADE Clinical Studies (full analysis set)

	Pooled Monotherapy[a] N=942	**JADE COMPARE N=837**	**JADE TEEN N=285**
Age, y, mean (SD) or median (IQR)	35.0 (15.9)	37.7 (14.7)	15.0 (IQR: 13.0-17.0)
Age <18 y, n (%)	124 (13.2)	0	284 (99.6)
Duration of disease, y, mean (SD)	23.0 (15.5)	22.7 (15.4)	10.0 (5.2)
EASI score, mean (SD)	28.8 (12.7)	30.9 (12.8)	29.9 (12.5)
PP-NRS total score, mean (SD)	7.0 (1.9)	7.3 (1.7)	7.0 (1.8)
DLQI total score, mean (SD)	14.6 (6.9)	15.7 (6.6)	NA
CDLQI total score, mean (SD)	12.7 (6.0)	NA	14.0 (6.6)
PSAAD Item #2 score, mean (SD)	5.6 (2.5)[b]	5.6 (2.6)[c]	5.0 (2.6)[d]

CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IQR, interquartile range; NA, not applicable; PP-NRS, Peak Pruritus Numerical Rating Scale; PSADD, Pruritus and Symptom Assessment for Atopic Dermatitis; SD, standard deviation.

[a]Pooled monotherapy population includes patients from the phase 2b, and phase 3 JADE MONO-1, and JADE MONO-2 trials; [b]N=802; [c]N=780; [d]N=254.

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