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Long-Term Efficacy of Abrocitinib in Patients With Moderate-to-Severe Atopic Dermatitis Who Had Prior Exposure to Systemic Therapies: A Post Hoc Analysis of JADE EXTEND

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INTRODUCTION

- Patients with moderate-to-severe atopic dermatitis (AD) with inadequate response to topical therapies may require treatment with systemic therapies[1]
- Abrocitinib, an oral, once-daily, Janus kinase 1-selective inhibitor is approved for the treatment of adults and adolescents with moderate-to-severe AD[2-4]
  - Prior exposure to systemic therapies impacts the efficacy of subsequent systemic treatment in patients with other chronic inflammatory conditions such as psoriasis[5]
  - Prior use of oral systemic or biologic therapies did not seem to impact the efficacy of abrocitinib in patients with moderate-to-severe AD treated over 48 weeks[5]

OBJECTIVE

- To evaluate the efficacy of abrocitinib up to 112 weeks of treatment in patients with moderate-to-severe AD with or without prior exposure to systemic therapies

METHODS

Study Design and Patients

- Data were included from adults and adolescents randomly assigned to abrocitinib (200 mg or 100 mg) or placebo in the phase 2a trial JADE MOA (NCT03915496) and phase 3 JADE MONO-1 (NCT03349060), JADE MONO-2 (NCT03575871), JADE COMPARE (NCT03720470), JADE TEEN (NCT03796676), and JADE DARE (NCT04345367) trials and subsequently enrolled in the ongoing extension study, JADE EXTEND (NCT03422822; data cutoff: September 5, 2022) (**Supplementary Figure S1,** accessed via QR code)
- Patients may have received their first abrocitinib dose in JADE EXTEND if they had placebo in the qualifying phase 3 trials
- For this analysis, patients were classified by prior exposure to oral corticosteroids, methotrexate (MTX, administered via all routes), systemic cyclosporine A (CsA), biologics (benralizumab, dupilumab, etanercept, monoclonal antibody OX40, omalizumab, risankizumab, secukinumab and tralokinumab), ≥2 systemic therapies, or no systemic therapies (systemic therapy naive) before enrollment in the qualifying trial

Assessments

- This analysis assessed the proportion of patients achieving the following endpoints at Weeks 2 through 112 of abrocitinib treatment, stratified by type of prior medication exposure before enrollment in the qualifying study:
  - ≥50%, ≥75%, and ≥90% improvement from baseline in Eczema Area and Severity Index (EASI-50, EASI-75, and EASI-90, respectively)
  - Investigator's Global Assessment score of 0 (clear) or 1 (almost clear) with ≥2-point improvement from baseline (IGA 0/1)
  - ≥4-point improvement from baseline in Peak Pruritus Numerical Rating Scale score (PP-NRS4; used with permission from Regeneron Pharmaceuticals, Inc., and Sanofi)
  - PP-NRS score of 0 or 1 with ≥2-point reduction from baseline (PP-NRS 0/1; ie, itch-free state)

Statistical Analysis

- Data are reported as observed values calculated up to Week 112 of abrocitinib treatment, with any missing data excluded from the analysis
  - Baseline was defined as the baseline visit from the relevant qualifying parent trial, and Day 1 as the first day of receiving abrocitinib
  - The baseline value of the efficacy assessments was defined as the last predose assessment in the qualifying parent trial

RESULTS

Patients

- A total of 1930 patients were included in this analysis, of whom 1054 patients were not previously treated with systemic therapy (ie, systemic therapy naive) and 876 had prior exposure to systemic therapy (oral corticosteroids [n=446)], MTX [n=21], systemic CsA [n=213], biologics [n=70], and ≥2 systemic therapies [n=126]) (**Table 1**)
  - Baseline demographics were generally comparable across treatment groups when stratified according to prior medication (**Table 1**)

Table 1. Patient Demographics by Prior Medication

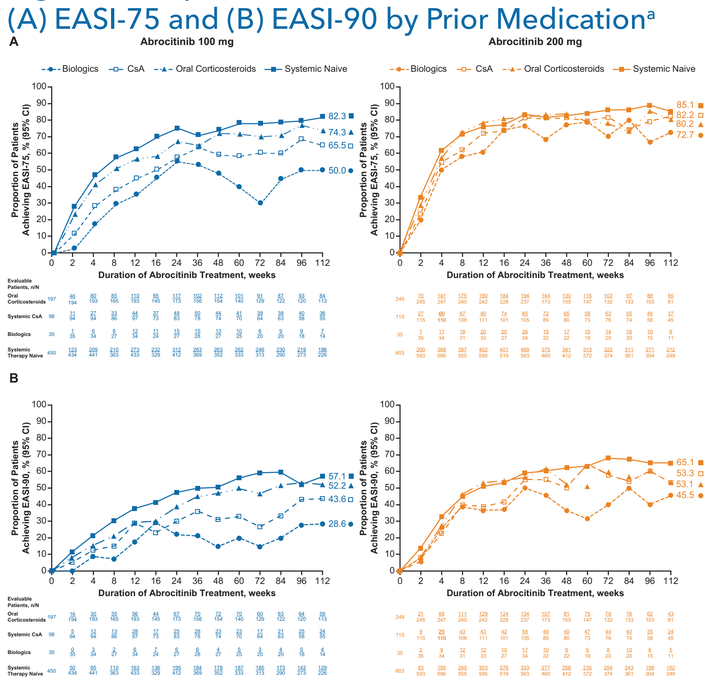
	Systemic Therapy Naive		Oral Corticosteroids		MTX		Systemic CsA		Biologics		≥2 Systemic Therapies	
	Abrocitinib 100 mg n=451	Abrocitinib 200 mg n=603	Abrocitinib 100 mg n=197	Abrocitinib 200 mg n=249	Abrocitinib 100 mg n=10	Abrocitinib 200 mg n=11	Abrocitinib 100 mg n=98	Abrocitinib 200 mg n=115	Abrocitinib 100 mg n=35	Abrocitinib 200 mg n=35	Abrocitinib 100 mg n=60	Abrocitinib 200 mg n=66
Age, mean ± SD, y	30.1 ± 15.9	32.6 ± 16.3	34.1 ± 14.5	34.8 ± 15.4	31.9 ± 14.5	28.9 ± 14.3	32.6 ± 14.7	32.9 ± 14.4	37.8 ± 13.9	38.2 ± 15.6	32.5 ± 12.3	35.4 ± 16.6
Sex, n (%)												
Male	241 (53.4)	309 (51.2)	115 (58.4)	151 (60.6)	3 (30.0)	6 (54.5)	60 (61.2)	67 (58.3)	27 (77.1)	19 (54.3)	35 (58.3)	40 (60.6)
Female	210 (46.6)	294 (48.8)	82 (41.6)	98 (39.4)	7 (70.0)	5 (45.5)	38 (38.8)	48 (41.7)	8 (22.9)	16 (45.7)	25 (41.7)	26 (39.4)
Race, n (%)												
Asian	102 (22.6)	133 (22.1)	53 (26.9)	57 (22.9)	1 (10.0)	4 (36.4)	23 (23.5)	38 (33.0)	8 (22.9)	12 (34.3)	14 (23.3)	21 (31.8)
Black or African American	31 (6.9)	34 (5.6)	3 (1.5)	9 (3.6)	2 (20.0)	0	1 (1.0)	0	4 (11.4)	2 (5.7)	2 (3.3)	2 (3.0)
White	314 (69.6)	414 (68.7)	136 (69.0)	173 (69.5)	7 (70.0)	5 (45.5)	74 (75.5)	76 (66.1)	22 (62.9)	21 (60.0)	44 (73.3)	42 (63.6)
Other[a]	4 (0.9)	22 (3.7)	5 (2.5)	10 (4.0)	0	2 (18.2)	0	1 (0.9)	1 (2.9)	0	0	1 (1.5)

CsA, cyclosporine A; MTX, methotrexate; y, years.
[a]Other includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, multiracial, and not reported.

Efficacy Responses up to Week 112 of Abrocitinib Treatment

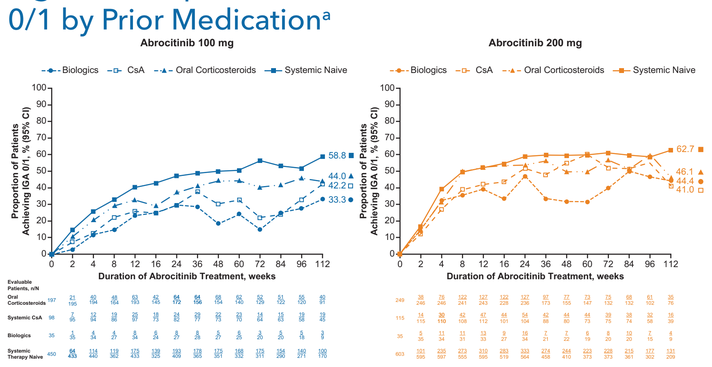
- Efficacy responses were sustained through 112 weeks of continuous treatment with abrocitinib 200 mg and 100 mg across all subgroups of prior treatment exposure (**Figures 1-3**; **Supplementary Figure S2**; **Tables S1-S2,** accessed via QR code); similar observations were previously reported up to Week 48 of abrocitinib treatment[5]
  - Notably, at Week 112 of abrocitinib treatment 43.6%-53.3% of patients achieved a stringent response of EASI-90, 27.8%-39.0% of patients achieved an itch-free state (ie, PP-NRS 0/1) with both abrocitinib doses in subgroups of prior exposure to oral corticosteroids and systemic CsA (**Figures 1 and 3**)
  - Similar trends were observed for EASI-90 and itch-free responses in patients with prior exposure to MTX and ≥2 systemic therapies; however, the sample size for these subgroups was small (**Supplementary Tables S1-S2,** accessed via QR code)
  - In patients who received prior biologic therapy, 4/14 patients (28.6%) in the abrocitinib 100 mg and 5/11 patients (45.5%) in the abrocitinib 200 mg treatments arms achieved EASI-90; 3/9 patients (33.3%) in each treatment arm achieved an itch-free state (**Figures 1 and 3**)
- The pattern of response over time was similar across different subgroups of prior treatment exposure
  - Similar to previously published Week 12 and Week 48 responses,[5] Week 112 efficacy responses with abrocitinib tended to be lower in patients with prior exposure to oral corticosteroids, systemic CsA, biologics, or ≥2 systemic therapies compared with those who were systemic therapy naive, except in the MTX subgroup, likely due to the small sample size (**Figures 1-3**; **Supplementary Tables S1-S2,** accessed via QR code)
  - These observations were more pronounced for high-threshold endpoints (EASI-90, IGA 0/1 and PP-NRS 0/1) and in patients treated with abrocitinib 100 mg versus 200 mg (**Figures 1-3**; **Supplementary Tables S1-S2,** accessed via QR code)

Figure 1. Proportions of Patients Who Achieved (A) EASI-75 and (B) EASI-90 by Prior Medication[a]



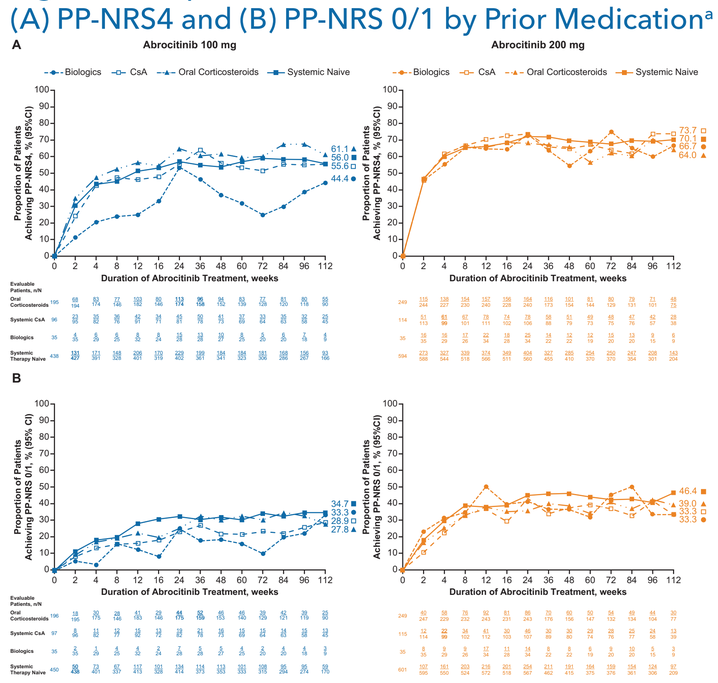
CsA, cyclosporine A; EASI-75/-90, ≥75/90% improvement from baseline in Eczema Area and Severity Index.
[a]Confidence intervals (not shown) of data points for efficacy assessments were large due to small sample sizes and generally overlapped across prior treatment subgroups; small sample sizes in some subgroups limited the analysis.

Figure 2. Proportions of Patients Who Achieved IGA 0/1 by Prior Medication[a]



CsA, cyclosporine A; IGA 0/1, Investigator's Global Assessment score of 0 (clear) or 1 (almost clear) with ≥2-point improvement from baseline.
[a]Confidence intervals (not shown) of data points for efficacy assessments were large due to small sample sizes and generally overlapped across prior treatment subgroups; small sample sizes in some subgroups limited the analysis.

Figure 3. Proportions of Patients Who Achieved (A) PP-NRS4 and (B) PP-NRS 0/1 by Prior Medication[a]



CsA, cyclosporine A; PP-NRS4, ≥4-point improvement from baseline in Peak Pruritus Numerical Rating Scale score; PP-NRS 0/1, Peak Pruritus Numerical Rating Scale score of 0 or 1 with ≥2-point reduction from baseline (itch-free state).
[a]Confidence intervals (not shown) of data points for efficacy assessments were large due to small sample sizes and generally overlapped across prior treatment subgroups; small sample sizes in some subgroups limited the analysis.

CONCLUSIONS

- Previous exposure to systemic therapies had a modest impact on long-term abrocitinib response
- For patients with previous exposure to systemic therapies, abrocitinib 200 mg dosing more consistently provided better skin clearance and pruritus control than abrocitinib 100 mg
- It is unclear from this analysis whether patients whose symptoms failed to respond to treatment with biologics reflect more severe disease or a more unique or broader endotype
- Importantly, abrocitinib at either dose provided sustained long-term efficacy for >2 years in patients with moderate-to-severe AD, regardless of prior exposure to systemic therapies
- This analysis is limited by small sample sizes in some subgroups

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ACKNOWLEDGMENTS

Editorial/medical writing support under the guidance of the authors was provided by Chantell Hayward, PharmD, and Megan K. Elder, PhD, at ApotheCom, San Francisco, CA, USA, and was funded by Pfizer Inc., New York, NY, USA, in accordance with Good Publication Practice (GPP 2022) guidelines (*Ann Intern Med.* 2022;10.7326/M22-1460).
This study was funded by Pfizer Inc.

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Presented at the 33rd Annual European Academy of Dermatology and Venereology (EADV) Congress; September 25-28, 2024; Amsterdam, the Netherlands