Treatment Response Trajectories and Safety Outcomes of Oral Janus Kinase Inhibitors in Older Adults with Moderate-to-Severe Atopic Dermatitis: Findings from a Real-World Prospective Cohort

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ABSTRACT Managing moderate-to-severe AD in older adults is complicated by age-related physiological decline, coexisting illnesses, and shifts in immune function. Oral JAK inhibitor use has grown in this population, yet controlled trial data on their sustained effectiveness and safety in the elderly remain scarce. This was a prospective cohort study of elderly patients with moderate-to-severe AD treated with abrocitinib or upadacitinib in routine clinical practice. In total, 90 individuals entered the cohort, of whom 80 remained through the full 36-week observation period and were retained for the final analysis. Severity indices, quality-of-life measures, and lab values were tracked across the treatment course, and linear mixed-effects modeling was applied to examine how baseline factors related to changes in EASI. Clinical outcomes improved and remained stable during follow-up in both treatment groups. Most EASI responses were achieved within the first 16 weeks of treatment, followed by a relatively stable response through Week 36. Both treatments demonstrated rapid early improvement; however, the difference between the two drugs decreased at the final visit. Sustained improvements in SCORAD and DLQI scores were observed over the long-term follow-up. A shorter disease history, upadacitinib treatment, and a higher BMI were each linked to greater gains in EASI scores. Safety profiles were generally acceptable, although more cases of herpes zoster were reported in the upadacitinib group. Across the 36-week study period, both agents produced durable clinical benefit with manageable safety in this older AD population. Upadacitinib achieved earlier gains than abrocitinib, though this gap narrowed as follow-up continued. These real-world data support considering oral JAK inhibitors for extended use in elderly patients with moderate-to-severe disease.

INDEX TERMS atopic dermatitis; JAK inhibitors; upadacitinib; abrocitinib; elderly patients

I. INTRODUCTION

THE study does not cover older people. Atopic dermatitis (AD) is a chronic inflammatory skin disease, which is accompanied by recurrent eczematous lesions, severe itching, and remitting/recurring clinical course [1]–[3]. It has been spreading across the world in recent years. Its onset and progression involve an interplay of skin barrier breakdown, dysregulated immune signaling, hereditary predisposition, and exposure-related triggers [4]. The disease course is sometimes long, inflammatory activity is often continuing in elderly patients, there may be a multitude of comorbid conditions and treatment may be more complicated. Disease presentation and functional status differ in older adults, reflecting skin aging, a weakening immune response, and coexisting chronic illnesses [5].

Treating AD in older patients is further complicated by common concurrent conditions such as high blood pressure, diabetes, kidney impairment, and cardiovascular disease [6]. Further, there may be aging-related physiological changes in hepatic and renal function that impact drug metabolism and predispose to the occurrence of adverse events caused by treatment. Systemic immunosuppression such as the use

of corticosteroids, cyclosporine and methotrexate are still good treatments for AD, though the older patients may be more susceptible to side effects, infection and drug interactions, and intolerance when used for a longer period [7]. This highlights the need for therapies capable of sustaining disease control over time without meaningfully raising the risk of harm in this age group. Advances in targeted therapy have expanded treatment options for moderate-to-severe disease. Dupilumab, which blocks IL-4/IL-13 signaling, has meaningfully improved outcomes and is now a standard systemic option [4], [8], [9]. However, the specific advantages discussed for dupilumab vary among patients and some may require alternative therapies because they have inadequate response to the drug or side effects, such as conjunctivitis [10]. These clinical challenges highlight the need to improve the availability of options for treatment and care of the many forms and needs of AD. Oral JAK inhibitors such as upadacitinib and abrocitinib act by blocking JAK-mediated cytokine signaling, dampening inflammatory cascades driven by IL-4, IL-13, and IL-31 [11], [12]. Trial evidence shows these drugs rapidly reduce disease severity and itch, though known safety signals include infection risk, lipid changes, and transaminase elevation [13], [14]. In older adults—often immunosenescent and burdened with comorbidities—careful real-world assessment of benefit and risk becomes especially important [15].

Although oral JAK inhibitors are increasingly incorporated into routine management of AD, prospective real-world evidence describing their long-term treatment response and safety characteristics in elderly patients remains insufficient. Treatment evaluation in older patients requires additional consideration because aging is often accompanied by immune senescence and multiple chronic comorbidities, which may influence both therapeutic response and treatment-related risks. In this prospective cohort study, 90 elderly patients with moderate-to-severe AD receiving upadacitinib or abrocitinib were observed for 36 weeks. We aimed to characterize treatment response patterns, identify factors associated with clinical improvement, and evaluate the safety profiles of these oral JAK inhibitors in a real-world setting.

II. METHOD

A. ENROLLMENT

This prospective, real-world observational cohort was conducted between September 2024 and September 2025 at the Affiliated Hospital of Xuzhou Medical University. Consecutive elderly patients diagnosed with moderate-to-severe AD who were initiating oral JAK inhibitor therapy were enrolled. Of the 90 participants at baseline, 44 were assigned to Group A (abrocitinib) and 46 to Group B (upadacitinib). During the period of 36 weeks, ten participants (four from Group A, six from Group B) withdrew before the Week 12 assessment, mainly citing financial or personal reasons. These withdrawals were not thought to be treatment response-related. The safety and efficacy analysis of the group combined is consequently not representative of the group of patients who received CQRS. There were 80 patients (40 patients in each treatment group), who completed the relapse evaluation and were used for the final analysis.

B. STUDY POPULATION

Inclusion required a diagnosis of moderate-to-severe AD warranting JAK inhibitor treatment, age of 65 years or older, and both willingness and capacity to attend scheduled follow-up visits. Patients with factors which may compromise treatment safety and/or assessment of the study were excluded, which included contraindications for JAK inhibitors, active infection, severe organ dysfunction, malignancy or being unable to complete baseline disease assessment. Participants found to be inappropriate for continued participation due to poor response, significant adverse events, interfering medical events, protocol deviations, inadequate adherence to protocol, personal reasons, or investigator assessment during follow-up were considered to have experienced withdrawal during follow-up.

C. INTERVENTIONS

Oral JAK inhibitors were used during the study and topical corticosteroids were offered to patients with severe localized lesions. Other systemic anti-pruritic, immunosuppressive and injection therapies were not used. Products details from Group A were given as a single 100 mg massed every day, versus 15 mg of upadacitinib each day in Group B. No dose was adjusted in Week 0–16 period. Following this, any patient with EASI50 response and clinical stability received a consideration of switching to alternate-day dosing with continued efficacy and safety monitoring. Patients who responded with EASI50 and were clinically stable were evaluated for changing to an alternate-day dosing regimen after this duration with regard to its efficacy and safety. A flare was defined as an EASI score that was $\geq 50\%$ higher than at the previous clinic visit or if the EASI score was back to the level of disease before reduction.

D. OUTCOME MEASURES AND FOLLOW-UP

Treatment efficacy was assessed throughout follow-up, with EASI50, EASI75, and EASI90 response rates specifically compared at Weeks 16 and 36. Changes in disease severity, quality of life, and longitudinal EASI scores were recorded during the observation period. Patients attended clinical assessments at 4-week intervals, whereas laboratory examinations were conducted at baseline and subsequently every 12 weeks. Following treatment discontinuation, patients were monitored at Weeks 4 and 12 to identify possible relapse. Relapse was considered when AD lesions reappeared or deteriorated and additional therapeutic intervention was required.

F. DATA COLLECTION

The collected information included demographic data, disease severity assessments, relevant comorbid conditions,

laboratory measurements, and adverse events during treatment. The severity of adverse events was graded according to CTCAE v5.0

E. STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS version 29.0 (IBM Corp., Armonk, NY, USA). Variables were described according to their distribution and data type. Continuous data were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), while categorical data were summarized as frequencies and percentages. The McNemar test was applied to evaluate longitudinal changes in EASI50, EASI75, and EASI90 response rates within each group. Comparisons between groups were conducted using the chi-square test or Fisher's exact test when appropriate. Longitudinal variations in EASI scores were assessed using linear mixed-effects models. Safety outcomes, including adverse events and laboratory abnormalities, were analyzed descriptively. Statistical significance was defined as a two-sided P value < 0.05.

G. ETHICAL CONSIDERATIONS

Ethical approval was granted by the Xuzhou Medical University Ethics Committee, and written informed consent was obtained from every participant. As the treatment methods followed routine clinical care and no additional interventions were introduced during the study, it was considered a minimal-risk study and complied with relevant ethical requirements.

III. RESULTS AND DISCUSSION

A. BASELINE CHARACTERISTICS

After the follow-up, 40 patients were included in the abrocitinib group and 40 in the upadacitinib group for analysis. There were 70.0% males in the study population. Baseline age, sex distribution, disease duration, BMI, comorbidity burden, and severity indices (EASI, SCORAD, DLQI) did not differ meaningfully between the two treatment arms (Table S1).

TABLE S1. BASELINE CHARACTERISTICS OF THE STUDY POPULATION

Variable	Abrocitinib ($n = 40$)	Upadacitinib ($n = 40$)	Total ($n = 80$)
Sex			
Male	27 (67.5%)	29 (72.5%)	56 (70.0%)
Female	13 (32.5%)	11 (27.5%)	24 (30.0%)
Age (years)	71.00 (5.50)	70.00 (5.75)	70.00 (5.75)
Disease duration (years)	8.63 ± 33.26	8.06 ± 30.12	8.34 ± 31.36
BMI (kg/m^2)	25.45 ± 10.81	25.51 ± 16.02	25.48 ± 13.25
Cardiovascular disease	26 (65.0%)	24 (60.0%)	50 (62.5%)
Diabetes mellitus	12 (30.0%)	9 (22.5%)	21 (26.3%)
EASI score	31.62 ± 35.06	33.01 ± 42.55	31.95 ± 38.43
SCORAD score	62.40 ± 100.29	65.35 ± 267.77	63.87 ± 183.92
DLQI score	20.55 ± 7.64	20.45 ± 5.69	20.50 ± 6.58

B. EFFICACY OUTCOMES

Primary efficacy outcomes—Response patterns varied and were found to differ across the three EASI thresholds evaluated during follow-up. EASI50 rose quickly through the first 16 weeks, rising from 30.0% at Week 4 to 88.75% at Week 16, and then remaining high for the rest of the study at Week 36 (87.5%). EASI75 showed a slower improvement with a final score at Week 16 of 56.25%, a score of approximately 58–60% showed little additional improvement after that point. EASI90 had a delayed response with rates rising from 0% at Week 4 to 8.75% at Week 16, and further increase levels in subsequent weeks (8.75–11.25%). Overall, clinical improvement occurred primarily during the first 16 weeks of the study, and maintained a relatively flat phase of clinical response thereafter. Dose tapering (88.75%) was performed at Week 16 and disease flares were not detected in the follow up. The clinical efficacy was demonstrated in subgroup analysis, similarly, in both treatment groups, with the response profile of upadacitinib being faster and deeper. By Week 12, EASI50 responses were higher in the abrocitinib group: 70.0%, and in the group were 95–100% by Week 20. Upadacitinib group had a better response rate, which reached 40% at Week 4 and 80% at Week 12, and remained stable at 97.5–100% thereafter. After Week 20, response rates were at ∼50–55% in the abrocitinib group and achieved a higher plateau of ∼62.5–65% in the upadacitinib group with EASI75. The EASI90 responses in both treatment groups were modest, and slightly greater in the Upadacitinib group than in the Abrocitinib group, in later follow up (Figure 1).

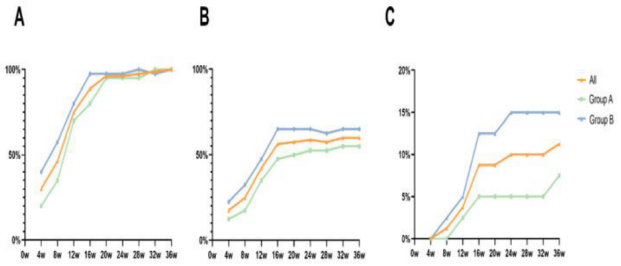

FIGURE 1. Changes in EASI50, EASI75 and EASI90 responses over 36 weeks' follow up.

(A) EASI50 response rates rose almost monotonically across overall cohort and each treatment group.

(B) EASI75 response rates rose primarily within the first 16 weeks, and then stayed the same between all groups.

(C) EASI90 responses appeared later, with higher response rates observed in Group B during follow-up. Lines are shown for the cohort in total, Group A, and Group B. Patterns of disease control were assessed at Week 16 and 36 with Week 4 as the basis for comparison.

Disease control was assessed by comparing response rates at Weeks 16 and 36 with those observed at Week 4. Response proportions across all three EASI thresholds rose significantly between Weeks 4 and 16 ($P < 0.01$ for each), then plateaued through Week 36 with no further significant change.

At Week 16, EASI50 attainment was significantly higher in Group B than Group A ($P = 0.029$), whereas EASI75 and EASI90 rates were statistically similar between arms ($P = 0.176$ and $P = 0.432$). At the Week 36 assessment, all patients in both groups achieved EASI50 response, and no significant differences were detected between the groups for either EASI75 or EASI90 responses ($P = 0.364$ and 0.481, respectively).

SCORAD fell progressively over the study, with significant drops from baseline evident at both Week 16 and Week 36 ($P < 0.001$ each). Upadacitinib-treated patients recorded lower SCORAD values than abrocitinib-treated patients at both checkpoints, pointing to a deeper severity reduction (Table S2).

TABLE S2. SCORAD SCORES OVER TIME

Time point	A	B	Total
0 w	62.40 ± 100.29	65.35 ± 267.77	63.87 ± 183.92
4 w	43.46 ± 184.68	36.13 ± 69.42	39.79 ± 139.50
8 w	35.85 ± 163.27	26.17 ± 38.45	31.00 ± 123.29
12 w	28.27 ± 92.12	19.69 ± 21.69	23.98 ± 74.81
16 w	24.75 ± 81.13	14.54 ± 10.66	19.64 ± 71.72
20 w	22.98 ± 73.76	11.80 ± 7.83	17.39 ± 71.94
24 w	22.18 ± 67.97	9.69 ± 4.74	15.93 ± 75.34
28 w	21.17 ± 63.84	8.50 ± 4.40	14.83 ± 74.31
32 w	19.76 ± 45.45	7.13 ± 2.74	13.45 ± 64.19
36 w	19.29 ± 43.96	6.55 ± 2.27	12.92 ± 63.88

DLQI scores declined progressively during follow-up, with significant improvements observed at Weeks 16 and 36 compared with baseline (both $P < 0.001$). When looking at the patient-conditioned quality of life data (DLQI), in both time periods, Group B had lower DLQI scores than Group A indicating higher improvement in patient-reported quality of life (Table S3).

TABLE S3. DLQI SCORES OVER TIME

Time point	A	B	Total
0 w	20.55 ± 7.64	20.45 ± 5.69	20.50 ± 6.58
4 w	16.38 ± 18.34	13.63 ± 5.27	15.00 ± 13.57
8 w	14.55 ± 20.66	9.58 ± 2.51	12.06 ± 17.71
12 w	12.10 ± 17.73	7.35 ± 1.52	9.73 ± 15.22
16 w	10.10 ± 14.86	5.48 ± 1.02	7.79 ± 13.26
20 w	9.10 ± 16.09	4.45 ± 0.46	6.78 ± 13.65
24 w	8.30 ± 14.01	3.63 ± 0.29	5.96 ± 12.59
28 w	7.65 ± 13.57	3.25 ± 0.50	5.45 ± 11.85
32 w	7.23 ± 13.56	2.63 ± 0.24	4.93 ± 12.17
36 w	6.80 ± 13.14	2.58 ± 0.25	4.69 ± 11.13

C. EASI IMPROVEMENT RATE MIXED-EFFECTS

In the mixed-effects model, BMI, treatment assignment, and disease duration all emerged as significant predictors of EASI change: higher BMI predicted better improvement ($P = 0.011$), while longer-standing disease predicted a blunted response ($P < 0.001$). Compared with Group B, patients in Group A showed a lower rate of EASI improvement ($P < 0.001$). No significant associations were found for age, sex, IgE levels, cardiovascular disease, or diabetes (all $P > 0.05$). Residual variance narrowed as follow-up progressed—patient-to-patient variability was highest during Weeks 4–8 and settled into a consistently low pattern from Week 16 onward (Tables 1 and 2).

TABLE 1. Fixed Effects

Model term	Coefficient	Standard error	t	P	95% CI (Lower)	95% CI (Upper)
Intercept	0.813	0.0738	11.023	< 0.001	0.668	0.958
Age	−0.001	0.001	−0.485	0.628	−0.003	0.002
Male	0.013	0.0101	1.327	0.185	−0.006	0.033
Female	—	—	—	—	—	—
BMI	0.003	0.0013	2.549	0.011	0.001	0.006
Group A (Abrocitinib)	−0.042	0.009	−4.605	< 0.001	−0.059	−0.024
Group B (Upadacitinib)	—	—	—	—	—	—
Disease duration	−0.014	0.0009	−14.335	< 0.001	−0.015	−0.012
IgE	8.438E-6	1.0300E-5	0.819	0.413	-1.178E-5	2.866E-5
No cardiovascular disease	0.006	0.0094	0.654	0.514	−0.012	0.024
Cardiovascular disease	—	—	—	—	—	—
No diabetes mellitus	−0.006	0.0105	−0.569	0.569	−0.027	0.015
Diabetes mellitus	—	—	—	—	—	—

TABLE 2. Residual Effects

Residual effect	Estimate	Standard error	Z	P	95% CI (Lower)	95% CI (Upper)
Var (Week 4)	0.146	0.023	6.251	< 0.001	0.106	0.199
Var (Week 8)	0.078	0.013	6.203	< 0.001	0.057	0.107
Var (Week 12)	0.03	0.005	6.154	< 0.001	0.022	0.042
Var (Week 16)	0.015	0.002	6.274	< 0.001	0.011	0.02
Var (Week 20)	0.011	0.002	6.313	< 0.001	0.008	0.015
Var (Week 24)	0.01	0.002	6.296	< 0.001	0.007	0.014
Var (Week 28)	0.01	0.002	6.253	< 0.001	0.007	0.013
Var (Week 32)	0.01	0.002	6.154	< 0.001	0.007	0.013
Var (Week 36)	0.01	0.002	6.077	< 0.001	0.007	0.014

D. SAFETY

AE profiles were broadly similar across arms over the 36 weeks. Group A patients most often reported headache (12.5%), nausea (10%), GI discomfort (7.5%), upper respiratory infection (7.5%), and herpes simplex (2.5%). For Group B, upper respiratory tract infection (15%), headache (10%), and gastrointestinal discomfort (7.5%) were reported, with herpes zoster occurring in three patients (7.5%) and nausea occurring in two patients (5%).

The majority of AEs were grade 1–2 and resolved with symptomatic management. No patient discontinued treatment because of an adverse event, and no serious events—opportunistic infection, major cardiac events, VTE, or clinically significant liver/kidney impairment—were recorded.

Laboratory assessments were performed at baseline and Weeks 12, 24, and 36, including hematological, hepatic, renal, lipid, coagulation, and infection-related parameters. Thrombocytopenia occurred in three Group A patients by Week 12 (nadir platelet count 90×10^9/L), resolving spontaneously with no recurrence thereafter.

Lipid changes were more evident in Group B. At Week 12, 12 patients showed lipid increases of $> 20\%$ from baseline, including 4 patients with levels exceeding 3.40 mmol/L (maximum 3.81 mmol/L). Lipid levels subsequently declined at Weeks 24 and 36, with all values remaining below 3.4 mmol/L. Group A showed no clinically relevant lipid abnormalities.

Mild transaminase elevations occurred in both groups without clinical consequences or additional treatment requirements. No abnormalities were detected in tuberculosis screening, hepatitis B/C viral load, or other monitored safety parameters during follow-up (Figures 2 and 3).

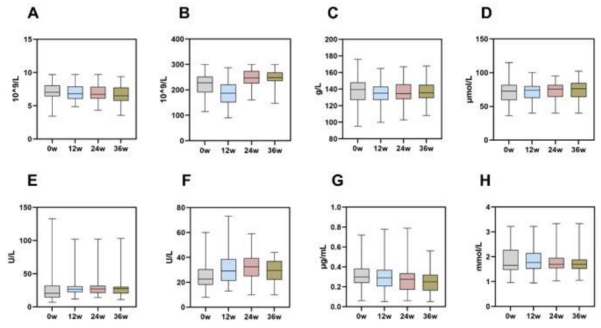

FIGURE 2. Longitudinal changes in laboratory parameters in Group A during JAK inhibitor therapy.

Laboratory parameter changes in Group A during JAK inhibitor treatment. Measurements were obtained at baseline and Weeks 12, 24, and 36. (A–H) WBC, PLT, Hb, Scr, AST, ALT, D-dimer, and LDL-C levels, respectively.

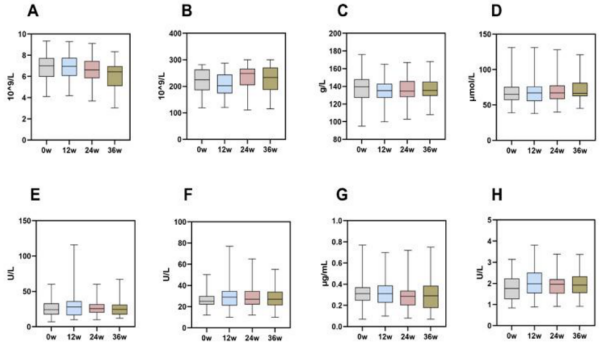

FIGURE 3. Longitudinal changes in laboratory parameters in Group B during JAK inhibitor therapy.

Laboratory parameter changes in Group B during JAK inhibitor treatment. Data were collected at baseline and Weeks 12, 24, and 36. (A–H) WBC, PLT, Hb, Scr, AST, ALT, D-dimer, and LDL-C levels, respectively.

F. RELAPSE

No relapses were seen in the first 4 weeks post-discontinuation; by 12 weeks off treatment, a small subset experienced mild, localized flare-ups (2/40 in Group A, 3/40 in Group B), predominantly in flexural sites. All cases were controlled with topical therapy and did not require re-initiation of systemic treatment.

IV. CONCLUSION

In this prospective, real-world cohort, we characterized both efficacy and safety of upadacitinib and abrocitinib among elderly patients with moderate-to-severe AD. Over the 36-week observation window, both drugs produced early clinical gains that were sustained through follow-up [16]. The EASI50/75/90 rates we observed align with prior published figures, supporting the view that JAK inhibitor efficacy is preserved in older patients even amid comorbid conditions. Most clinical improvement occurred within the first 16 weeks, followed by a stable response phase, as supported by the sustained reductions in SCORAD and DLQI scores. Although both treatments achieved similar outcomes by Week 36, differences were observed during the early treatment period. Upadacitinib's advantage lay in speed—larger early drops in SCORAD and DLQI and a higher Week-16 EASI50 rate than abrocitinib—suggesting it may be preferable when rapid control is clinically needed, such as in patients who failed prior therapy [17].

Regarding safety, the observed adverse event profile in both groups was comparable with previously reported findings [6], [18], Some adverse events appeared to occur more frequently in older patients. In the abrocitinib group, headache, nausea, and gastrointestinal discomfort were the predominant events, with most cases being mild and self-limited. In the upadacitinib group, upper respiratory tract infection was the most commonly reported AE. Three patients (7.5%) developed herpes zoster—numerically above the 1–3% typically reported in RCTs [19], [20]. This elevated rate is plausibly attributable to the combination of older age, greater baseline vulnerability to viral reactivation, and JAK inhibition's effect on antiviral signaling pathways such as interferon–STAT. While these zoster cases were all clinically manageable, they reinforce the value of screening infection history and monitoring zoster risk before and during JAK inhibitor therapy in older AD patients [13], [14].

In clinical practice, additional attention may be required for infection-related risks in elderly patients receiving JAK inhibitors, particularly for herpes zoster. In our cohort, these events were generally manageable and did not lead to treatment interruption or severe complications. Ongoing assessment of safety parameters may help guide the individualized use of JAK inhibitors in older patients with AD.

Repeated lab monitoring revealed no safety signal of clinical concern. A subset of patients showed transient shifts in liver enzymes, lipids, or platelets, all of which normalized over time without accompanying organ dysfunction. LDL elevation at Week 12 was more pronounced with upadacitinib, mirroring lipid changes already documented for this drug class. As lipid levels declined at later visits, these findings support continued monitoring and individualized management rather than routine treatment withdrawal [21]. Lipid profiles should be periodically reviewed in elderly patients receiving JAK inhibitors, allowing early recognition and management of potential abnormalities.

During the observation period, tuberculosis testing and hepatitis B/C monitoring remained negative, with no evidence of infection reactivation.

Few patients experienced relapse after treatment with-

drawal, and the recurrent lesions were mild and controlled with topical therapy alone. These findings suggest that some patients may maintain disease stability after achieving adequate control and dose reduction.

The mixed-effects analysis linked EASI trajectory to both treatment assignment and disease duration—upadacitinib outperformed abrocitinib, and a shorter disease history predicted a more favorable response. A modest positive relationship emerged between BMI and improvement, whereas age, sex, IgE level, and common comorbidities showed no significant effect on efficacy [22]. In this cohort, differences in treatment regimen and disease characteristics appeared to explain more variation in EASI changes than demographic factors. The lower residual variance observed after Week 16 reflected a reduction in response variability between patients, which coincided with the maintenance period of treatment..

Several limitations warrant consideration. We lacked a comparator arm on conventional systemics or biologics, and the single-site design constrained cross-therapy comparison. Sample size was also relatively small, which may limit generalizability. In addition, the absence of inflammatory biomarker, skin barrier, and pharmacokinetic data limited our ability to probe the mechanistic drivers of response [23]. Although the current follow-up captured changes in efficacy and safety over 36 weeks, longer observation will be required to determine the persistence of clinical benefits. Studies including more diverse patient populations and prolonged follow-up may provide additional evidence regarding the long-term use of JAK inhibitors in older patients with AD.

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