

Early Clinical Response Predicts Treatment Persistence in Advanced Therapy-naïve Atopic Dermatitis

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Treatment persistence is a key real-world outcome integrating effectiveness and tolerability in moderate-to-severe atopic dermatitis (AD). We conducted a retrospective multicentre cohort study in 146 advanced therapy-naïve patients with moderate-to-severe AD initiating dupilumab, anti-IL-13 agents or JAK inhibitors (JAKi) between April 2022 and April 2025 at 2 secondary-care hospitals in Madrid, Spain. Overall persistence rates were 82.9%, 69.8%, 59.5% and 54.5% at 6, 12, 18 and 24 months, respectively, with significant differences across therapeutic groups (log-rank $p=0.025$). In multivariable Cox regression, JAKi were associated with higher discontinuation risk compared with dupilumab (HR 1.79; 95% CI 1.05–3.05; $p=0.034$) and male sex was independently associated with increased discontinuation risk (HR 2.20; 95% CI 1.27–3.81; $p=0.005$). Early clinical response at week 16 was the strongest predictor: each 1% increase in EASI improvement was associated with a 3% reduction in discontinuation risk (HR 0.97; 95% CI 0.96–0.98; $p<0.001$). A parallel gradient was observed using patient-reported pruritus (NRS), confirming the predictive value of both objective and patient-reported measures. Baseline biomarkers were not independently associated with persistence. These findings support week 16 as a clinically meaningful decision point for response-guided treatment evaluation in routine practice.

Key words: atopic dermatitis; biological products; Janus kinase inhibitors; medication adherence; medication persistence; pharmacoepidemiology.

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Moderate-to-severe atopic dermatitis (AD) is a chronic relapsing skin disease with marked quality-of-life impairment. Over the past decade,

SIGNIFICANCE

Many patients with severe eczema need long-term treatments to keep their skin condition under control. This study followed 146 patients starting a new type of targeted treatment for the first time and asked: who keeps taking it and who stops? We found that the most important factor was how well the treatment was working at 4 months – patients who responded well early on were much more likely to stay on treatment long term. This information can help doctors and pharmacists identify early which patients may need a change of treatment, improving care for people living with severe eczema.

dupilumab (an interleukin [IL]-4/IL-13 inhibitor), tralokinumab and lebrikizumab (IL-13 inhibitors) and Janus kinase inhibitors (JAKi) (upadacitinib, baricitinib, abrocitinib) have expanded management options for AD (1–4). However, clinical trial data do not fully capture routine practice, where long-term outcomes are shaped by adherence, tolerability and patient-related factors over extended follow-up (5–7).

Treatment persistence – the time from initiation to discontinuation – integrates effectiveness and tolerability and has emerged as a key real-world outcome (8). Registries such as BioDay and SwedAD have provided clinical data (9–12), but most cohorts include patients with heterogeneous prior therapy exposure, limiting comparisons across mechanisms and the identification of actionable predictors. Studies restricted to patients naïve to advanced therapies are scarce, and it remains unclear whether early clinical response predicts long-term persistence better than baseline biomarkers (13, 14).

Since week 16 represents the standard chronological milestone for primary efficacy assessment in most AD guidelines and clinical trials, establishing its predictive value in real-world naïve cohorts is crucial. We therefore evaluated treatment persistence in a multicentre cohort of patients with moderate-to-severe AD initiating their first advanced therapy, aiming to assess whether early response at week 16 predicts long-term persistence and to identify predictors of discontinuation.

MATERIALS AND METHODS

Study design and population

We conducted a retrospective multicentre cohort study including consecutive patients aged ≥ 16 years with moderate-to-severe AD initiating advanced therapies between April 2022 and April 2025 at 2 secondary-care hospitals in Madrid, Spain. All were naïve to advanced therapies and had previously failed, had a contraindication to or were intolerant to ciclosporin. Treatment was selected at the dermatologist's discretion. The inclusion window was defined to coincide with the availability of all 3 mechanisms, ensuring a minimum follow-up of 12 months for patients remaining on treatment at study closure: 30 April 2026. All consecutive eligible patients identified during the study period were included; no patients were excluded due to incomplete records, and the cohort therefore represents the complete eligible population at both centres. The study was approved by the CEIm of Hospital Universitario Fundación Alcorcón (approval number 26/63); informed consent was waived given its retrospective design and use of anonymised data.

Treatment groups

Patients were classified by mechanism of action into 3 groups: IL-4/IL-13 inhibitor (dupilumab), IL-13 inhibitors (tralokinumab or lebrikizumab) and JAKi (upadacitinib, baricitinib or abrocitinib), all initiated at approved doses.

Variables collected

Data were extracted from electronic medical records. Variables included demographics (age, sex), baseline clinical measures (Eczema Area and Severity Index (EASI), Investigator Global Assessment (IGA), body surface area (BSA), Numeric Rating Scale (NRS) for pruritus and sleep), atopic comorbidities, eosinophil count, total immunoglobulin E (IgE) and treatment-related data (drug, duration, discontinuation reason, switching). Early clinical response was defined as percentage EASI improvement from baseline to week 16 (15, 16).

Definition of outcome variables

The primary outcome was treatment persistence, defined as the time from treatment initiation to discontinuation. Discontinuation was recorded as a documented suspension in the medical record or an interruption exceeding 90 days (grace period), consistent with previous pharmacological persistence studies (17) and recommendations for survival analyses in chronic inflammatory diseases (18).

Reasons for discontinuation were categorised as inefficacy (primary or secondary), adverse events, loss to follow-up, or other causes.

Statistical analysis

Persistence was estimated using Kaplan–Meier curves and compared with the log-rank test at 6, 12, 18 and 24 months. Multivariable Cox regression identified factors independently associated with discontinuation (73 events, 6 variables; ~ 12 events per variable). Variables included treatment group, age, sex, baseline EASI, early clinical response and prior ciclosporin exposure. The proportional hazards assumption was verified. Clinical response was also analysed categorically ($<50\%$, $50\text{--}74\%$, $\geq 75\%$ EASI improvement). A sensitivity analysis grouped biologics vs JAKi; a landmark analysis at week 16 evaluated persistence beyond the initial treatment phase. Missing data were handled by complete case analysis (Cox model variables $\leq 3.4\%$ missing; IgE 24.7%, sleep NRS 34.9% and BMI 6.2% excluded from the multivariable model). Statistical significance was set at $p < 0.05$. Analyses were performed using Stata 17.0 (StataCorp, TX, USA).

RESULTS

Patient characteristics

A total of 146 patients with moderate-to-severe AD were included and classified into 3 groups: dupilumab ($n=51$), anti-IL-13 agents ($n=46$) and JAKi ($n=49$). Mean age was 36.4 ± 16.1 years and 60.3% were male.

Baseline characteristics were similar across groups regarding disease severity and biomarkers, though differences were observed in age and prior systemic treatment history. Patients in the JAKi group were significantly younger (30.6 ± 12.6 years) than those receiving dupilumab (38.1 ± 17.2) or anti-IL-13 agents (40.8 ± 16.8 ; $p=0.005$) and had a higher rate of prior ciclosporin use (98.0% vs 86.3% and 82.6%, respectively; $p=0.042$). No significant differences were observed in baseline disease severity (EASI, BSA, IGA) or biomarkers (**Table I**). Pruritus scores and atopic comorbidity prevalence were similar across groups.

Follow-up

Median follow-up was 18.0 months (interquartile range [IQR] 9.7–31.8 months).

Treatment persistence

Persistence differed significantly across groups over the entire follow-up period (log-rank $p=0.025$), with the highest rates observed for dupilumab, followed by anti-IL-13 agents, and the lowest for JAKi.

Table I. Baseline characteristics of patients according to initial treatment group

Variable	Dupilumab (n=51)	Anti-IL-13 agents (n=46)	JAK inhibitors (JAKi) (n=49)	p-value
Demographics				
Age, years, mean (SD)	38.1 (17.2)	40.8 (16.8)	30.6 (12.6)	0.005
Male sex, n (%)	35 (68.6)	28 (60.9)	25 (51.0)	0.197
Atopic profile				
Childhood-onset AD (<18 years), n (%)	19 (37.3)	17 (37.0)	13 (26.5)	0.441
Any atopic comorbidity, n (%)	45 (88.2)	37 (80.4)	41 (83.7)	0.569
Disease severity				
EASI, mean (SD)	25.4 (6.6)	27.3 (7.7)	27.8 (9.7)	0.277
BSA, %, mean (SD)	32.7 (18.3)	38.9 (24.0)	40.3 (20.7)	0.164
Pruritus NRS (0–10), mean (SD)	7.8 (1.4)	7.9 (1.8)	8.4 (1.8)	0.200
Biomarkers				
Eosinophils, cells/μL, median (IQR)	400 (200–635)	340 (200–475)	400 (200–700)	0.226
Total IgE, IU/mL, median (IQR)	1140 (238–3595)	502 (172–1918)	844 (264–3361)	0.613
Treatment-related variables				
Prior ciclosporin use, n (%)	44 (86.3)	38 (82.6)	48 (98.0)	0.042

p-values: ANOVA for continuous normally distributed variables; Kruskal–Wallis for non-normally distributed variables; chi-square test for categorical variables. BSA: body surface area; EASI: Eczema Area and Severity Index; IQR: interquartile range; JAK: Janus kinase; NRS: Numeric Rating Scale; SD: standard deviation.

Overall persistence rates were 82.9%, 69.8%, 59.5% and 54.5% at 6, 12, 18 and 24 months. At 12 months, rates were 76.5% for dupilumab, 69.3% for anti-IL-13 agents and 63.3% for JAKi, widening at 24 months to 62.2%, 58.5% and 43.1%, respectively (Fig. 1).

A prespecified subgroup analysis was performed in patients aged <40 years.

Among the 86 patients under 40 years, persistence remained higher with biological therapies than with JAKi across all timepoints. Twelve-month rates were 77.4% and 62.2%, respectively, consistent with the main analysis.

Discontinuation rates and reasons

Cumulative discontinuation rates over the entire follow-up period up to study closure were 41.2% for dupilumab, 45.7% for anti-IL-13 agents and 63.3% for JAKi.

Reasons for discontinuation differed across groups. In dupilumab-treated patients, inefficacy and adverse events contributed similarly, whereas inefficacy predominated in the anti-IL-13 and JAKi groups.

When inefficacy was classified as primary or secondary failure, secondary failure predominated across all groups at the time of treatment discontinuation (80%, 83% and 75% of inefficacy-related discontinuations in the dupilumab, anti-IL-13 and JAKi groups, respectively).

Timing of discontinuation varied by cause and treatment. Adverse events in the JAKi group occurred early (median 2.2 [IQR 2.0–4.8] months), with 5 of 6 cases within the first 6 months, in contrast to the dupilumab group where adverse event-related discontinuations occurred later (median 8.4 [IQR 4.7–13.1] months), consistent with the known delayed onset of ocular complications. Primary failure was also an early phenomenon across all groups (overall median 3.5 [IQR 2.8–4.8] months). In contrast, secondary failure

was a late event across all groups, with median times to discontinuation of 15.8 [IQR 10.1–18.3], 16.2 [IQR 9.0–23.3] and 14.0 [IQR 9.8–19.9] months for dupilumab, anti-IL-13 agents and JAKi, respectively.

Adverse event-related discontinuation during follow-up occurred in 15.7% of patients on dupilumab, 8.7% on anti-IL-13 agents and 12.2% on JAKi. Within the JAKi group, rates were 11.5% for upadacitinib and 21.4% for abrocitinib; no cases were observed with baricitinib. The overall incidence of adverse events was similar between male and female patients (44.3% vs 50.0%), as was the proportion of discontinuations attributable to adverse events among those who discontinued (24.0% vs 26.1%).

The nature of adverse events differed by treatment. In the dupilumab group, conjunctivitis was the leading cause, followed by arthralgias. In the anti-IL-13

Table II. Multivariable Cox regression analysis of factors associated with treatment discontinuation in patients with atopic dermatitis

Variable	HR	95% CI	p-value
Treatment group			
Dupilumab	Reference	—	—
Anti-IL-13 agents	1.32	0.78–2.24	0.302
JAK inhibitors	1.79	1.05–3.05	0.034
Sex (male vs female)			
Female	Reference	—	—
Male	2.20	1.27–3.81	0.005
Age (per year increase)			
	0.99	0.97–1.01	0.214
Baseline EASI (per point increase)			
	1.01	0.98–1.03	0.462
Early clinical response at week 16 (per 1 % increase in EASI improvement)			
	0.97	0.96–0.98	<0.001
Prior ciclosporin exposure			
No	Reference	—	—
Yes	2.33	0.80–6.77	0.117

Hazard ratios (HR) were estimated using a multivariable Cox proportional hazards model adjusted for treatment group, age, sex, baseline EASI, early clinical response and prior ciclosporin exposure. The proportional hazards assumption was assessed and met. CI: confidence interval; EASI: Eczema Area and Severity Index; HR: hazard ratio; JAK: Janus kinase.

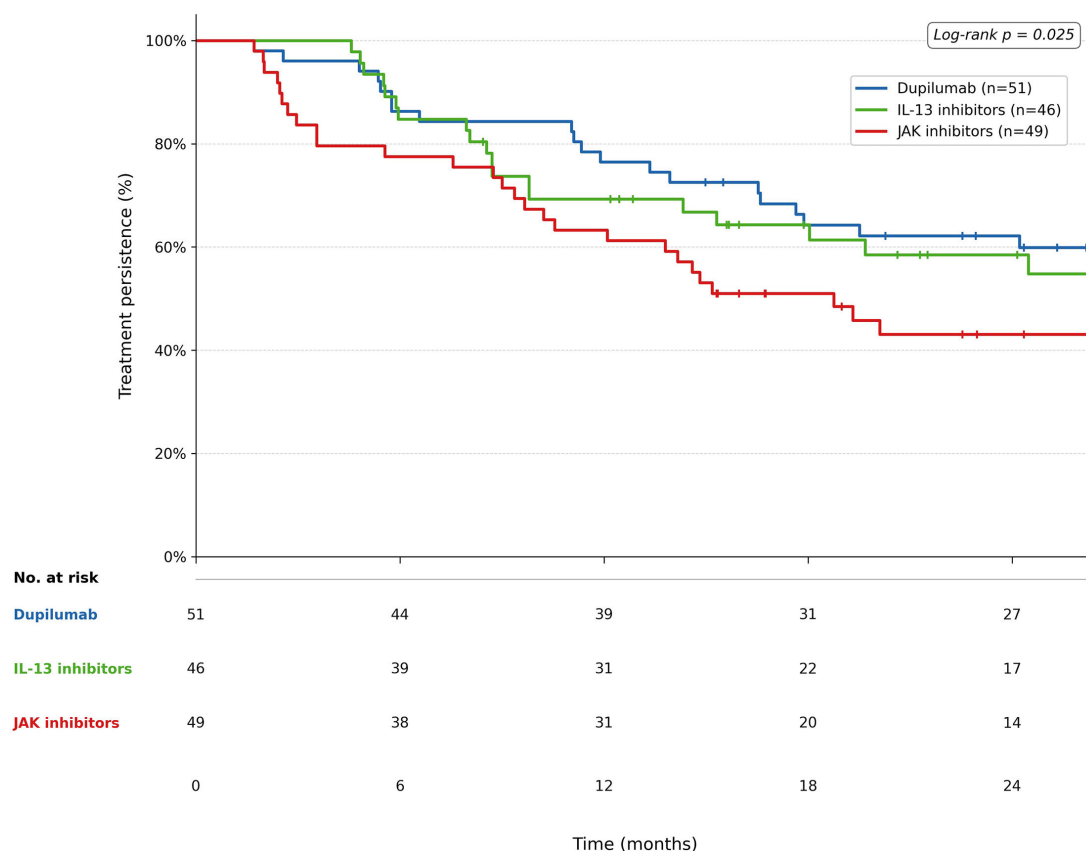


Fig. 1. Treatment persistence according to mechanism of action in advanced therapy-naïve atopic dermatitis. Kaplan-Meier curves showing treatment persistence in patients with moderate-to-severe atopic dermatitis initiating advanced therapies, stratified by mechanism of action (dupilumab, anti-IL-13 agents and JAK inhibitors [JAKi]). Differences between groups were assessed using the log-rank test. Median treatment persistence was not reached in any group during the available follow-up. Number at risk is shown below the plot.

group, these included conjunctivitis, arthralgias and a paradoxical psoriasiform reaction. In the JAKi group, no ocular events led to discontinuation; metabolic alterations, headache and infections predominated.

Factors associated with discontinuation

In multivariable Cox regression, treatment type, sex and early clinical response were independently associated with discontinuation (**Table II**).

Compared with dupilumab, JAKi were associated with higher discontinuation risk (hazard ratio [HR] 1.79; 95% confidence interval [CI] 1.05–3.05; $p=0.034$), while anti-IL-13 agents showed an intermediate risk. Male sex was also associated with a higher risk (HR 2.20; 95% CI 1.27–3.81; $p=0.005$).

Early clinical response was the strongest predictor: each 1% increase in EASI improvement at week 16 was associated with a 3% reduction in discontinuation risk (HR 0.97; 95% CI 0.96–0.98; $p<0.001$), equivalent to approximately a 30% reduction per 10% increase in EASI improvement.

Prior ciclosporin exposure, baseline disease severity and biomarkers were not independently associated with persistence (Table II).

Relationship between clinical response and persistence

A consistent gradient was observed between early response and long-term persistence. Two-year persistence rates were 10.0%, 30.1% and 65.2% in patients with <50%, 50–74% and $\geq 75\%$ EASI improvement at week 16, respectively.

A similar gradient was observed using patient-reported pruritus (NRS), available in 128 patients (91.4%) at week 16: persistence rates of 36.7%, 51.9% and 73.1% for NRS improvement <50%, 50–74% and $\geq 75\%$, respectively. NRS and EASI improvement were moderately correlated ($r=0.648$; $p<0.001$) (Fig. S1).

The NRS trajectory across 3 timepoints – baseline, week 16 and at discontinuation – provided further insight into the nature of treatment failure. Patients discontinuing due to adverse events showed progressive pruritus reduction (NRS: 8.2 $\rightarrow$ 2.9 $\rightarrow$ 1.3), with well-controlled disease at discontinuation (mean EASI 5.3). Those discontinuing due to secondary failure showed initial improvement (NRS: 8.8 $\rightarrow$ 3.5) but maintained substantial pruritus control at discontinuation (NRS 2.4) despite worsening objective disease (mean EASI 14.5), suggesting a

dissociation between patient-reported and clinician-assessed outcomes. Patients with primary failure showed virtually no NRS improvement at week 16 ($7.7 \rightarrow 7.2$) and persistently high disease activity at discontinuation (mean EASI 24.7).

Landmark analysis

In the landmark analysis restricted to patients who reached week 16 ($n=134$), 12-month persistence rates from the landmark timepoint were similar for dupilumab (77.6%) and JAKi (76.9%), and lower for anti-IL-13 agents (69.3%).

At 24 months, the pattern observed in the main analysis re-emerged (62.3%, 58.5% and 54.1%, respectively), supporting the robustness of the findings.

Disease activity at discontinuation

Disease activity at the time of treatment discontinuation differed by reason for stopping. Patients stopping due to adverse events had lower disease activity at that point than those stopping for inefficacy (median EASI 3.0 vs 17.0; $p<0.001$), despite greater relative improvement (Fig. 2).

Switching patterns

Among 73 patients who discontinued, 60 (82.2%, including patients lost to follow-up in the denominator) switched to another advanced therapy. Dupilumab, upadacitinib and tralokinumab were equally the most common second-line agents ($n=15$ each), followed by baricitinib and abrocitinib ($n=6$ each), and lebrikizumab ($n=3$).

Switching followed a mechanism-based pattern: among patients discontinuing biologics, 21 (63.6%) switched to a JAKi and 12 (36.4%) to another biologic; conversely, among those stopping a JAKi, 21 (77.8%) switched to a biologic and only 6 (22.2%) to another JAKi. This asymmetry – with JAKi failures more frequently switching to biologics than vice versa – is consistent with a biologic-first sequencing preference in real-world clinical practice.

Switching rates varied markedly by reason for discontinuation: all patients with primary inefficacy switched (10/10, 100%), as did the vast majority of those with secondary inefficacy (34/36, 94.4%) and adverse events (15/18, 83.3%), whereas none of the patients lost to follow-up or discontinuing for other reasons did so. Of those initiating a second-line therapy, 36 (60%) remained on that treatment at study closure (30 April 2026), although this figure should be interpreted with caution given the heterogeneous follow-up times on second-line treatment.

Sensitivity analysis

In the sensitivity analysis grouping biological therapies vs JAKi, persistence remained higher in the biologics group (HR 0.54; 95% CI 0.31–0.92; $p=0.010$), confirming the robustness of the results.

DISCUSSION

Our results align with the Swedish SwedAD registry (11) and Dutch cohorts (12). Lower rates likely reflect patient selection rather than drug performance (11, 12). Our restriction to advanced therapy-naïve patients allows evaluation in a true first-line setting, free from

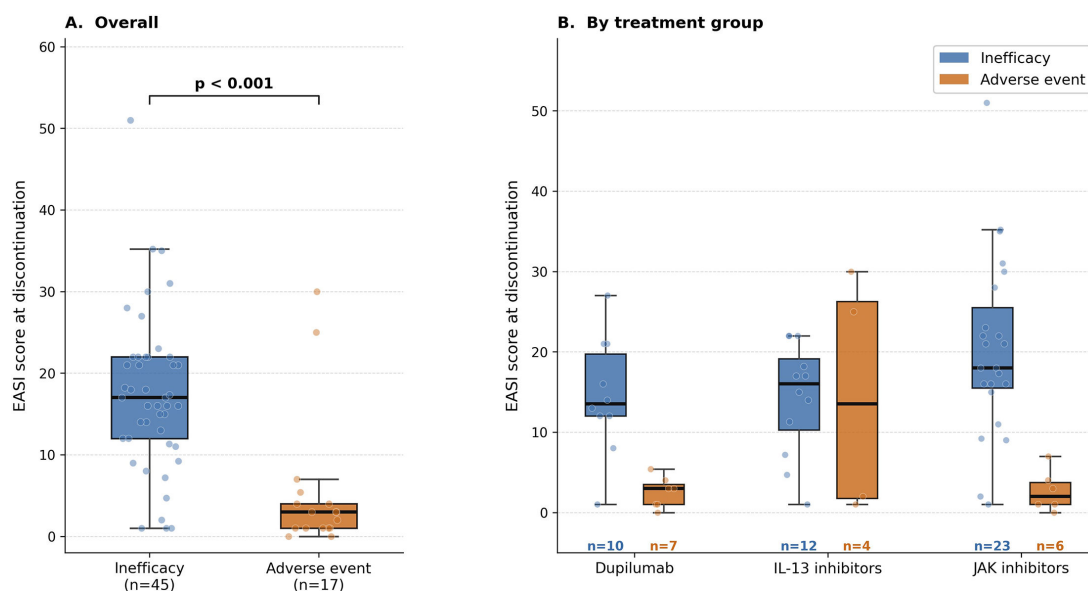


Fig. 2. Disease activity at treatment discontinuation according to reason for discontinuation. Patients discontinuing due to adverse events had lower EASI scores compared with those discontinuing due to inefficacy, indicating that discontinuation due to adverse events often occurs in the context of well-controlled disease. EASI: Eczema Area and Severity Index.

prior exposure (13, 14). Baseline differences in age and prior ciclosporin use reflected routine prescribing but were not independently associated with discontinuation. Residual confounding remains possible, as factors like disease trajectory and clinician preference are not fully captured.

Early clinical response was the strongest predictor of persistence. Patients achieving <50% EASI improvement at week 16 showed a markedly different trajectory than those reaching $\geq 75\%$, a gradient that persisted after adjustment. Similar patterns in data from the BioDay cohort confirm that early nonresponse drives inefficacy-related discontinuation (14, 19). These data support week 16 as a key window where the clinical signal is already informative for routine treatment reassessment (13, 14, 19).

The alignment between EASI and NRS trajectories at week 16 is consistent, but the moderate correlation ($r=0.648$) also shows they do not simply track each other. Skin score and itch can diverge – a patient with controlled pruritus may still have significant objective disease, or vice versa. Relying on a single measure at reassessment visits risks missing part of the picture, which is relevant when the decision to continue or change treatment is being made.

The longitudinal NRS pruritus trajectory reveals distinct patterns of treatment failure beyond a single endpoint. Patients with primary inefficacy showed minimal pruritus improvement at week 16 and persistently high disease activity. Those with secondary failure achieved initial pruritus control but later worsened in objective disease, highlighting a dissociation between patient-reported and clinician-assessed outcomes. Patients discontinuing due to adverse events maintained both low pruritus and low EASI scores despite treatment cessation. These trajectories define clinically distinct phenotypes of discontinuation with different underlying mechanisms and management implications, supporting longitudinal pruritus assessment in routine care.

Across treatment groups, persistence was highest with dupilumab, followed by anti-IL-13 agents, with JAKi showing the greatest attrition. This pattern was consistent across analyses, including the sensitivity analysis. The landmark analysis at week 16 requires careful interpretation. Of the 12 patients who did not reach week 16, 10 (83%) were receiving JAKi, most discontinuing early due to primary failure or adverse events. Excluding these patients introduces a selection bias, explaining the apparent convergence at 12 months; with longer follow-up, differences re-emerged. Persistence should not be interpreted as a direct proxy for intrinsic efficacy, but as a composite outcome influenced by multiple factors, and findings should be interpreted at the level of mechanism of action rather

than as head-to-head comparisons, particularly given the heterogeneity within JAKi.

The association between male sex and higher discontinuation risk (HR 2.20) was not explained by differences in adverse events, baseline severity or treatment allocation, and the pattern was consistent across treatment groups. Notably, loss to follow-up was disproportionately more frequent in male patients (6/88 vs 1/58), whereas adherence (PDC 95.7 % vs 94.9 %; $p=0.656$) (20) and early clinical response (80.8% vs 80.9 %; $p=0.991$) were comparable between sexes, suggesting that engagement with follow-up visits, rather than drug-related factors, may underlie this association. However, this finding should be interpreted with caution: the number of events within each sex-by-treatment subgroup is small, and residual confounding by unmeasured behavioural or socioeconomic factors cannot be excluded.

The temporal pattern of discontinuation highlights 2 clinically relevant phases. Early discontinuations, mainly within the first 6 months, particularly in the JAKi group, were largely driven by adverse events. Later discontinuations, typically after 12 months, were predominantly due to secondary loss of efficacy across all treatments. The relatively low rate of primary failure suggests that patients achieving an early response are likely to maintain at least partial benefit over time.

The safety profile observed aligns with existing evidence. Ocular adverse events were more frequent with dupilumab and anti-IL-13 agents, whereas infections and metabolic alterations predominated with JAKi, particularly upadacitinib and abrocitinib (21). The high switching rate after discontinuation — 82% of patients moved on to another advanced therapy — reflects how these treatments are used in practice: not as a last resort, but as part of a sequence. Switching followed a mechanism-based pattern, consistent with current guidance recommending a change of mechanism after insufficient response (22).

Among the strengths of this study, the restriction to advanced therapy-naïve patients is the most important methodologically. It removes the noise of prior treatment exposure and allows a cleaner comparison across mechanisms in a true first-line setting. Consecutive recruitment reduces selection bias, and the joint analysis of persistence, response and switching provides a comprehensive picture. The persistence rates observed are notably lower than those reported in pivotal trials, providing clinicians with more realistic expectations regarding long-term drug survival in daily practice.

Several limitations should be acknowledged. The observational design introduces the possibility of residual confounding, and the absence of randomisation limits causal inference. The sample size, although

adequate for primary analyses, limits precision in some subgroups, particularly within the baricitinib-treated subgroup. The absence of a formal quality-of-life instrument such as the Dermatology Life Quality Index (DLQI) limits patient-centred interpretation. Although biomarkers were collected at baseline, they were not independently associated with persistence, consistent with previous literature (23). Patient-reported pruritus severity was systematically assessed using an NRS at baseline, week 16 and at the time of discontinuation, providing a clinically meaningful longitudinal complement to objective disease severity.

Overall, these findings support a response-guided approach to treatment decisions in AD. Week 16 emerges as a relevant decision point: patients without early improvement are unlikely to persist, whereas those achieving a strong response are more likely to maintain benefit over time, with secondary loss of efficacy representing the main long-term challenge.

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Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics committee: The study was approved by the Research Ethics Committee (CEIm) of Hospital Universitario Fundación Alcorcón (approval number 26/63). The study was conducted in accordance with the principles of the Declaration of Helsinki. Given its retrospective design and the use of fully anonymised data, the requirement for informed consent was waived.

Conflict of interest: José Javier Martínez Simón reports personal fees from AstraZeneca, Sanofi, LEO Pharma and GSK, and support for attending meetings from MSD, outside the submitted work. Lucía Carrasco Piernavieja reports honoraria from Johnson & Johnson and support for attending meetings from AbbVie, Johnson & Johnson, LEO Pharma and Sanofi, outside the submitted work. Estefanía Zhan Zhou reports honoraria from Johnson & Johnson, GlaxoSmithKline, AstraZeneca and Novartis, and participation on advisory boards for Novartis, GlaxoSmithKline and AstraZeneca, outside the submitted work. Marta Isabel Andreu Barasoain reports consulting fees from LEO Pharma, honoraria from LEO Pharma and AbbVie, and support for attending meetings from Lilly, Pfizer, Almirall and Sanofi, outside the submitted work. Araceli Sánchez Gilo reports consulting fees and honoraria from AbbVie, Galderma, Lilly, LEO Pharma, Pfizer and Sanofi-Regeneron, outside the submitted work. Elena García Zamora reports no conflicts of interest. Virginia Collados Arroyo reports honoraria from Johnson & Johnson and support for attending meetings from AbbVie, Johnson & Johnson, LEO Pharma and Sanofi, outside the submitted work. Montserrat Pérez Encinas reports support for attending meetings from Pfizer and Almirall, outside the submitted work. Francisco Javier Vicente Martín reports no conflicts of interest. José Luis López Esteban served as

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