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ORIGINAL RESEARCH

JAK Inhibitors in Atopic Dermatitis: Does Weight Matter? A Real-World, Nationwide Retrospective Study: IL-AD (Italian Landscape Atopic Dermatitis)

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ABSTRACT

Introduction: Janus kinase (JAK) inhibitors are effective systemic treatments for moderate-to-severe atopic dermatitis (AD), rapidly controlling symptoms and improving quality of life. However, the impact of body mass index (BMI) on therapeutic response remains unclear.

Methods: This multicenter retrospective study analyzed data from 388 adult AD patients treated with upadacitinib, abrocitinib, or baricitinib

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across 25 Italian dermatology centers between May 2022 and July 2024. Patients were classified as overweight (BMI ≥ 25) or non-overweight (BMI < 25), with disease severity assessed using EASI, IGA, and Numerical Rating Scales (NRS) for pruritus and sleep disturbance over 104 weeks. The effect of different treatment dosages was also evaluated.

***Results*:** No significant BMI-related differences in clinical outcomes were noted at most timepoints. However, in the upadacitinib 15 mg group, non-overweight patients showed greater EASI and pruritus improvements at Week 4 ($p = 0.037$, $p = 0.039$), although these differences resolved subsequently. At Week 104, higher BMI modestly reduced EASI improvement ($p = 0.045$) in multivariable analysis.

***Conclusions*:** Treatment dosage consistently influenced clinical improvement regardless of BMI. These findings confirm the efficacy of JAK inhibitors across BMI categories, suggesting minimal short-term BMI influence but highlighting potential long-term considerations in overweight patients, emphasizing personalized dosing strategies and prolonged monitoring.

Keywords: Atopic dermatitis; JAK inhibitors; Body mass index; Obesity; Real-world study; Upadacitinib; Abrocitinib; Baricitinib; Treatment efficacy; Dermatology

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Key Summary Points

Why carry out this study?

Given the rising use of JAK inhibitors and the high prevalence of overweight and obesity in atopic dermatitis, it is clinically important to understand whether body mass index affects treatment outcomes, particularly as real-world data on this relationship remain limited.

Does baseline BMI influence the short and long term clinical response to JAK inhibitors in adults with moderate to severe AD?

What was learned from the study?

Across 388 patients, BMI did not significantly impact early or mid-term clinical outcomes (EASI, IGA, NRS pruritus/sleep); a modest but significant negative effect on EASI response was observed only at 104 weeks (p = 0.045). JAK inhibitors appear effective across BMI categories in the short to mid-term, supporting their broad utility. A delayed negative effect of high BMI may warrant closer long-term monitoring or tailored dosing strategies in overweight patients.

INTRODUCTION

Atopic dermatitis (AD) is a chronic, inflammatory skin disease characterized by intense pruritus and eczema, often with a relapsing course. In moderate-to-severe cases, systemic therapies are required to control symptoms and improve quality of life. The introduction of dupilumab, the first biologic approved for the treatment of moderate-to-severe AD, represented a major advancement in the management of the disease [1]. This was followed by the approval of tralokinumab, and, subsequently, lebrikizumab, expanding the landscape of targeted biologic therapies for AD. More recently, small molecules named oral Janus kinase (JAK) inhibitors—including upadacitinib, abrocitinib, and baricitinib—have emerged as effective alternatives, showing rapid onset of action and favorable efficacy profiles in both clinical trials and real-world settings [2–5].

Despite the growing use of JAK inhibitors, little is known about the impact of body mass index (BMI) on treatment response to these drugs in AD. Obesity has been associated with chronic low-grade inflammation and may alter the pharmacokinetics and pharmacodynamics of systemic therapies, potentially reducing clinical efficacy [6]. While the impact of BMI has been extensively studied in other inflammatory diseases such as psoriasis [7], evidence remains limited and inconclusive in the context of AD—particularly with regard to JAK inhibitors.

Recent evidence also suggests that JAK inhibitors—particularly those targeting JAK2—may induce weight gain, raising questions about the potential interplay between body weight, metabolic effects, and treatment outcomes [8]. Given the increasing prevalence of overweight and obesity in patients with AD [9], understanding whether BMI influences therapeutic outcomes is of both clinical and pharmacological relevance. To address this gap, we conducted a multicenter, real-world study across 25 Dermatology units in Italy, as part of the IL-AD (Italian Landscape Atopic Dermatitis) group, to evaluate the impact of BMI on the clinical response to JAK inhibitors in adult patients with moderate-to-severe AD. The analysis included both global and dose-stratified comparisons, with a focus on longitudinal response dynamics and multivariable modeling.

METHODS

This retrospective study included adult patients (≥ 18 years) diagnosed with AD who were treated with a JAK inhibitor—upadacitinib, abrocitinib, or baricitinib—between May 2022 and July 2024. Treatment eligibility followed the criteria outlined by both the Italian Medicines Agency and the EuroGuiDerm guidelines for AD, which define the clinical indications for initiating JAK inhibitor therapy in appropriate candidates. These include a diagnosis of severe AD [Eczema Area and Severity Index (EASI) score ≥ 24] requiring systemic treatment, with either an

inadequate response, intolerance, or contraindications to cyclosporine A, or prior use of biologics or small molecules that proved ineffective or led to adverse events. Topical treatments such as corticosteroids and calcineurin inhibitors were applied only for short-term management of acute flares in limited skin areas. No patients received additional systemic therapies during the study period. Patient data were extracted from medical records. To be included, individuals were required to have at least one follow-up visit after baseline, with a minimum follow-up duration of 4 months. Additional scheduled follow-up assessments occurred at week 16, 36, 52, and 104.

In accordance with Good Clinical Practice guidelines, disease severity was evaluated using the EASI at baseline and each follow-up visit. Patient-reported symptoms were assessed using the peak pruritus and sleep disturbance Numerical Rating Scales (NRS).

Continuous variables were reported as mean ± standard deviation (SD) if normally distributed, or as median and range if non-normally distributed. Categorical variables were expressed as frequencies and percentages. The Kruskal–Wallis test was used to compare medians across timepoints. Linear regression analysis was performed to assess the independent effects of BMI and dosage. A p-value < 0.05 was considered statistically significant.

Ethical Approval

Ethical approval was not required, as the study involved retrospective data collection without deviation from routine clinical care. All participants had provided written informed consent for the use of their anonymized clinical data during standard clinical visits. The study was conducted in accordance with the principles of the Declaration of Helsinki and relevant regulations regarding data protection and patient confidentiality. Data collection complied with all applica ble regulations on patient protection and privacy.

RESULTS

A total of 388 patients were included (Table 1), with a mean age of 40.67 years (± 15.93 SD); 211 were male (54.4%) and 177 were female (45.6%). The median age at disease onset was 9.0 years (range 0–80). Regarding clinical phenotype, the majority (84.0%) of patients presented with flexural AD. Less common phenotypes included the generalized lichenoid form (4.1%), nummular eczema (3.6%), prurigo-like (3.4%), palmar-plantar involvement (2.8%), and erythroderma (2.1%). Involvement of sensitive or highly visible anatomical areas was common, with lesions most frequently observed on the face and neck (63.1%), hands (50.3%), and genital area (15.5%). A personal history of atopy was reported in 72.4% of patients, with associated comorbid atopic conditions such as rhinitis (42.3%), asthma (28.9%), and conjunctivitis (22.2%). Other main comorbidities included hypertension (11.6%), hypercholesterolemia (7.5%), diabetes (4.9%), and cardiovascular disease (3.6%). Nasal polyps were reported in 3.9% of patients. A substantial proportion of patients had received one or more systemic or targeted treatments prior to initiating JAK inhibitor therapy. The most frequently previously used conventional systemic agent was cyclosporine, prescribed in 75% of patients ($n = 291$). Systemic corticosteroids had been used in 28.6% of the cohort ($n = 111$). Among targeted biologic therapies, dupilumab had been administered in 39.2% of cases ($n = 152$), while phototherapy was reported in 7.0% of patients ($n = 27$). At the time of study inclusion, other prior treatments included baricitinib (10.3%, $n = 40$), abrocitinib (5.2%, $n = 20$), upadacitinib (2.3%, $n = 9$), methotrexate (2.9%, $n = 11$), acitretin (1.6%, $n = 6$), and tralokinumab (0.8%, $n = 3$). At baseline, the most frequently prescribed JAK inhibitor was upadacitinib 15 mg, administered to 225 patients (58.0%), followed by upadacitinib 30 mg in 78 patients (20.1%) and abrocitinib 100 mg in 50 patients (12.9%). Smaller proportions of patients received abrocitinib 200 mg ($n = 7$, 1.8%), baricitinib 4 mg ($n = 26$, 6.7%), or baricitinib 2 mg ($n = 2$, 0.5%). No patients were treated with abrocitinib 50 mg. At baseline,

Table 1 Baseline demographics and disease characteristics

Parameters	*N* = 388
Gender, *n* (%)	
Male	211 (54.4)
Female	177 (45.6)
Age (years), mean (SD)	40.67 (15.93)
Disease onset (years), median (range)	9 (0–80)
Phenotype, *n* (%)	
Classic	326 (84.0)
Generalized lichenoid	16 (4.1)
Prurigo-like	14 (3.6)
Nummular eczema	13 (3.4)
Palmo-plantar	11 (2.8)
Erythroderma	8 (2.1)
Sensitive or highly visible anatomical areas, *n* (%)	
Face and neck	245 (63.1)
Hands	195 (50.3)
Genitalia	60 (15.5)
Atopic comorbidities, *n* (%)	281 (72.4)
Rhinitis	164 (42.3)
Asthma	112 (28.9)
Conjunctivitis	86 (22.2)
Other comorbidities, *n* (%)	
Hypertension	45 (11.6)
Hypercholesterolemia	29 (7.5)
Diabetes	19 (4.9)
Cardiovascular disease	14 (3.6)
Nasal polyps	15 (3.9)
Previous therapy, *n* (%)	
Cyclosporine	291 (75)
Systemic corticosteroids	111 (28.6)
Dupilumab	152 (39.2)
Phototherapy	27 (7)
Baricitinib	40 (10.3)
Abrocitinib	20 (5.2)
Upadacitinib	9 (2.3)
Methotrexate	11 (2.9)
Acitretin	6(1.6)
Tralokinumab	3 (0.8)
Ongoing therapy at baseline	
Upadacitinib 15 mg/day	225 (58)
Upadacitinib 30 mg/day	78 (20.1)
Abrocitinib 100 mg/day	50 (12.9)
Abrocitinib 200 mg/day	7 (1.8)
Baricitinib 2 mg/day	2 (0.5)
Baricitinib 4 mg/day	26 (6.7)
Baseline BMI, *n* (%)	
< 18.5	11 (2.8)
18.5–24.9	247 (63.7)
≥ 25	130 (33.5)
Baseline EASI, median (range)	24 (0–64)
Baseline IGA, median (range)	3 (0–4)
Baseline NRS pruritus, median (range)	8 (0–10)
Baseline NRS sleep disturbance, median (range)	7 (0–10)

BMI Body Mass Index, *EASI* Eczema Area and Severity Index, *IGA* Investigator's Global Assessment, *NRS* Numerical Rating Scale

the BMI distribution indicated that 11 patients (2.8%) were underweight (BMI < 18.5), 247 (63.7%) had a normal weight (BMI 18.5–24.9), and 130 (33.5%) had a BMI ≥ 25, including 59 overweight (BMI 25–29.9), 45 with class I obesity (BMI 30–34.9), 17 with class II obesity (BMI 35–39.9), and 9 with class III obesity (BMI ≥ 40). Given the low number of underweight patients,

underweight and normal-weight individuals were combined into a single category referred to as non-overweight for statistical analysis. Based on this classification, 258 patients (65.5%) were categorized as non-overweight, while 130 patients (33.5%) were overweight. All patients with a body weight over 90 kg were classified as obese according to their BMI; no normal-weight individuals exceeded this weight threshold. The median baseline EASI score was 24.0 (range 0–64), while the median IGA score was 3 (range 0–4). The median NRS pruritus score was 8 (range 0–10), and the median NRS sleep disturbance score was 7 (range 0–10).

Evaluation of Clinical Response According to BMI: Pooled and Dose-Stratified Analyses

No significant differences in clinical outcomes were observed between non-overweight and overweight patients across all treatments and timepoints, as assessed by the Kruskal–Wallis test (Table 2). Changes in EASI scores did not differ significantly between groups at Week 4 ($p = 0.656$), Week 16 ($p = 0.639$), Week 36 ($p = 0.659$), or Week 52 ($p = 0.803$), nor at Week 104 (p = 0.068). Similarly, no significant differences were found in IGA scores at Week 4 ($p = 0.622$), Week 16 ($p = 0.804$), Week 36 ($p = 0.720$), Week 52 ($p = 0.443$), or Week 104 ($p = 0.444$). Patient-reported outcomes followed the same trend. NRS pruritus showed no significant differences between groups at Week 4 ($p = 0.30$), Week 16 ($p = 0.947$), Week 36 ($p = 0.410$), Week 52 ($p = 0.925$), or Week 104 ($p = 0.808$). NRS sleep were also comparable at Week 4 ($p = 0.879$), Week 16 ($p = 0.783$), Week 36 ($p = 0.669$), Week 52 ($p = 0.529$) and Week 104 ($p = 0.146$).

Among patients receiving low-dose regimens (upadacitinib 15 mg, abrocitinib 100 mg, or baricitinib 2 mg), EASI score improvements were comparable between non-overweight and overweight individuals at all timepoints, with Kruskal–Wallis *p*-values ranging from 0.189 (Week 4) to 0.811 (Week 52) (Table 3). A non-significant trend was noted at Week 104 ($p = 0.090$), with overweight patients showing slightly lower

Table 2 Kruskal–Wallis test analysis of clinical and patient-reported outcomes between non-overweight and overweight patients across JAK inhibitor treatments and timepoints

Parameters	Baseline		Week 4			Week 16			Week 36			Week 52			Week 104		
Median (range)	Non-overweight ($n = 258$)	Overweight ($n = 130$)	Non-overweight ($n = 258$)	Overweight ($n = 130$)	*p*-value	Non-overweight ($n = 222$)	Overweight ($n = 104$)	*p*-value	Non-overweight ($n = 177$)	Overweight ($n = 75$)	*p*-value	Non-overweight ($n = 127$)	Overweight ($n = 55$)	*p*-value	Non-overweight ($n = 48$)	Overweight ($n = 27$)	*p*-value
EASI	24 (0–64)	24 (0–46)	4 (0–26)	4 (0–40)	0.656	1 (0–24)	1 (0–30)	0.639	1 (0–18)	1 (0–30)	0.659	0 (0–16)	0 (0–8)	0.803	0 (0–10)	0 (0–20)	0.068
IGA	3 (0–4)	3 (0–4)	1 (0–4)	1 (0–4)	0.622	0 (0–4)	0 (0–4)	0.804	0 (0–3)	0 (0–4)	0.702	0 (0–3)	0 (0–2)	0.443	0 (0–2)	0 (0–3)	0.444
NRS pruritus	8 (0–10)	8 (0–10)	2 (0–10)	2 (0–8)	0.30	0 (0–10)	0 (0–8)	0.947	0 (0–7)	0 (0–7)	0.410	0 (0–6)	0 (0–7)	0.925	0.5 (0–7)	0 (0–6)	0.808
NRS sleep	7 (0–10)	6 (0–10)	0 (0–8)	0 (0–10)	0.879	0 (0–10)	0 (0–8)	0.783	0 (0–8)	0 (0–9)	0.669	0 (0–7)	0 (0–3)	0.529	0 (0–8)	0 (0–6)	0.146

EASI Eczema Area and Severity Index, *IGA* Investigator's Global Assessment, *NRS* Numerical Rating Scale

improvement, although this did not reach statistical significance. Similarly, in the high-dose group (upadacitinib 30 mg, abrocitinib 200 mg, or baricitinib 4 mg), no significant differences were found between BMI categories at any timepoint. Kruskal–Wallis p-values ranged from 0.264 at Week 4 to 0.942 at Week 36, indicating consistent clinical efficacy regardless of BMI status under high-dose therapy. In addition to EASI, BMI-related differences were also investigated for IGA, NRS pruritus, and NRS sleep scores using the Kruskal–Wallis test. No statistically significant differences were observed between non-overweight and overweight patients at any timepoint, regardless of treatment dose group (all p-values >0.05).

Evaluation of Clinical Response by BMI Category Across Specific JAK Inhibitors

To evaluate the potential impact of BMI on clinical outcomes, differences in EASI score improvement between non-overweight and overweight patients were assessed for each JAK inhibitor and timepoint using the Kruskal–Wallis test (Tables 4, 5, 6). Among patients treated with upadacitinib 15 mg, a statistically significant difference was observed at Week 4 ($p=0.037$), with non-overweight individuals achieving greater clinical improvement. This difference was not maintained at subsequent assessments, with no significant differences at Week 16 ($p=0.405$), Week 36 ($p=0.578$), Week 52 ($p=0.564$), or Week 104 ($p=0.733$). In patients receiving upadacitinib 30 mg, EASI score improvements did not differ significantly by BMI at any timepoint (all p-values between 0.413 and 0.927). Similarly, no BMI-related differences were observed in the abrocitinib 100 mg or 200 mg groups (all $p>0.3$), or in patients treated with baricitinib 2 mg or 4 mg, although the small sample size in these subgroups limits interpretation. Regarding patient-reported outcomes, a significant difference in NRS pruritus was found only at Week 4 for patients on upadacitinib 15 mg ($p=0.039$), again favoring non-overweight individuals. No further significant differences in pruritus scores were noted across treatments or timepoints. For IGA, no significant BMI-related differences were observed at any assessment or in any treatment group (all $p>0.05$). Similarly, NRS sleep scores did not differ between BMI groups at any timepoint, with all p-values above the conventional threshold for significance.

Multivariable Analysis of BMI and Dosage on Clinical Response

To assess the independent effects of BMI and treatment dosage on clinical outcomes, linear regression models were applied for each timepoint, with change in EASI, IGA, NRS pruritus, and NRS sleep scores as dependent variables (Table 7). All models included BMI category (non-overweight *vs* overweight) and dosage group (low *vs* high) as predictors. For EASI, treatment dosage was consistently and significantly associated with clinical improvement up to Week 52 (p-values: 0.015 at Week 4, 0.015 at Week 16, 0.006 at Week 36, 0.0009 at Week 52), with lower efficacy observed in patients on low-dose regimens. BMI category was not a significant predictor at each timepoint from W4 to W52 (all p-values >0.05), while became statistically significant at Week 104 ($p=0.045$), indicating a modest but independent negative effect of higher BMI on long-term clinical response. Similar trends were observed for other clinical endpoints. For IGA, BMI category had no significant impact at any timepoint (all $p>0.05$). Dosage was significantly associated with greater IGA improvement at Week 16 ($p=0.031$) and Week 52 ($p=0.008$), supporting a dose–response effect. For NRS pruritus and NRS sleep, no significant associations were detected between BMI category and symptom improvement across any timepoint.

Table 3 Kruskal–Wallis test analysis of clinical and patient-reported outcomes between non-overweight and overweight patients receiving low-dose of high-dose JAK inhibitor treatments across all timepoints

Low-Dose JAK inhibitor regimens																
Parameters	**Baseline**		**Week 4**			**Week 16**			**Week 36**			**Week 52**			**Week 104**		
median (range)	Non-overweight ($n=184$)	Overweight ($n=93$)	Non-overweight ($n=184$)	Overweight (n=93)	*p*-value	Non-overweight ($n=156$)	Overweight ($n=70$)	*p*-Value	Non-overweight ($n=128$)	Overweight ($n=56$)	*p*-Value	Non-overweight ($n=94$)	Overweight ($n=44$)	*p*-Value	Non-overweight ($n=34$)	Overweight ($n=21$)	*p*-Value
EASI	22 (0–64)	24 (0–46)	4 (0–25)	5 (0–21)	0.189	1 (0–24)	1 (0–10)	0.318	1 (0–18)	0 (0–17)	0.704	0 (0–16)	0 (0–5)	0.811	0 (0–8)	0 (0–20)	
IGA	3 (0–4)	3 (0–4)	1 (0–4)	1 (0–3)	0.419	0 (0–4)	0 (0–2)	0.535	0 (0–3)	0 (0–4)	0.761	0 (0–3)	0 (0–2)	0.248	0 (0–2)	0 (0–3)	0.975
NRS pruritus	8 (0–10)	8 (0–10)	2 (0–10)	2 (0–8)	0.377	0 (0–10)	0 (0–8)	0.391	0 (0–7)	0 (0–7)	0.131	0 (0–6)	0 (0–7)	0.256	0.5 (0–7)	0 (0.6)	0.613
NRS sleep	7 (0–10)	7 (0–10)	0 (0–8)	0 (0–10)	0.399	0 (0–10)	0 (0–6)	0.085	0 (0–8)	0 (0–9)	0.362	0 (0–7)	0 (0–3)	0.261	0 (0–8)	0 (0–6)	0.912
High-Dose JAK Inhibitor Regimens																	
Parameters	**Baseline**		**Week 4**			**Week 16**			**Week 36**			**Week 52**			**Week 104**		
Median (range)	Non-overweight ($n=74$)	Overweight ($n=37$)	Non-overweight ($n=74$)	Overweight ($n=37$)	*p*-value	Non-overweight ($n=66$)	Overweight ($n=34$)	*p*-Value	Non-overweight ($n=49$)	Overweight ($n=19$)	p-calue	Non-overweight ($n=33$)	Overweight ($n=11$)	*p*-value	Non-overweight ($n=14$)	Overweight ($n=6$)	*p*-value
EASI	26 (0–58)	24 (4–46)	4 (0–26)	5 (0–40)	0.264	0.3 (0–13)	2 (0–30)	0.537	0.2 (0–16)	1 (0–30)	0.941	0 (0–16)	0 (0–5)	0.804	0 (0–10)	1 (0–10)	0.401
IGA	4 (0–4)	4 (2–4)	1 (0–4)	1 (0–4)	0.27	0 (0–4)	0 (0–4)	0.804	0 (0–3)	0 (0–4)	0.252	0 (0–3)	0 (0–2)	0.698	0 (0–2)	0 (0–2)	0.794
NRS pruritus	8 (0–10)	8 (2–10)	2 (0–9)	2 (0–8)	0.895	0 (0–8)	0 (0–8)	0.330	0 (0–7)	0 (0–7)	0.587	0 (0–6)	0 (0–5)	0.845	0.5 (0–7)	0 (0.6)	0.475
NRS sleep	7 (0–10)	6 (0–10)	0 (0–8)	0 (0–7)	0.722	0 (0–8)	0 (0–8)	0.301	0 (0–8)	0 (0–8)	0.055	0 (0–7)	0 (0–3)	0.712	0 (0–7)	0 (0–5)	0.278

EASI Eczema area and severity index, *IGA* Investigator'sglobal assessment, *NRS* Numerical rating scale

Table 4 Kruskal–Wallis test comparison of clinical and patient-reported outcomes between non-overweight and overweight patients treated with upadacitinib 15 mg or 30 mg once daily across all timepoints

Upadacitinib 15 mg					
	BMI group	**EASI**		**NRS pruritus**	
		Median (range)	***p*-value**	**Median (range)**	***p*-value**
Baseline	Non-overweight ($n = 149$)	23 (0–64)	NA	8 (0–10)	NA
	Overweight ($n = 76$)	22.4 (0–45)		8 (0–10)	
Week 4	Non-overweight ($n = 149$)	4.0 (0–25)	0.037*	2 (0–10)	0.039*
	Overweight ($n = 76$)	4.0 (0–28)		2 (0–10)	
Week 16	Non-overweight ($n = 125$)	1.0 (0–18)	0.405	0 (0–10)	0.572
	Overweight ($n = 60$)	0.0 (0–16)		0 (0–7)	
Week 36	Non-overweight ($n = 104$)	0.0 (0–18)	0.578	0 (0–10)	0.884
	Overweight ($n = 52$)	0.0 (0–17)		0 (0–9)	
Week 52	Non-overweight ($n = 83$)	0.0 (0–12)	0.564	0 (0–7)	0.357
	Overweight ($n = 42$)	0.0 (0–8)		0 (0–7)	
Week 104	Non-overweight ($n = 34$)	0.0 (0–6)	0.733	0 (0–8)	0.914
	Overweight ($n = 20$)	0.0 (0–20)		0 (0–6)	
	BMI group	**IGA**		**NRS sleep**	
		Median (range)	***p*-value**	**Median (range)**	***p*-value**
Baseline	Non-overweight ($n = 149$)	3 (0–4)	NA	7 (0–10)	NA
	Overweight ($n = 76$)	3 (0–4)		7 (0–10)	
Week 4	Non-overweight ($n = 149$)	1 (0–4)	0.527	1 (0–8)	0.373
	Overweight ($n = 76$)	1 (0–4)		0 (0–10)	
Week 16	Non-overweight ($n = 125$)	0 (0–3)	0.768	0 (0–10)	0.415
	Overweight ($n = 60$)	0 (0–3)		0 (0–8)	
Week 36	Non-overweight ($n = 104$)	0 (0–3)	0.618	0 (0–8)	0.623
	Overweight ($n = 52$)	0 (0–4)		0 (0–9)	
Week 52	Non-overweight ($n = 83$)	0 (0–3)	0.983	0 (0–8)	0.71
	Overweight ($n = 42$)	0 (0–2)		0 (0–3)	
Week 104	Non-overweight ($n = 34$)	0 (0–2)	0.25	0 (0–8)	0.818
	Overweight ($n = 20$)	0 (0–3)		0 (0–6)	
Upadacitinib 30 mg					
	BMI group	**EASI**		**NRS pruritus**	
		Median (range)	***p*-value**	**Median (range)**	***p*-value**
Baseline	Non-overweight ($n = 51$)	24 (0–58)	NA	8 (0–10)	NA

Table 4 continued

Upadacitinib 30 mg					
	BMI group	**EASI**		**NRS pruritus**	
		Median (range)	***p*-value**	**Median (range)**	***p*-value**
	Overweight ($n = 27$)	24 (10–46)		8 (2–10)	
Week 4	Non-overweight ($n = 51$)	3.4 (0–26)	0.701	2 (0–8)	0.393
	Overweight ($n = 27$)	4.0 (0–40)		1 (0–8)	
Week 16	Non-overweight ($n = 51$)	1.0 (0–24)	0.838	0 (0–10)	0.753
	Overweight ($n = 27$)	2.0 (0–30)		0 (0–8)	
Week 36	Non-overweight ($n = 42$)	1.0 (0–16)	0.972	1 (0–10)	0.915
	Overweight ($n = 17$)	1.0 (0–30)		1 (0–8)	
Week 52	Non-overweight ($n = 31$	1.0 (0–16)	0.56	1 (0–10)	0.192
	Overweight ($n = 10$)	0.5 (0–6)		0 (0–5)	
Week 104	Non-overweight ($n = 13$)	1.5 (0–10)	0.927	2 (0–7)	0.917
	Overweight ($n = 6$)	1.5 (0–10)		2 (0–7)	
	BMI group	**IGA**		**NRS sleep**	
		Median (range)	***p*-value**	**Median (range)**	***p*-value**
Baseline	Non-overweight ($n = 51$)	4 (0–4)	NA	7 (0–10)	NA
	Overweight ($n = 27$)	4 (2–4)		7 (0–10)	
Week 4	Non-overweight ($n = 51$)	1 (0–3)	0.641	0 (0–10)	0.416
	Overweight ($n = 27$)	1 (0–4)		0 (0–10)	
Week 16	Non-overweight ($n = 51$)	0 (0–4)	0.686	0 (0–8)	0.668
	Overweight ($n = 27$)	0 (0–4)		0 (0–7)	
Week 36	Non-overweight ($n = 42$)	1 (0–3)	0.95	0 (0–9)	0.349
	Overweight ($n = 17$)	1 (0–4)		0 (0–8)	
Week 52	Non-overweight ($n = 31$	1 (0–3)	0.186	0 (0–8)	0.404
	Overweight ($n = 10$)	0 (0–1)		0 (0–8)	
Week 104	Non-overweight ($n = 13$)	1 (0–2)	0.962	0 (0–6)	0.886
	Overweight	0.5 (0–2)		0 (0–2)	

EASI Eczema Area and Severity Index, *IGA* Investigator's Global Assessment, *NRS* Numerical Rating Scale, *NA* not applicable

Table 5 Kruskal–Wallis test comparison of clinical and patient-reported outcomes between non-overweight and overweight patients treated with abrocitinib 100 mg or 200 mg once daily across all timepoints

Abrocitinib 100 mg					
		EASI		**NRS pruritus**	
	BMI group	**Median (range)**	***p*-value**	**Median (range)**	***p*-value**
Baseline	Non-overweight ($n = 35$)	20 (2–40)	NA	8 (3–10)	NA
	Overweight ($n = 15$)	26 (11–30)		7 (0–10)	
Week 4	Non-overweight ($n = 35$)	3.8 (0–14)	0.56	3 (0–7)	0.958
	Overweight ($n = 15$)	4.0 (0–15)		2 (0–8)	
Week 16	Non-overweight ($n = 31$)	2.0 (0–10)	0.619	1 (0–7)	0.161
	Overweight ($n = 8$)	2.5 (0–8)		2 (0–8)	
Week 36	Non-overweight ($n = 24$)	2.0 (0–6)	0.26	1 (0–7)	0.264
	Overweight ($n = 3$)	2.0 (2–4)		2 (2–3)	
Week 52	Non-overweight ($n = 11$)	2.0 (0–3)	0.125	0 (0–6)	0.418
	Overweight ($n = 1$)	3.0		0	
Week 104	Non-overweight ($n = 0$)	NA (NA)	NA	NA (NA)	NA
	Overweight ($n = 0$)	NA (NA)		NA (NA)	
	BMI group	**IGA**		**NRS sleep**	
		Median (range)	***p*-value**	**Median (range)**	***p*-value**
Baseline	Non-overweight ($n = 35$)	3 (1–4)	NA	6 (0–10)	NA
	Overweight ($n = 15$)	3 (2–4)		6 (0–10)	
Week 4	Non-overweight ($n = 35$)	1 (0–3)	0.957	0 (0–7)	0.412
	Overweight ($n = 15$)	1 (0–3)		1 (0–5)	
Week 16	Non-overweight ($n = 31$)	1 (0–2)	0.852	0 (0–6)	0.716
	Overweight ($n = 8$)	0.5 (0–2)		0 (0–2)	
Week 36	Non-overweight ($n = 24$)	1 (0–2)	0.073	0 (0–6)	0.495
	Overweight ($n = 3$)	1 (1–2)		0 (0–3)	
Week 52	Non-overweight ($n = 11$)	1 (0–1)	0.398	0 (0–2)	0.655
	Overweight ($n = 1$)	1		0	
Week 104	Non-overweight ($n = 0$)	NA (NA)	NA	NA (NA)	NA
	Overweight ($n = 0$)	NA (NA)		NA (NA)	
Abrocitinib 200 mg					

Table 5 continued

	BMI group	EASI		NRS pruritus	
		Median (range)	*p*-value	Median (range)	*p*-value
Baseline	Non-overweight ($n = 5$)	24 (12–40)	NA	8 (3–10)	NA
	Overweight ($n = 2$)	25.5 (17–34)		8.5 (8–9)	
Week 4	Non-overweight ($n = 5$)	3.0 (0–5)	0.355	0.5 (0–2)	0.06
	Overweight ($n = 2$)	15.5 (3–28)		3.5 (3–4)	
Week 16	Non-overweight ($n = 3$)	0.8 (0–1)	0.564	0 (0–0)	0.182
	Overweight ($n = 2$)	4.0 (0–8)		3 (0–3)	
Week 36	Non-overweight ($n = 0$)	NA (NA)	NA	NA (NA)	NA
	Overweight ($n = 1$)	3.0		2	
Week 52	Non-overweight ($n = 0$)	NA (NA)	NA	NA (NA)	NA
	Overweight ($n = 1$)	4.0		3	
Week 104	Non-overweight ($n = 0$)	NA (NA)	NA	NA (NA)	NA
	Overweight ($n = 0$)	NA (NA)		NA (NA)	
	BMI group	**IGA**		**NRS sleep**	
		Median (range)	*p*-value	Median (range)	*p*-value
Baseline	Non-overweight ($n = 5$)	4 (2–4)	NA	7 (0–10)	NA
	Overweight ($n = 2$)	3.5 (3–4)		5.5 (3–8)	
Week 4	Non-overweight ($n = 5$)	1 (0–1)	0.171	0 (0–0)	0.128
	Overweight ($n = 2$)	2 (1–3)		3.5(2–5)	
Week 16	Non-overweight ($n = 3$)	0.5 (0–1)	0.543	0 (0–0)	0.414
	Overweight ($n = 2$)	1 (0–2)		0 (0–4)	
Week 36	Non-overweight ($n = 0$)	NA (NA)	NA	NA (NA)	NA
	Overweight ($n = 1$)	1		0	
Week 52	Non-overweight ($n = 0$)	NA (NA	NA	NA (NA)	NA
	Overweight ($n = 1$)	2		0	
Week 104	Non-overweight ($n = 0$)	NA (NA)	NA	NA (NA)	NA
	Overweight ($n = 0$)	NA (NA)		NA (NA)	

EASI Eczema Area and Severity Index, *IGA* Investigator's Global Assessment, *NRS* Numerical Rating Scale, *NA* Not Applicable

Table 6 Kruskal–Wallis test comparison of clinical and patient-reported outcomes between non-overweight and overweight patients treated with baricitinib 2 mg or 4 mg once daily across all timepoints

Baricitinib 2 mg					
		EASI		**NRS pruritus**	
	BMI group	**Median (range)**	***p*-value**	**Median (range)**	***p*-value**
Baseline	Non-overweight (n = 0)	NA (NA)	NA	NA (NA)	NA
	Overweight (n = 2)	16.5 (15–18)		8 (7–9)	
Week 4	Non-overweight (n = 0)	NA (NA)	NA	NA (NA)	NA
	Overweight (n = 2)	7.5 (5–10)		4 (3–5)	
Week 16	Non-overweight (n = 0)	NA (NA)	NA	NA (NA)	NA
	Overweight (n = 2)	2.0 (2–2)		2.5 (2–3)	
Week 36	Non-overweight (n = 0)	NA (NA)	NA	NA (NA)	NA
	Overweight (n = 1)	4.0		1	
Week 52	Non-overweight (n = 0)	NA (NA)	NA	NA (NA)	NA
	Overweight (n = 1)	3.0		1	
Week 104	Non-overweight (n = 0)	NA (NA)	NA	NA (NA)	NA
	Overweight (n = 1)	8.0		1	
		IGA		**NRS sleep**	
	BMI group	**Median (range)**	***p*-value**	**Median (range)**	***p*-value**
Baseline	Non-overweight (n = 0)	NA (NA)	NA	NA (NA)	NA
	Overweight (n = 2)	2 (2–2)		6 (6–6)	
Week 4	Non-overweight (n = 0)	NA (NA)	NA	NA (NA)	NA
	Overweight (n = 2)	1 (1–1)		2 (1–3)	
Week 16	Non-overweight (n = 0)	NA (NA)	NA	NA (NA)	NA
	Overweight (n = 2)	0.5 (0–1)		1 (0–2)	
Week 36	Non-overweight (n = 0)	NA (NA)	NA	NA (NA)	NA
	Overweight (n = 1)	1		0	
Week 52	Non-overweight (n = 0)	NA (NA)	NA	NA (NA)	NA
	Overweight (n = 1)	1		0	
Week 104	Non-overweight (n = 0)	NA (NA)	NA	NA (NA)	NA
	Overweight (n = 1)	2 (2–2)		0 (0–0)	
Baricitinib 4 mg					

Table 6 continued

		EASI		NRS pruritus	
	BMI group	**Median (range)**	***p*-value**	**Median (range)**	***p*-value**
Baseline	Non-overweight ($n = 18$)	24 (1–30)	NA	7 (2–10)	NA
	Overweight ($n = 8$)	15.5 (4–30)		7.5 (2–10)	
Week 4	Non-overweight ($n = 18$)	4.0 (0–17)	0.095	2 (0–9)	0.872
	Overweight (n = 8)	10.0 (0–15)		3 (0–4)	
Week 16	Non-overweight ($n = 12$)	2.4 (0–10)	0.873	2.5 (0–8)	0.165
	Overweight ($n = 5$)	2.0 (0–10)		1 (0–5)	
Week 36	Non-overweight ($n = 7$)	1.5 (0–4)	0.182	1 (0–9)	0.368
	Overweight ($n = 1$)	4.0		4	
Week 52	Non-overweight ($n = 2$)	1.0 (0–2)	NA	3.5 (0–7)	NA
	Overweight ($n = 0$)	NA (NA)		NA (NA)	
Week 104	Non-overweight ($n = 1$)	0.0	NA	7	NA
	Overweight ($n = 0$)	NA (NA)		NA (NA)	
		IGA		**NRS sleep**	
	BMI group	**Median (range)**	***p*-value**	**Median (range)**	***p*-value**
Baseline	Non-overweight ($n = 18$)	3.5 (1–4)	NA	6.5 (0–10)	NA
	Overweight ($n = 8$)	3 (2–4)		5 (0–8)	
Week 4	Non-overweight ($n = 18$)	1 (0–3)	0.221	0 (0–8)	0.285
	Overweight ($n = 8$)	2 (0–3)		3 (0–3)	
Week 16	Non-overweight ($n = 12$)	1 (0–3)	0.783	0 (0–8)	0.422
	Overweight ($n = 5$)	1 (0–3)		0 (0–2)	
Week 36	Non-overweight ($n = 7$)	1 (0–2)	0.817	0 (0–0)	0.008
	Overweight ($n = 1$)	1		1	
Week 52	Non-overweight ($n = 2$)	0 (0–1)	NA	0 (0–0)	NA
	Overweight ($n = 0$)	NA (NA)		NA (NA)	
Week 104	Non-overweight ($n = 1$)	0	NA	0	NA
	Overweight ($n = 0$)	NA (NA)		NA (NA)	

EASI Eczema Area and Severity Index, *IGA* Investigator's Global Assessment, *NRS* Numerical Rating Scale, *NA* not applicable

Table 7 Multivariable linear regression analysis of the independent effects of BMI and treatment dosage on clinical outcomes across timepoints

	Low-dose *p*-value	High-dose *p*-value	BMI ≥ 25 vs < 25 *p*-value
EASI			
Week 4	0.006*	0.280	0.877
Week 16	0.015*	0.105	0.910
Week 36	0.006*	0.021	0.971
Week 52	0.001*	0.215	0.913
Week 104	0.421	0.334	0.045*
IGA			
Week 4	0.247	0.136	0.498
Week 16	0.030*	0.099	0.764
Week 36	0.380	0.336	0.550
Week 52	0.008*	0.212	0.812
Week 104	0.760	0.254	0.210
NRS pruritus			
Week 4	0.599	0.461	0.967
Week 16	0.581	0.393	0.836
Week 36	0.975	0.453	0.931
Week 52	0.900	0.598	0.928
Week 104	0.328	0.482	0.279
NRS sleep			
Week 4	0.522	0.629	0.586
Week 16	0.461	0.892	0.568
Week 36	0.534	0.701	0.560
Week 52	0.285	0.981	0.561
Week 104	0.715	0.782	0.113

EASI Eczema Area and Severity Index, *IGA* Investigator's Global Assessment, *NRS* Numerical Rating Scale

DISCUSSION

This real-world, multicenter study confirms the clinical effectiveness of JAK inhibitors in adult patients with moderate-to-severe atopic dermatitis, regardless of BMI category. While no significant differences were observed in EASI, IGA, or patient-reported outcomes between overweight and non-overweight patients at early and mid-term timepoints, a weak but statistically significant association emerged at Week 104 in multivariable analysis, suggesting a potential long-term impact of higher BMI on clinical response. Conversely, dose-dependent efficacy was evident in the multivariable model, supporting the relevance of appropriate dosing, particularly in the early months of treatment. The dosage showed a consistent and significant effect on clinical improvement up to Week 52, confirming the importance of adequate systemic exposure during the first year of therapy. This observation raises the hypothesis that, once stable clinical remission is achieved it may be possible to consider step-down dosing strategies in selected patients, especially if sustained disease control is maintained beyond the first year of treatment. Prospective studies are warranted to evaluate the safety and effectiveness of long-term dose adjustment according to clinical response and patient characteristics. The early-phase difference observed in EASI and pruritus scores among patients treated with upadacitinib 15 mg indicates that lower doses may be less effective in overweight individuals during the initial treatment phase. However, this trend did not persist beyond Week 4 and was not confirmed across other JAK inhibitors or dosages. Overall, these findings support the effectiveness of JAK inhibitors in a real-world population, regardless of BMI status, while highlighting the relevance of dosing strategies in the early treatment phase. The delayed association between BMI and EASI response observed at one year suggests that long-term pharmacodynamic effects may warrant closer monitoring in overweight patients.

These findings align with previous evidence from other immune-mediated inflammatory diseases. Data from psoriatic arthritis suggest that high BMI may reduce treatment response to JAK inhibitors, particularly at lower doses [10]. In a pooled analysis of phase 3 trials, patients with BMI ≥ 35 showed diminished clinical outcomes with tofacitinib 5 mg, while responses were

preserved at 10 mg. However, such stratification was not feasible in our study due to the limited number of patients in the highest BMI categories. As a result, BMI was analyzed using broader categories to preserve statistical power. Nonetheless, our findings similarly point to a modest, delayed impact of BMI on long-term response, supporting the need for individualized treatment strategies in overweight populations.

In a recent study on 81 patients with rheumatoid arthritis (RA) [11], obesity and adipokine profiles were not found to significantly influence the response to JAK inhibitors (baricitinib, tofacitinib, filgotinib, and upadacitinib). Specifically, the authors observed no difference in clinical outcomes between normal-weight and overweight/obese patients, and circulating levels of leptin and adiponectin showed no correlation with treatment response over a six-month period. This suggests that the mechanism of action of JAK inhibitors may remain effective regardless of adipose tissue–related inflammatory signals. In a pooled analysis of over 3800 patients with RA treated with tofacitinib in phase 3 trials [12], no clinically meaningful differences in clinical response were observed across BMI categories. While patients with obesity showed slightly lower numerical response rates, these differences were consistently below the threshold of clinical relevance. Moreover, radiographic progression was even lower among obese patients receiving the higher tofacitinib dose. These results support the idea that JAK inhibitors maintain their therapeutic effect regardless of BMI. In contrast to previous studies showing no major impact of BMI on JAK inhibitor efficacy, recent real-world data in RA suggest otherwise. A Korean registry analysis found that obese patients (BMI ≥ 30) treated with non-TNF-targeted agents, including JAK inhibitors, experienced reduced clinical improvement and significantly higher discontinuation rates [13]. This supports the possibility that higher BMI may affect long-term treatment persistence. However, a retrospective cohort study on tofacitinib in RA found no significant association between obesity and drug survival in multivariate analysis, despite a numerically higher 12-month retention rate among obese patients [14].

Consistent evidence from other immune-mediated inflammatory diseases supports the notion that body weight may not significantly affect the efficacy of JAK inhibitors. In ulcerative colitis, a post hoc analysis of the phase 3 OCTAVE clinical program showed that tofacitinib maintained its efficacy across all BMI categories, with no consistent trend in clinical outcomes related to BMI [15]. Regression analyses confirmed that BMI was not a significant predictor of clinical remission, endoscopic improvement, or steroid-free response. In contrast to this study, a recent U.S. cohort study in ulcerative colitis reported worse outcomes in obese patients treated with advanced therapies, including JAK inhibitors [16]. Obesity was associated with higher risks of corticosteroid use, treatment switch, and colectomy, even after adjusting for comorbidities. While these findings suggest that obesity may impair treatment effectiveness in IBD, the milder and delayed impact observed in our atopic dermatitis cohort points to possible disease-specific differences.

These results, although coming from studies on diseases with pathogenic mechanisms different from AD, mirror our findings in AD, where BMI did not significantly influence treatment outcomes at early timepoints and only showed a weak association with reduced EASI improvement at Week 104. Together, these data suggest that JAK inhibitors exert robust anti-inflammatory effects regardless of body composition, reinforcing their value as weight-independent systemic therapies in chronic inflammatory diseases. This aligns with previous studies on dupilumab, which reported no significant impact of BMI on treatment efficacy [17].

This study is strengthened by its multicenter design, the inclusion of multiple JAK inhibitors, and the longitudinal follow-up extending to two years. However, limitations include the retrospective nature of data collection, the observational design, and no pharmacokinetic assessments to explore drug distribution or metabolism, which precludes causal inference. Moreover, the small number of patients in some subgroups, may also limit the generalizability of dose-specific findings. Finally, not all

patients had completed the 104-week follow-up by the time of data cutoff, and the number of evaluable cases progressively declined over time. Therefore, observations related to long-term outcomes—especially those at two years—should be interpreted with appropriate caution. Additional data from longer-term follow-up may help to further validate these findings.

CONCLUSIONS

In conclusion, while BMI did not significantly influence short- or mid-term outcomes, a modest association with reduced long-term efficacy emerged at two years. These findings support the overall effectiveness of JAK inhibitors regardless of body weight, but also highlight the importance of long-term monitoring and individualized dosing strategies, particularly in overweight patients. Future prospective studies are needed to better elucidate the pharmacokinetic and immunologic mechanisms underlying the impact of BMI on long-term response to JAK inhibitors in AD.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflicts of Interest. Mariateresa Rossi has received personal fees for advisory board meetings from Sanofi, AbbVie, Novartis, and Cantabria. Alessandra Narcisi has served on advisory boards and received honoraria and research grants from multiple companies including Almirall, AbbVie, Leo Pharma, Celgene, Eli Lilly, Janssen, Novartis, Sanofi Genzyme, Amgen, and Boehringer Ingelheim. Antonio Costanzo has served as an advisory board member and consultant, and has received fees, speaker's honoraria, or participated in clinical trials for AbbVie, Almirall, Biogen, LEO Pharma, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi Genzyme, and UCB Pharma. Silvia Mariel Ferrucci has been principal investigator in clinical trials for multiple companies including AbbVie, Almirall, Galderma, Leo Pharma, Sanofi, Amgen, Novartis, and Bayer, and has received honoraria for lectures from Novartis and Menarini. Francesca Manzo Margiotta has nothing to declare. Simone Ribero has received honoraria and served as a consultant or advisory board member for companies including

AbbVie, Almirall, Leo Pharma, Eli Lilly, Novartis, Pfizer, and Sanofi Genzyme. Michela Ortoncelli has served as a consultant or advisory board member for AbbVie, Leo Pharma, and Sanofi Genzyme. Maddalena Napolitano has acted as speaker, consultant, and/or advisory board member for AbbVie, Eli Lilly, Leo Pharma, Novartis, and Sanofi. Anna Balato has received honoraria for participation in advisory boards or as a speaker for several pharmaceutical companies including AbbVie, Celgene, Janssen Cilag, Eli Lilly, Novartis, Pfizer, Sanofi Genzyme, and UCB Pharma. Francesco Loconsole received honoraria or served on advisory boards for AbbVie, Janssen Cilag, Novartis, Eli Lilly, and Sanofi. Piergiorgio Malagoli has been a speaker for AbbVie, Eli Lilly, Novartis, Janssen Cilag, Celgene, Leo Pharma, and Almirall. Maria Letizia Musumeci has served as an advisory board member and consultant and has received speaker's honoraria and trial fees for AbbVie, Almirall, Biogen, Eli Lilly, Janssen Cilag, Leo Pharma, and Novartis. Caterina Foti has received honoraria for participation in advisory boards, meetings, or lectures for AbbVie, Amgen, Pfizer, Sanofi, Novartis, Eli Lilly, Leo Pharma, Incyte, and Boehringer Ingelheim. Andrea Carugno has been a consultant, speaker, or participant in advisory boards for AbbVie, Almirall, Amgen, Boehringer Ingelheim, Eli Lilly, Janssen-Cilag, Leo Pharma, Novartis, Sanofi, and UCB Pharma. Massimo Gola has been a consultant and/or speaker, participated in advisory boards, and received personal fees from AbbVie, Almirall, Leo Pharma, Pfizer, and Sanofi. Mario Bruno Guanti has served as an advisory board member and/or consultant and received fees, honoraria, or participated in clinical studies for AbbVie, Leo Pharma, Sanofi Genzyme, Novartis, Cantabria, and Eli Lilly. Elena Pezzolo has been a consultant and speaker for Sanofi Genzyme, AbbVie, Leo Pharma, Novartis, Janssen, Almirall, Pfizer, Galderma, and Boehringer Ingelheim. Stefano Bighetti, Matteo Bianco, Francesco Messina, Francesca Gaiani, Angelo Valerio Marzano, Francesca Barei, Francesco Leo, Andrea Cosenza, Cataldo Patruno, Claudio Sciarrone, Federica Veronese, Anna Graziella Burroni, Carlotta Gurioli, Flavia Manzo Margiotta, Francesca Satolli, Giuseppe Amoruso, Maria Esposito, Paolo Pella, Nicola Zerbinati, Martina Maurelli, Ilaria Trave, Luca Bettolini have nothing to disclose. Mariateresa Rossi, Anna Campanati and PierGiacomo Calzavara-Pinton are Editorial Board members for *Dermatology and Therapy*. They were not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions.

Ethical Approval. Ethical approval was not required, as the study involved retrospective data collection without deviation from routine clinical care. All participants had provided written informed consent for the use of their anonymized clinical data during standard clinical visits. The study was conducted in accordance with the principles of the Declaration of Helsinki and relevant regulations regarding data protection and patient confidentiality. Data collection complied with all applicable regulations on patient protection and privacy. Informed consent was obtained from all subjects involved in the study.

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