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RESEARCH ARTICLE

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Baricitinib for adult atopic dermatitis: real-world effectiveness, safety, and response predictors

Niccolò Gori[a,b], Lucia Di Nardo[a], Elena Ippoliti[b], Flaminia Antonelli[b], Luisa Boeti[b], Anna Balato[c], Eugenia Veronica Di Brizzi[c], Maddalena Nicoletti[c], Maria Esposito[d,e], Maria Concetta Fargnoli[d], Andrea De Berardinis[d,e], Lina Maria Magnanimi[d,e], Marco Galluzzo[f,g], Claudia Paganini[f,g], Marina Talamonti[g], Luca Bianchi[f,g], Maddalena Napolitano[h,i], Cataldo Patruno[i], Giuseppe Lauletta[h], Francesca di Vico[h] and Ketty Peris[a,b]

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ABSTRACT

Objectives: Baricitinib has shown efficacy and a favorable safety profile in randomized trials for moderate-to-severe atopic dermatitis (AD), but real-world evidence is limited. We conducted a multicenter, retrospective and prospective study aimed at evaluating the long-term effectiveness and safety profile of baricitinib in the treatment of adult patients affected from AD, with the additional goal of identifying potential predictors of treatment response.

Methods: We included adult AD patients treated with baricitinib between January 2023 and November 2024 at five Italian tertiary centers. Disease severity and patient-reported outcomes, including the Eczema Area and Severity Index (EASI), Body Surface Area (BSA), Itch Numeric Rating Scale (Itch-NRS), Sleep Numeric Rating Scale (Sleep-NRS), Dermatology Life Quality Index (DLQI), Patient-Oriented Eczema Measure (POEM), and Minimal Disease Activity (MDA, defined as EASI ≤3 and Itch-NRS ≤1), were assessed at baseline and weeks 4, 16, 32, and 52.

Results: The 52 patients enrolled showed significant and sustained improvements in physician- (BSA, EASI) and patient-reported outcomes (Itch-NRS, Sleep-NRS, DLQI, POEM). At week 16, atopic comorbidities increased the odds of achieving MDA (OR: 10.9; $p = 0.033$), whereas head and neck involvement reduced the likelihood of response (OR: 0.07 $p = 0.028$). Thirty-two mild to moderate adverse events occurred in 28 patients, none requiring treatment discontinuation.

Conclusion: In this real-world study, baricitinib provided substantial long-term effectiveness with a favorable safety profile in moderate-to-severe AD, and atopic comorbidities emerged as a predictor of optimal clinical response at week 16.

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Introduction

Atopic dermatitis (AD) is a common inflammatory skin disease in both children and adults, whose incidence has markedly increased in the last decades (1,2). AD clinical manifestations and associated comorbidities are often the cause of a marked impairment in patients' quality of life (QoL) (1,2).

Over one third of adult patients suffer from a moderate to severe form of AD, the long-term management of which remains challenging due to the chronic, recurrent nature of the disease (1,3). Recent advances in AD pathogenesis have led to the introduction of novel therapeutic agents, including three biologics (dupilumab, tralokinumab and lebrikizumab) and three Janus kinase (JAK) inhibitors (3), thus allowing a significant progress in the therapeutic management of AD and achievement of long-term disease control (3,4).

Baricitinib is a selective oral JAK1/JAK2 inhibitor indicated for the treatment of moderate to severe AD (5–8). The broad inhibitory activity of baricitinib toward multiple cytokines (IL-4, IL-13, IL-22, INFγ, IL-9 and IL-31), which play a role in the pathogenesis of AD, is reflected in the significant reduction of patients' clinical signs and symptoms observed in phase III clinical trials (7,8).

Considering the wide range of available treatments for AD, it is essential to identify the most appropriate treatment for each patient. In this context, a post-hoc analysis using an artificial intelligence program identified an 'itch-dominant' sub-cohort, characterized by a body surface area (BSA) involvement of 10–40% and a baseline itch numerical rating scale (NRS) score of ≥7, as the most responsive to baricitinib treatment (9). However, data regarding clinical predictors of baricitinib response in real-world AD patients are still lacking.

The aim of this multicenter, real-world study is to evaluate the effectiveness and safety profile of baricitinib as well as clinical predictors of drug response up to 52 weeks of treatment.

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Material and methods

In this retrospective and prospective study, adult patients with moderate to severe AD treated with baricitinib, were recruited at five Italian University Hospitals from January 2023 to November 2024. The objective of the study was to evaluate the effectiveness and safety of baricitinib, up to 52 weeks of observation, in the treatment of adult patients affected by moderate to severe AD, with a view toward the identification of clinical predictors of drug response. In the study population, baricitinib was prescribed at a daily dosage of 2 mg or 4 mg, in patients with an Eczema Area and Severity Index (EASI) score ≥24 and a medical history of inefficacy, intolerance or contraindication to Cyclosporine A (CsA), as required by the Italian Medical Agency (AIFA). A starting dose of 2 mg once daily was prescribed, in accordance with the Summary of Product Characteristics, as the patient fell into a group for whom this dose may be considered: aged ≥75 years, at increased risk for adverse events (such as serious infections or thrombotic events), or with moderate hepatic impairment. For all the other patients, the recommended starting dose of 4 mg once daily was prescribed.

All patients were recommended to apply moisturizers daily; topical corticosteroids or calcineurin inhibitors were used by patients as needed. Patients with at least 16 weeks of follow-up were included in the study. The following clinical and demographic characteristics were registered: age, sex, body mass index (BMI), clinical phenotype classified according to Silvestre Salvador JF et al. (10), involvement of sensitive body areas (including head and neck, hands and genitalia), atopic comorbidities, non-atopic comorbidities, previous treatments for AD. Clinical response was assessed at 16, 32 and 52 weeks during treatment using the following scores: Body Surface Area (BSA), ranging from 0 to 100; Eczema Area and Severity Index (EASI), ranging from 0 to 72 points; itch and sleep Numeric Rating Scale (NRS), ranging from 0 to 10 points; Dermatology Life Quality Index (DLQI), ranging from 0 to 30 points; Patient Oriented Eczema Measure (POEM), ranging from 0 to 30 (11). Super responder patients were considered those achieving a minimal disease activity (MDA) according to Silverberg JI et al. (12), defined as the simultaneous achievement of EASI ≤3 and itch-NRS ≤1.

Evaluation of safety was conducted, encompassing the incidence of treatment-related adverse events (AE), objective examinations, and laboratory tests (complete blood count, aspartate transaminase, alanine transaminase, gamma-glutamyl transferase, creatinine, creatine phosphokinase (CPK), triglycerides, total cholesterol, LDL cholesterol, HDL cholesterol, hepatitis B and C markers, Quantiferon-TB test, Human Immunodeficiency Virus antibody tests). The severity of each event was classified as mild (minimal impact, no specific treatment required), moderate (some impact, requiring symptomatic treatment), or severe (marked impact, requiring medical intervention and/or treatment discontinuation).

Statistical analysis

Descriptive statistics were used to summarize baseline demographic and clinical characteristics. Continuous variables were expressed as means with standard deviations (SD), while categorical variables were reported as absolute frequencies and their percentages. The efficacy of baricitinib was assessed through changes in clinical scores (EASI, Itch-NRS, Sleep-NRS, DLQI, POEM) at multiple time points (weeks 4, 16, 32, and 52), using paired *t*-tests or Wilcoxon signed-rank tests, as appropriate, to evaluate intra-group differences. Differences in treatment response between bio-naïve and bio-experienced patients were assessed using unpaired *t*-tests or Mann–Whitney *U* tests. To identify independent predictors of achieving MDA at week 16, univariable analyses were performed using chi-squared or Fisher's exact tests for categorical variables and logistic regression for continuous variables. Variables with $p < 0.1$ were included in a multivariable logistic regression model. Results are reported as odds ratios (OR) with 95% confidence intervals (CI), and statistical significance was set at $p < 0.05$. Analyses were conducted using STATA version 17 (StataCorp, College Station, TX).

All efficacy outcomes were analyzed using the *as-observed* method, except for EASI-50, EASI-75, and EASI-90 responses at weeks 32 and 52, which were calculated using both the *as-observed* method and the *last observation carried forward* (LOCF) approach.

Results

Population characteristics

Overall, 52 adult patients (22 females and 30 males, mean age: 41.2 years (SD ±14.6), with moderate to severe AD were included in the study. Patients' baseline characteristics are reported in Table 1. The flexural phenotype was the most common clinical presentation (41/52; 78.8%), followed by nummular eczema (4/52; 7.7%), prurigo nodularis-like AD (4/52; 7.7%), and erythrodermic AD (3/52; 5.8%).

Table 1. Clinical and demographic characteristics of patients.

Overall population	52 patients
Males, *n* (%)	30/52 (57.7)
Age, mean ± SD	41.2 ± 14.6
BMI, mean ± SD	25.5 ± 4.9
Atopic comorbidities, *n* (%)	22/52 (42.3)
• Allergic rhinitis, *n* (%)	18/52 (34.5)
• Asthma, *n* (%)	10/52 (19.2)
• Conjunctivitis, *n* (%)	9/52 (17.3)
Other comorbidities, *n* (%)	22/52 (42.3)
• Hypothyroidism, *n* (%)	3/52 (5.8)
• Alopecia areata, *n* (%)	3/52 (5.8)
• Hypertension, *n* (%)	3/52 (5.8)
• Dyslipidaemia, *n* (%)	1/52 (1.9)
• Alopecia areata, *n* (%)	3/52 (1.9)
• Psoriasis, *n* (%)	1/52 (1.9)
• Suppurative hidradenitis, *n* (%)	1/52 (1.9)
• Vitiligo, *n* (%)	1/52 (1.9)
• Celiac disease, *n* (%)	1/52 (1.9)
• Spontaneous Urticaria, *n* (%)	1/52 (1.9)
• Diabetes, *n* (%)	1/52 (1.9)
• Bipolar disorder, *n* (%)	1/52 (1.9)
• Restless leg syndrome, *n* (%)	1/52 (1.9)
• Bell paralysis, *n* (%)	1/52 (1.9)
• Interstitial lung disease, *n* (%)	1/52 (1.9)
• Irritable bowel syndrome, (%)	1/52 (1.9)
• Diverticulitis, *n* (%)	1/52 (1.9)
• Fatty liver disease, *n* (%)	1/52 (1.9)
• Multiple uterine fibroids, *n* (%)	1/52 (1.9)
• Arthrosis, *n* (%)	1/52 (1.9)
• Hypogammaglobulinemia, *n* (%)	1/52 (1.9)
Early onset (<18 years old), *n* (%)	22/52 (42.3)
Late onset (≥18 years old), *n* (%)	30/52 (57.7)
Flexural phenotype, *n* (%)	41/52 (78.8)
Nummular eczema, *n* (%)	4/52 (7.7)
Prurigo nodularis-like AD, *n* (%)	4/52 (7.7)
Erythrodermic AD, *n* (%)	3/52 (5.8)
Head and neck involvement, *n* (%)	34/52 (65.4)
Hand involvement, *n* (%)	25/52 (48.1)
Genital involvement, *n* (%)	7/52 (13.4)
Previous treatments	
CsA, *n* (%)	31/52 (59.6)
Dupilumab, *n* (%)	29/52 (55.7)
Tralokinumab, *n* (%)	7/52 (13.5)
Upadacitinib, *n* (%)	4/52 (7.7)
Abrocitinib, *n* (%)	2/52 (3.8)

BMI: Body Max Index; CsA: cyclosporine A.

At least one atopic comorbidity was observed in 42.3% of patients; allergic rhinitis was the most frequently reported (34.6%), followed by allergic asthma (19.2%) and allergic conjunctivitis (17.3%).

In addition, 44.2% of patients had at least one non-atopic comorbidity, including cardiovascular/metabolic, autoimmune, and psychiatric disorders, among others (Table 1). Regarding traditional systemic therapies prior to initiating baricitinib, CyA had been used in 31/52 (58.5%) patients and systemic corticosteroids in 33/52 (62.3%). Regarding previous biologic and small molecule therapies, dupilumab had been used in 29/52 patients (54.7%), tralokinumab in 7/52 (13.2%), upadacitinib in 4/52 (7.5%), and abrocitinib in 2/52(3.8%) patients. Notably, 6 patients had been treated with more than one advanced systemic agent. The reasons for switching from dupilumab to baricitinib were inefficacy in 24/29 (82.7%) patients, and the occurrence of AEs in 5/29 (17.2%) cases, including three patients with conjunctivitis, one case of reactive generalized lymphadenopathy, and one case of red face. Previous treatment with tralokinumab and/or abrocitinib was discontinued in all cases due to lack of efficacy, while upadacitinib was suspended due to inefficacy in three cases and abnormal haematological tests in one case.

Baricitinib effectiveness

At baseline patients showed moderate extension and severity of the eczematous lesions [BSA: 19.1 (10.1); EASI: 18.9 (9.1)], intense itching [Itch-NRS: 8.2 (1.5)] and significant impairment of their QoL [DLQI: 20.5 (7.7)] (Table 2). Notably, 48/52 patients (90.6%) started treatment with baricitinib at a dosage of 4 mg/day, which was then maintained throughout the study period.

Significant improvements in both physician-reported outcomes (BSA, EASI) and patient-reported outcomes (Itch-NRS, Sleep-NRS, DLQI, and POEM) were consistently observed over the 52-week follow-up. No significant differences in clinical response, as assessed by BSA, EASI, POEM and DLQI scores, were observed between bio-naïve and bio-experienced patients at week 4 and week 16 (Figure 1).

Table 2. Assessment of disease amelioration at the various timepoints using physician and patient's reported outcome.

Responso endpoints	Week 0 ($n=52$)°	Week 4 ($n=52$)°	Week 16 ($n=52$)°	Week 32 ($n=28$)	Week 54(n Week 52 ($n=16$)
EASI [mean (SD)]*	18.9 (9.1)	8.4 (6.3)	5.3 (4.5)	3.3 (3.5)	3.2 (5.4)
BSA, mean (SD)	19.1 (10.1)	9.7 (8.1)	3.3 (2.6)	2.2 (2.6)	2.0 (3.4)
Itch-NRS, mean (SD)*	8.2 (1.5)	3.8 (2.4)	2.5 (2.8)	2.3 (2.9)	1.4 (2.8)
Sleep-NRS, mean (SD)*	6.6 (2.9)	2.6 (2.2)	1.4 (2.1)	0.8 (2.0)	0.2 (0.8)
DLQI, mean (SD)*	20.5 (7.7)	8.4 (4.9)	2.6 (3.2)	1.7 (3.4)	1.1 (1.8)
POEM, mean (SD)*	24.3 (3.6)	7.3 (4.2)	2.7 (4.2)	2.0 (4.9)	0.7 (1.4)
EASI50 *n* (%)		32/49 (65.3)	41/52 (78.8)	24/28 (85.7)	15/16 (93.7)
EASI75 *n* (%)		9/49 (18.4)	32/52 (61.5)	20/28 (71.4)	14/16 (87.5)
EASI90 *n* (%)		3/49 (6.1)	11/52 (21.1)	14/28 (50.0)	9/16 (56.3)
MDA *n* (%)		3/49 (6.1)	16/52 (30.8)	14/28 (50.0)	10/16 (62.5)

SD: Standard Deviation; BSA: body surface area; EASI: Eczema Area and Severity Index; NRS: Numeric Rating Scale; DLQI: Dermatology Life Quality Index; POEM: Patient oriented Eczema Measure; MDA: Minimal Disease Activity.
*Paired *t* test for the comparison between baseline and subsequent timepoints shows $p<0.001$.
° The reduction in the number of patients at each follow-up visit was due to the fact that patients started treatment at different times and that not all patients had completed 12 months of treatment by the time of the present study.

A significant response was observed as early as week 4 of treatment, with 32/49 (65.3%) and 9/49 (18.4%) patients achieving EASI 50 and EASI 90, respectively. At week 16, EASI 75 and EASI 90 were achieved by 32/52 (61.5%) and 11/52 (21.1%) patients, respectively. Clinical results were sustained through week 52, with 14/16 (87.5%) and 9/16 (56.3%) patients achieving EASI 75 and EASI 90, respectively. A slightly lower but still significant proportion of patients achieved EASI-75 and EASI-90 at both weeks 32 and 52 in the last observation carried forward (LOCF) analysis (Figure 2).

MDA was detected in 16/52 (30.8%) patients at week 16 and 10/16 (62.5%) patients at week 52.

Patients experienced a marked and rapid reduction in AD symptoms, with Itch and Sleep NRS scores decreasing from 8.2 (±1.5) and 6.6 (±2.9) at baseline, to 3.8 (±2.4) and 2.6 (±2.2) at week 4, and further to 2.5 (±2.8) and 1.4 (±2.1) at week 16, respectively. The amelioration of AD signs and symptoms was reflected in the patients' perception of disease severity and its impact on their QoL, with DLQI and POEM scores dropping from 20.5 (7.7) and 24.3 (3.6) at baseline, to 8.4 (4.9) and 7.3 (4.2) at week 4, and 2.6 (3.3) and 2.7 (4.2) at week 16.

Throughout the study period, 11 patients discontinued treatment due to lack of effectiveness: 6 within the first 16 weeks, and 5 during the subsequent period up to week 52. All patients had data available at week 16, while data were available for 28 patients (54%) at week 32 and 16 patients (31%) at week 52. Missing data at later time points mainly reflect patients who had not yet reached the respective follow-up visits.

Analysis of clinical predictors of MDA achievement

The univariable analysis revealed that the presence of atopic comorbidities tends to be associated with a higher proportion of patients achieving MDA, (64.3% versus 35.7%, $p=0.055$), while no significant difference was observed according to baseline clinical severity of the disease, BSA ($p=0.082$) or EASI ($p=0.385$). In the multivariable logistic regression ($N=49$; Prob > χ^2 = 0.0127; Pseudo R^2 = 0.2171) including treatment status (bio-experienced versus bio-naive), atopic comorbidities, and difficult-to-treat areas (head and neck and hand), a significantly higher probability to reach MDA was observed at week 16 among patients with atopic comorbidities (OR= 10.9, 95% CI= 1.21–97.04, $p=0.033$), whereas a reduced likelihood to reach this outcome was observed among patients with head and neck eczema (OR = 0.07, 95% CI= 0.007–0.753, $p=0.028$) (Table 3).

Table 3. Factors associated with treatment response: Multivariate logistic regression analysis.

Variabile	Odds Ratio	Std. Err.	Z	P-valore	95% CI (Basso)	95% CI (Alto)
Bioexperienced (yes)	0.60	0.45	−0.68	0.497	0.14	2.59
Atopic comorbidities (yes)	10.86	12.13	2.13	0.033	1.22	97.04
Head and neck involvement (yes)	0.07	0.09	−2.20	0.028	0.007	0.75
Hands involvement (yes)	0.36	0.29	−1.25	0.212	0.07	1.80

Safety

During the study period up to week 52, a total of 32 AEs were observed in 28 patients. Of these, 24 occurred in the first 6 months of treatment, including acneiform eruption ($n=4$), upper respiratory

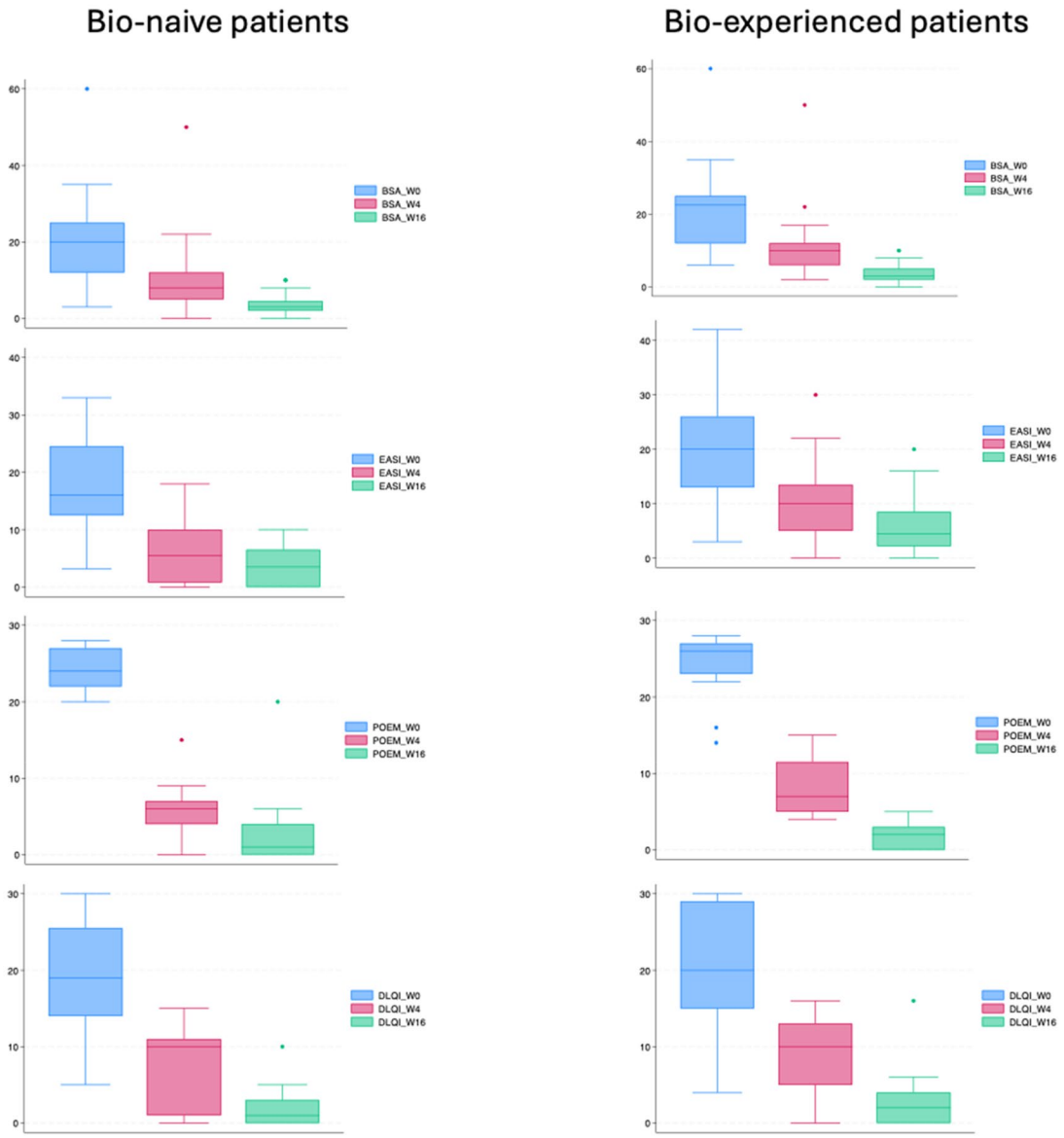

Figure 1. Objective severity scores (BSA, EASI) and patient-reported outcomes (POEM, DLQI) reduction over time in bio- experience and bio—naïve patients.

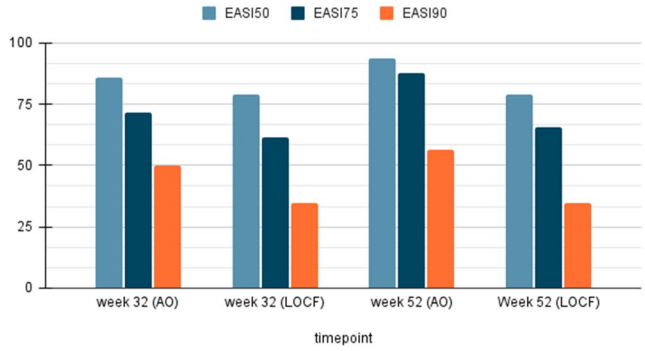

Figure 2. EASI-50, EASI-75, and EASI-90 responses at weeks 32 and 52, analyzed both as-observed and using last observation carried forward (LOCF).

tract infections (URTIs) ($n=2$), herpes simplex ($n=2$), and modest laboratory abnormalities ($n=16$) consisting of hypercholesterolemia ($n=9$), elevations in CPK ($n=6$), hypertriglyceridemia ($n=2$), elevated transaminases ($n=2$), and anemia ($n=1$). Between weeks 36 and 52, 8 additional AEs were reported including acneiform eruption ($n=2$), 1 URTI ($n=1$), and laboratory abnormalities ($n=5$), including mild CPK elevations ($n=3$), hypercholesterolemia ($n=1$), hypertriglyceridemia ($n=1$), and anemia ($n=1$).

All AEs were mild to moderate in severity and did not require treatment discontinuation. In particular, hypercholesterolemia was managed with dietary modifications, omega-3 supplements, and statins, while acne was managed with topical antibiotics in all cases.

Discussion

AD is characterized, especially in the chronic phase, by the overexpression of multiple inflammatory pathways, including Th2, Th17, Th1 and Th9 (1), with the majority of inflammatory mediators signaling through the JAK1 and JAK2 enzymes (5).

Baricitinib, a JAK1 and JAK2 inhibitor, can suppress a broad range of cytokines and chemokines involved in the pathogenesis of AD, showing high clinical efficacy (6–9,13). In particular, in the

phase 3 randomized clinical trial, BREEZE-AD7, 48% of patients treated with baricitinib 4 mg/day and low to moderate potency corticosteroids achieved EASI 75 at week 16, while a significant reduction in pruritus was observed as early as week 2, with sustained improvement continuing throughout the study period. In a long-term extension trial, sustained clinical efficacy was observed, with 55.7% and 47.1% of patients treated with baricitinib 4 mg/day achieving EASI 75 and IGA 0/1 responses, respectively, after 68 weeks of treatment.

In our real-world study, we analyzed the effectiveness and safety of baricitinib in a cohort of 52 patients with moderate disease extension (mean: BSA: 19.1) and a high disease burden (mean EASI: 18.9; mean NRS-itch: 8.2; mean DLQI: 20.5). In line with previous randomized clinical trials, we demonstrated good effectiveness in reducing AD clinical manifestations, as evidenced by significant improvement in both clinician and patient-reported outcomes over the 52-week observation period. Notably, a 55% reduction in the mean EASI score (from 18.9 to 8.4) and a 53.7% reduction in the mean Itch-NRS (from 8.2 to 3.8) were observed at week 4 of treatment, with sustained improvements maintained throughout the whole study period. At week 16, EASI 75 and EASI 90 responses were achieved by 61.5% and 21.1% of patients, respectively, and at week 52, EASI 75 increased to 87.5% of patients and EASI 90 to 56.3%. The improvement obtained on clinical signs and symptoms was mirrored by a marked amelioration of the health-related quality of life, with an 87.4% reduction in the mean DLQI value at week 16 compared to baseline.

Interestingly, more than half of the patient population treated with baricitinib in this study may be considered difficult to treat, since they had failed at least one advanced systemic therapy, including dupilumab and tralokinumab. Despite this, no significant differences were observed in the reduction of patient- and physician- reported outcomes between bio-naïve and bio-experienced patients, suggesting that baricitinib may be a valid therapeutic option for the management of severe AD, both as a first- and second-line treatment. Similar to our finding, a real-world prospective study from the BioDay registry, involving 51 patients treated with baricitinib for up to 16 weeks, found no significant difference in clinical effectiveness between biologic-naïve ($n = 25$) and biologic-resistant ($n = 26$) patients (14). Given the current systemic treatment options for severe AD, the identification of clinical response predictors is essential for optimizing patient management. Within the framework of precision medicine, we assessed the clinical predictors of the achievement of MDA at week 16 (12). The presence of atopic comorbidities was associated with a higher likelihood of achieving MDA, showing a trend in the univariable analysis (64.3% vs 35.7%, $p = 0.055$) and reaching statistical significance in the multivariable model (OR 10.9; 95% CI: 1.21–97.04; $p = 0.033$). Consistently with our findings, a recently published real-world study reported a better long-term therapeutic response to dupilumab in AD patients with atopic comorbidities compared to those without (15). A predominantly type 2 immune endotype has been demonstrated in AD patients with atopic comorbidities (extrinsic phenotype), in contrast to those without atopic comorbidities (intrinsic phenotype), who exhibit a broader inflammatory profile characterized by the overexpression of additional pathways, including Th17 and Th1 (16,17). Despite the broader mechanism of action of baricitinib compared to biologics, our findings suggest that patients with an extrinsic phenotype are more likely to achieve an optimal disease control. This may be due to the narrower range of immune pathways involved in this AD subtype, potentially making it more responsive not only to targeted type 2 therapies but also to other immunomodulators such as JAK inhibitors. Nevertheless, considering the wide 95% confidence interval (1.21–97.04), further studies involving larger patient populations are necessary to confirm this finding.

In this study the involvement of the head and neck area was significantly associated with a reduced likelihood of achieving an optimal response (OR = 0.07; $p = 0.028$). Indeed, head and neck AD represents a complex clinical phenotype that is often difficult to manage with both topical and systemic therapies, including dupilumab, likely due to frequent exposure to irritants, allergens, and microbial agents that exacerbate the disease (18,19). The correct therapeutic management of AD affecting the head and neck area is important as this phenotype is considered the most highly burdensome in terms of patients' QoL (20). Despite our findings suggest a potential resistance of the head and neck area to baricitinib treatment, potentially limiting the achievement of an optimal response, a recent *post hoc* analysis on five clinical trials (BREEZE-AD1, -AD2, -AD4, -AD5, and -AD7) demonstrated favorable and consistent efficacy of baricitinib also on this anatomical area (21). In particular, across such studies, 93–98% of patients had head and neck involvement at baseline, and a comparable reduction in both total body EASI and H&N EASI scores was observed up to week 16 (21). In addition, the effectiveness of baricitinib in the H&N area is supported by real-world evidence (22,23) and a recent consensus guidelines recommend JAK inhibitors as first-line therapy for moderate-to-severe AD affecting this sensitive region (24). Our results, which seem to diverge from the current literature, may be explained by the fact that we adopted a particularly stringent outcome measure.

Notably, in our study, no significant difference was observed in achieving MDA at week 16 based on baseline clinical severity, neither for BSA ($p = 0.082$) nor for EASI ($p = 0.385$). Conversely, a *post hoc* analysis of the phase III study BREEZE-AD7, using a machine learning approach to identify the AD patients' profile with the highest likelihood of response to baricitinib, found baseline BSA and Itch-NRS as the most significant predictors of clinical response, with 69.2% of patients with a baseline BSA of 10–40% and an Itch NRS ≥7 achieving the primary endpoint (EASI 75) at week 16, compared to only 33% of patients with a BSA ≥40% and an Itch NRS <7 (9).

Ineffectiveness represented the most frequent reasons for treatment discontinuation in our study [11 out of 52 patients (21.1%)], in line with findings from other real-world experiences (14,25–27). In terms of safety, 53.8% of patients experienced at least one AE throughout the study period, which is consistent with the percentages reported in clinical trials (51.0–58.0%) (7,8,13). Consistent with findings from clinical trials and other real-world data (7,8,13,14, 25–27), the most commonly reported AEs in our study were acneiform eruption, herpes simplex, upper respiratory tract infections, and laboratory abnormalities, particularly hypercholesterolemia and elevated CPK levels. Notably, no treatment discontinuations were attributed to safety concerns, further supporting the favorable safety profile of the molecule, as observed in clinical trials and real-world experiences (7,8,13,14, 25–27).

The limitations of this study include its partially retrospective design, the limited patient cohort, the lack of a control group, and missing data, as not all patients completed the study due to its observational nature. Therefore, further studies involving larger AD populations are warranted to confirm the clinical predictors of treatment response. The study combined retrospective and prospective data collected under uniform conditions; while this approach maximized sample size, it may carry an inherent risk of selection bias.

In conclusion, this real-world study confirmed the marked effectiveness and favorable safety profile of baricitinib up to

52 weeks. Atopic comorbidities were significantly associated with achieving an optimal response at week 16, whereas prior systemic therapies and baseline disease extent and severity were not significantly associated with clinical outcomes.

Ethical approval and informed consent

The patients included in this study have given written informed consent to publication of their case details. Approval of this study was obtained by the Local Ethics Committee—Comitato Etico Territoriale (CET) Lazio Area 3, Prot. ID: 5909.

Disclosure statement

Outside of the submitted work, authors declare the following conflicts of interest: **Niccolò Gori** served as advisory board member for lectures for AbbVie, Sanofi, and Leo-Pharma. **Marco Galluzzo** has acted as a speaker and/or consultant for AbbVie, Almirall, Eli-Lilly, Johnson & Johnson, LeoPharma, Novartis, and Sanofi outside the submitted work and he has participated in clinical trials for AbbVie, Almirall, Boehringer-Ingelheim, Eli-Lilly, Incyte, Johnson & Johnson, Leo Pharma, Novartis and Sanofi. **Ketty Peris** has served on advisory board and received honoraria for lectures from Abbvie, Almirall, Lilly, Galderma, Leo Pharma, Pierre Fabre, Philogen, Novartis, Sanofi, Sun Pharma, Janssen. **Maddalena Napolitano** has served as a member of advisory board, consultant, speaker, and/or investigator for AbbVie, Almirall, Eli Lilly, Incyte, La Roche Posay, Leo Pharma, Novartis, Pfizer, Sanofi. **Maria Esposito** has served as speaker/consultant for Abbvie, Amgen, Almirall, Boehringer-Ingelheim, Eli Lilly, Janssen, Leopharma, Novartis, Pfizer, Sanofi Regeneron, UCB. **Maria Concetta Fargnoli** has served on advisory boards, received honoraria for lectures and/or research grants from AMGEN, Almirall, Abbvie, Boehringer-Ingelheim, BMS, Galderma, Kyowa Kyrin, Leo Pharma, Pierre Fabre, UCB, Lilly, Pfizer, Janssen, MSD, Novartis, Sanofi-Regeneron and Sunpharma. **Marina Talamonti** declares to have acted as speaker and/or consultant for AbbVie, Almirall, Eli Lilly, Johnson & Johnson, LEO Pharma, Novartis and Sanofi, outside the submitted work. Luca Bianchi declares to have acted as a speaker and/or consultant for AbbVie, Almirall, Eli Lilly, Johnson & Johnson, LEO Pharma, Novartis, Pfizer, Sanofi and UCB outside the submitted work. **Anna Balato** has served as consultant and/or has received fees from: Abbvie, Almirall, Amgen, BI, BMS, Eli-Lilly, Janssen, Incyte, LeoPharma, Novartis, Pfizer, Sanofi, UCB. The other authors have no competing interests to declare.

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Data availability statement

Enquiries related to the data generated or analyzed during this study can be directed to the corresponding author.

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