Prolonged real-life experience with baricitinib in patients with moderate-to-severe atopic dermatitis

Baricitinib is an oral selective Janus-kinase (JAK) 1 and 2 inhibitor for the treatment of moderate-to-severe atopic dermatitis (AD). Its efficacy and safety have previously been demonstrated in clinical trials [1, 2], but only in short-term real-life studies [3-5].

We retrospectively collected real-life data from a monocentric adult patients cohort treated with baricitinib for moderate-to-severe AD in Belgium from January 2021 to May 2023. Patients received baricitinib (4 mg daily, orally) after ineffectiveness or contra-indication of a previous systemic agent. The outcome for effectiveness was evaluated based on the percentage of patients who achieved a validated Investigator Global Assessment for AD (vIGA-AD) of 0 (clear) or 1 (almost clear) at the end of the follow-up. As the prescription was conducted in a real-life setting, patients were allowed to use topical steroids and/or calcineurin inhibitors.

Of the 19 patients included, 14 were male, median age±interquartile range (IQR) was 39.0±29.0 years and the median±IQR follow-up duration was 54.4 ± 64.2 weeks. Baseline demographic and clinical characteristics are summarized in *table 1A*. All patients were previously treated with cyclosporine, which was discontinued due to ineffectiveness or adverse events. One patient had received dupilumab, but stopped due to severe conjunctivitis. For all patients, baricitinib was the first JAK inhibitor prescribed.

At baseline, median vIGA-AD±IQR was 3.0 ± 1.0. The proportion of patients reaching a vIGA-AD of 0 (clear) or 1 (almost clear) was 47.4% (9/19 patients) at the end of the follow-up (May 2023). Improvement in vIGA-AD was significant ($p<0.001$, using a pairwise Wilcoxon signed-rank test) when comparing baseline values with last follow-up visit scores. Patients with less than a 2-point improvement were those with severe disease at baseline (vIGA-AD score of 4). Only one of the 7 patients (14.3%) with severe disease at baseline reached a vIGA-AD score of 0, compared to six of the 10 patients (60%) with moderate disease.

No serious adverse events (AEs) were reported. One patient presented with mild facial acne and another with nausea. Two patients presented with a transient increase of creatinine phosphokinase (10.5%, range: 186-301 units/L; normal value <170 units/L). Increased total cholesterol (>200 mg/dL) and triglycerides (>150 mg/dL) were observed in six patients (31.6%). The rate of all AEs (including biological changes) was 52.6%.

Seven patients (36.8%; six men with a mean age of 43.4 years, child-onset AD, and severe vIGA-AD score in four and moderate in three) discontinued treatment due to lack of effectiveness, with a mean duration of treatment±standard deviation before stopping of 19.6±13.3 weeks. Six of them then rapidly improved with upadacitinib at 30 mg daily, and one with dupilumab.

Five patients with concomitant alopecia areata (AA) showed signs of hair regrowth. At the end of the follow-up, three achieved a Severity of Alopecia Tool (SALT) score of 0 (complete regrowth), and two showed encouraging signs of regrowth, but SALT score remained >20. *Table 1B* summarizes the demographic and clinical characteristics of patients with concomitant AD and AA.

The results of this extended real-life study are consistent with those of BREEZE AD7 (31% of patients with vIGA-AD score of 0/1 at week 16) and the BREEZE AD3 long-term study (47.1% at week 68) [6]. Data on safety are consistent with the pooled safety analysis [7].

Table 1. A) Demographics and clinical characteristics of patients included in the study. B) Demographics and clinical characteristics of patients with concomitant atopic dermatitis and alopecia areata.

A

Variable	Value
Median age, years (± interquartile range)	39.0 (± 29.0)
Sex, male, *n*/*n* total	14/19
Age at onset of atopic dermatitis, *n* (%)	
Child	10 (52.6)
Teenager	2 (10.5)
Adult	7 (36.8)
History of personal atopy, *n* (%)	
Allergic asthma	3 (15.8)
Allergic rhino conjunctivitis	8 (42.1)
Not available	8 (42.1)
Previous topical treatments for atopic dermatitis, *n* (%)	
Emollients	11 (57.9)
Topical corticosteroids	11 (57.9)
Topical immunomodulators	4 (21.0)
Not available	7 (36.8)
Previous systemic treatments for atopic dermatitis, *n* (%)	
Corticosteroids	8 (42.1)
Cyclosporine	18 (94.7)
Phototherapy	4 (21.0)
Methotrexate	1 (5.3)
Dupilumab	1 (5.3)

B

Patient *n*°	Sex	Age (years)	AD severity at baseline (vIGA-AD score)	AA type[a]	AA duration	Previous treatments for AA	Time before hair regrowth with baricitinib treatment	Description of regrowth/SALT score	AD severity at last follow-up visit	Follow-up duration
1	F	27	3	Patchy (head)	15 years	Topical CS, intralesional CS injection, methylprednisolone infusion	6 weeks	Complete regrowth (SALT score = 0)	1	20 months
2	F	35	2	Patchy (head)	5 years	Topical CS, intralesional cs injection, minoxidil, cyclosporine	6 weeks	Complete regrowth (SALT score = 0)	0	13 months
3	F	18	2	Patchy (head)	9 years	Topical CS, isoprinosine, minoxidil 2%/5%	8 weeks	Complete regrowth (SALT score = 0)	0	13 months
4	H	70	3	Universalis	63 years	Unknown	12 weeks	Partial regrowth in the beard and occipital area (SALT score > 20)	1	3 months
5	H	21	3	Totalis	7 years	UV, intralesional CS injection, topical CS, minoxidil	4 weeks	Partial regrowth (SALT score > 20)	1	6 months

[a]*All patients had a Severity of Alopecia Tool (SALT) score of 50 or higher (range: 0 [no scalp hair loss] to 100 [complete scalp hair loss]) before baricitinib initiation. AA: alopecia areata; CS: corticosteroids; F: female; M: male; UV: ultraviolet; vIGA-AD: Validated Investigator Global Assessment for Atopic Dermatitis.*

Lipid level changes were the most frequent AE encountered but did not lead to treatment discontinuation or any major adverse cardiovascular event (MACE). However, the proportion of patients discontinuing treatment due to lack of effectiveness was 36.8%, compared to the 1-2% drop-out in clinical trials.

The effective shift of patients with a history of difficult-to-treat AD to another systemic immunomodulatory agent (upadactitinib or dupilumab) is consistent with a recent systematic review and network meta-analysis [8], as well as real-life data [9], assessing the superiority of these treatments, compared to baricitinib.

To conclude, baricitinib in a real-life setting seems to be more effective in treating patients with moderate rather than severe and long-lasting AD. Safety data are reassuring, in particular, no thromboembolic or cardiovascular AEs were observed, within the limits of the follow-up period. Lipid changes were the most frequent AE. The effectiveness of baricitinib as a treatment for hair regrowth among patients with concomitant AD and alopecia areata [10] may guide the choice towards baricitinib for this specific patient phenotype. ■

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None of the authors has scientific or financial conflicts of interests to declare in the current reported study.

Data Availability Statement: *The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.*

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Increasing trend in confirmed scabies cases in the only public dermatological institute of scientific research and care in Italy

Scabies, a parasitic skin infestation, caused by the mite *Sarcoptes scabiei var. hominis*, has been declared a neglected tropical disease by WHO in 2017 [1]. Although more common in developing countries and tropical areas, scabies has been increasingly observed in Europe over the last years [2, 3]. Increasing trends have been reported in several countries, even during the COVID-19 lockdowns [2, 4-6]. Noteworthy, the restrictive measures adopted during the pandemic also caused delayed diagnoses [7].

We conducted a retrospective observational study to investigate the trend of confirmed scabies diagnoses at the only public dermatological institution of scientific research and care in Italy over the last five years.

Data were retrieved from the records of the Microbiology Outpatient Service of the San Gallicano Dermatological Institute IRCCS (Rome, Italy). The records of all patients who underwent a parasitological examination between January 2019 and May 2023 with a suspicion of scabies were reviewed. Laboratory-confirmed diagnosis was based on the observation of mites, eggs or faeces in skin samples obtained by scarification and examined under a light microscope [8]. Socio-demographic data were retrieved for all cases with a positive microscopic examination.

Overall, 280 individuals underwent parasitological examination. Among them, 60 (21.4%) had a confirmed scabies diagnosis (age range: 3-85 years; median: 41 years, IQR: 22-58; 46 males [76.7%]). The highest number of diagnoses was observed during the first five months of 2023 (23/60, 38.3%), when the number of cases exceeded that of each of the previous four years: 6 (10.0%) in 2019, 5 (8.3%) in 2020, 8 (13.3%) in 2021, and 18 (30.0%) in 2022. The number of cases per semester over the entire study period is shown in *figure 1A*. Although the lesions mainly involved the classic sites (interdigital spaces, wrists, axillae, umbilical area, extremities and genitalia), unusual clinical presentations were observed in two cases in 2023. Atypical manifestations, including generalized pustular-like lesions on an erythematous base, as well as diffuse purpura-like lesions both required a biopsy. The presence of the mite allowed the diagnosis (*figure 1B*).

Overall, over half of the scabies patients (34/60, 56.7%) had been seen by practitioners of the Allergology Department, followed by the General Dermatology Department (14/60, 23.3%), and the sexually transmitted infection (STI) unit (9/60, 15.0%). The remaining three patients (5.0%) had been referred directly to the Microbiology Outpatient Service from general practitioners. Notably, patients from the STI unit were significantly younger than those from the other departments of the hospital (median age: 33 years *vs* 42 from the Allergology Department and 52 from the General Dermatology Department). Patients from the STI unit were all "men who have sex with men", for whom scabies infestation had occurred through sexual contact.

All patients were treated as recommended by the European guidelines (permethrin 5% cream, oral ivermectin, benzyl benzoate 10-25% lotion) [9]. After 2-4 weeks from treatment initiation, all patients showed

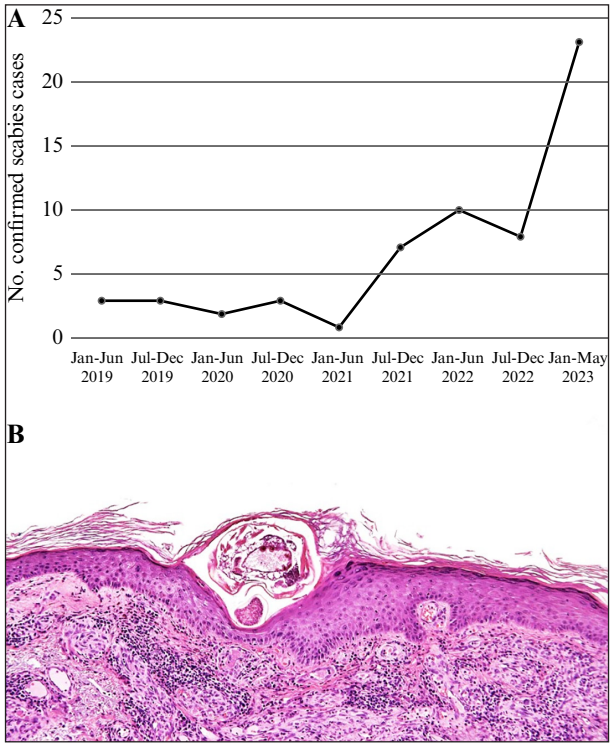

Figure 1. A) Number of laboratory-confirmed scabies cases per semester from January 2019 to May 2023 in an Italian public dermatological hospital. **B**) Skin biopsy showing scabies mites in the epidermis (haematoxylin-eosin stain; ×400).