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# Real-life effectiveness and safety of baricitinib in patients with severe alopecia areata: A 24-week Italian study

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## Abstract

**Background:** Alopecia areata is an autoimmune condition characterized by rapid hair loss in the scalp, eyebrows and eyelashes, for which treatments are limited. Baricitinib, an oral inhibitor of Janus kinases 1 and 2, has been recently approved to treat alopecia areata.

**Materials and Methods:** We conducted a retrospective study involving 23 medical centres across Italy, enrolling patients affected by severe alopecia areata (SALT >50), for more than 6 months. Clinical and trichoscopic assessment was performed at each visit and impact on quality of life, anxiety and depression were evaluated using the Skindex-16 and the Hospital Anxiety and Depression Scale (HADS), respectively.

**Results:** A total of 118 patients were enrolled, with a mean age of 39 years and a mean SALT >95. The mean value of the SALT score decreased from an average of 96.6 ( $\pm 8.23$  sd) to 48 ( $\pm 35.2$  sd) after 24 weeks of treatment and 42.3% of patients achieved a SALT 30, 31.3% a SALT 20 and 20.3% a SALT 10 by Week 24. Trichoscopic signs showed fewer yellow dots and black dots significantly earlier than hair regrowth. Adverse events during the treatment period (mild laboratory test abnormalities) were reported in 12.7% patients. No drop-out were registered.

For affiliations refer to page 1150.

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**Conclusions:** Data on the effectiveness and safety of baricitinib are promising and support the use of this drug in severe forms of AA, also in the early stages. We also suggest performing trichoscopy in order to reveal early response to therapy.

## INTRODUCTION

Alopecia Areata (AA) is an autoimmune disorder, with an estimated lifetime risk of approximately 2%. While the precise cause of AA is not fully understood, it is believed to result from a combination of genetic factors and environmental factors.<sup>1</sup> The prevalence of AA seems to exhibit variations across age groups and genders, being more prevalent among children and females.<sup>1-3</sup> It manifests as non-scarring hair loss, typically occurring in small patches on the scalp, though it can also affect other hair-bearing areas like eyelashes and eyebrows.<sup>3,4</sup> In severe cases, it can lead to total loss of scalp hair (known as alopecia areata totalis (AT)) or even complete loss of body hair (referred to as alopecia areata universalis (AU)). AA has a significant psychological impact, considerably impacting on quality of life and often resulting in depression and anxiety.<sup>2</sup> Diagnosis of AA primarily relies on clinical and trichoscopic evaluation, identifying hallmark signs like 'exclamation point' hairs in active patches and other indicative features such as black dots during acute phases and yellow dots in chronic AA.<sup>4</sup> Laboratory tests serve to exclude other autoimmune conditions, while histological examinations, albeit infrequent, may reveal inflammatory cell clusters around hair follicles in the so-called swarm of bee lymphocyte infiltration.<sup>4</sup> Traditionally, managing AA has been challenging, with treatments like topical steroids, systemic immunosuppressants and contact immunotherapy yielding inconsistent results.<sup>5,6</sup> Recently JAK inhibitors (JAKis) demonstrated high efficacy associated with a favourable safety profile. In particular, baricitinib, a first-generation JAK1 and JAK2 inhibitor<sup>7</sup> and ritlecitinib, a JAK3 and tyrosine kinase (TEC) inhibitor have been tested in randomized controlled clinical trials.<sup>7,8</sup> The double blind, randomized clinical trials BRAVE-AA1 and BRAVE-AA2 demonstrated that a daily 4 mg dose of baricitinib led to a notably higher proportion of adult patients with severe AA achieving a Severity Alopecia Tool (SALT) score of 20 or less compared to those on a 2-mg dose or placebo at Week 36.<sup>7,9</sup>

By conducting a retrospective study across 23 centres in Italy, we evaluated 118 adult AA-diagnosed patients undergoing treatment with a daily 4 mg dosage of baricitinib. Our study aimed to evaluate treatment effectiveness and tolerability, adverse events, and overall patient outcomes with this new drug in real life, shedding light on the practical implications of this novel therapeutic approach for AA.

## MATERIALS AND METHODS

A retrospective study involving 23 medical centres across Italy was conducted, encompassing 118 patients diagnosed

### Why was the study undertaken?

The study was conducted to assess the effectiveness and safety of baricitinib in alopecia areata.

### What does this study add?

Our results confirm the effectiveness and safety of baricitinib, and highlight that early response to treatment can be detected with trichoscopy.

### What are the implications of this study for disease understanding and/or clinical care?

The results confirm that baricitinib is an effective and safe treatment for AA and its use is promising.

with AA and undergoing treatment with baricitinib at a dosage of 4 mg per day for at least 24 weeks.

Patients were eligible if aged between 18 and 60 years, of both sexes, had a SALT score  $\geq 50$  ( $\geq 50\%$  scalp hair loss) and a current AA episode lasting  $>6$  months and  $<6$  years, without spontaneous improvement (i.e.  $\leq 10$ -point reduction in SALT score) over the 6 months prior to screening. Diagnosis of AA relied on clinical examination and trichoscopic assessment. We gathered demographic data from the patients as well as baseline clinical information related to AA and its treatment. The evolution of AA with baricitinib treatment and the outcomes of the patients were evaluated at specific intervals (T0, T4w, T12w and T24w) throughout the study, using the clinical SALT Score<sup>10</sup> trichoscopy, laboratory tests, Skindex-16 and Hospital Anxiety and Depression Scale (HADS).<sup>11</sup> SALT score is the worldwide severity score now utilized to grade AA severity.<sup>10</sup> It calculates the percentage of scalp involvement by AA by adding the percentages of hair loss of four different areas: vertex, lateral areas and back. SALT 0 corresponds to no hair loss and SALT 100 to complete loss of scalp hair. SALT  $>50\%$  characterizes severe AA, with SALT  $>95\%$  representing the very severe forms (AT and AU). A SALT  $\leq 20\%$  is usually considered a treatment success, associated with significant improvement in life quality index. Patients were also divided in early responders, that is, those who achieved SALT 30 within the first 12 weeks (Figure 1), and gradual responders, that is, those who achieved SALT 30 after Week 12 and up to Week 24 (Figure 2).

Trichoscopy was utilized to assess the course of AA during therapy: acute worsening AA shows trichoscopy signs such as black dots, exclamation point hair and dystrophic hair; conversely, chronic AA shows yellow dots and thin



**FIGURE 1** Early responder: (a, b) clinical presentation and (c) trichoscopy.



**FIGURE 2** Gradual responder: (a, b) clinical presentation and (c) trichoscopy.

**TABLE 1** Epidemiological data.

Center, <i>n</i>	23
Patients enrolled, <i>n</i> (%)	118 (100.0%)
Sex	
Female, <i>n</i> (%)	85 (72.0%)
Male, <i>n</i> (%)	33 (28.0%)
Age at enrolment, medium (IQR)	39 (26–50)
Age at diagnosis of AA, medium (IQR)	29 (16–42)
Familiarity for AA, <i>n</i> (%)	14 (11.9%)

Abbreviations: AA, alopecia areata; IQR, interquartile range.

nonpigmented hair; during the regrowing phase, upgrowing pointed hair may be observed. The presence of these signs at each follow-up visit and their changes were used to assess treatment response.

Skindex-16, Hospital Anxiety and Depression Scale (HADS) were utilized to assess changes in quality of life and psychological impact of AA patients, respectively. Skindex-16 consists of three domains (symptoms, emotions and functioning) with normalized scores ranging from 0 (no effect) to 96 (effect experienced all the time).<sup>11</sup> Values for the Hospital Anxiety and Depression Scale–Anxiety Total Score (HADS-A) and Hospital Anxiety and Depression Scale–Depression Total Score (HADS-D) range from 0 to 21, with higher scores indicating greater anxiety or depression. The HADS was used to identify patients with borderline or abnormal scores for anxiety or depression at baseline (HADS-A or HADS-D  $\geq$  8) with scores of  $<$ 8 considered normal.<sup>12</sup>

Adverse event experienced by the patients during the study period were documented at scheduled visits, as well as clinical laboratory tests and safety assessments. Reporting of adverse events and their severity was based on the investigator's subjective assessment.

Descriptive statistical analysis was used to summarize patient demographics, disease characteristics, treatment history, outcomes and adverse events. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the ethics committees of all participating centres. Furthermore, informed written consent was obtained from all patients who participated in the study.

## RESULTS

A total of 23 university hospitals from all the country participated in this study, enrolling 118 patients with AA, comprising 85 (72.0%) females and 33 (28.0%) males. The female-to-male ratio among patients was 2.6 (Table 1). The median age at enrolment was 39 years (interquartile range [IQR]: 26–50), while the median age at AA first diagnosis stood at 29 years (IQR: 16–42): the mean duration of AA was 9.7 years (IQR: 3–12). Familial occurrence of AA in was observed in 14 patients (11.9%).

**TABLE 2** Characteristics and previous treatment of alopecia areata.

Type of AA	
Alopecia in multiple patches, <i>n</i> (%)	12 (10.2%)
AT, <i>n</i> (%)	20 (16.9%)
AU, <i>n</i> (%)	86 (72.9%)
Years of duration of AA, medium (IQR)	9.7 (3–12)
Previous topical treatments	
High potency steroid cream, <i>n</i> (%)	113 (95.8%)
SADBE/DFC, <i>n</i> (%)	44 (37.3%)
Antralin, <i>n</i> (%)	10 (8.5%)
Intralesional triamcinolone acetonide, <i>n</i> (%)	3 (2.5%)
Previous systemic treatments	
Systemic steroid, <i>n</i> (%)	107 (90.7%)
CyA, <i>n</i> (%)	27 (22.9%)
MTX, <i>n</i> (%)	25 (21.2%)
Outcome of previous treatments	
NR, <i>n</i> (%)	101 (85.6%)
PR, <i>n</i> (%)	17 (14.4%)

Abbreviations: AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; CyA, cyclosporine A; DFC, diphenylcyclopropanone; IQR, interquartile range; MTX, methotrexate; NR, no response; PR, partial response; SADBE, squaric acid dibutyl ester.

**TABLE 3** Associated comorbidities.

Concomitant autoimmune diseases	
Autoimmune thyroiditis, <i>n</i> (%)	18 (15.3%)
Atopy, <i>n</i> (%)	8 (6.8%)
Celiac disease, <i>n</i> (%)	2 (1.7%)
Psoriasis, <i>n</i> (%)	2 (1.7%)
Vitiligo, <i>n</i> (%)	1 (0.8%)
Chronic spontaneous urticaria, <i>n</i> (%)	1 (0.8%)
Autoimmune polyendocrinopathy, <i>n</i> (%)	1 (0.8%)
Undifferentiated connectivitis, <i>n</i> (%)	1 (0.8%)
Other concomitant diseases	
Osteoporosis, <i>n</i> (%)	2 (1.7%)
Type 2 diabetes mellitus, <i>n</i> (%)	2 (1.7%)
Relapsing herpes simplex, <i>n</i> (%)	1 (0.8%)
Klippel–Trenaunay syndrome, <i>n</i> (%)	1 (0.8%)

Regarding the severity and type of AA, 12 (10.2%) patients showed patchy alopecia with SALT ranging from 100 to 58, 20 patients (16.9%) had AA totalis (AT) and 86 patients (72.9%) had AA universalis (AU). Previous treatments included high-potency topical steroids (95.8%), topical immunotherapy (squaric acid dibutyl ester or diphenylcyclopropanone) (37.3%), anthralin (8.5%) and intralesional corticosteroids (2.5%). Systemic treatments included steroids (90.7%), cyclosporine A (22.9%) and methotrexate (21.2%). Notably, the outcomes of previous treatments resulted in no response (85.6%) or only partial response (14.4%) (Table 2). Comorbidities observed among AA patients included

**TABLE 4** Scores.

	Skindex-16 (medium)	HADS depression (medium)	HADS anxiety (medium)	SALT (medium)
T0	58	6.86	7.36	96.6
T4w	51	5.60	6.61	89.3
T12w	44	5.02	5.81	69.0
T24w	38	5.18	5.65	48.0

Abbreviations: HADS, Hospital Anxiety and Depression Scale; SALT, Severity of Alopecia Tool.

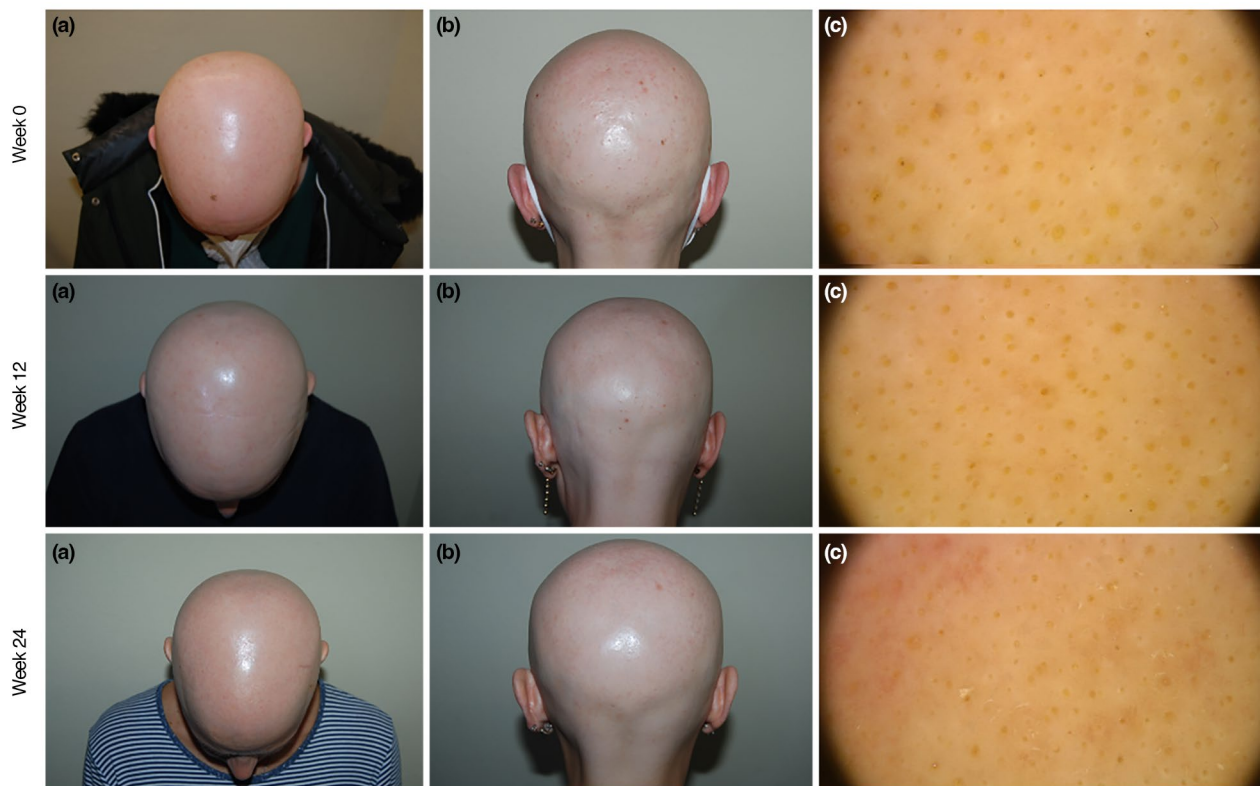
**FIGURE 3** Patient with SALT  $\geq 50$  after 24 weeks of treatment: (a, b) clinical presentation and (c) trichoscopy.

autoimmune thyroiditis (15.3%), atopy (6.8%), celiac disease (1.7%), psoriasis (1.7%), vitiligo (0.8%) and other rarer conditions. Other concomitant diseases noted were osteoporosis (1.7%), Type 2 diabetes mellitus (1.7%), relapsing herpes simplex (0.8%) and Klippel–Trenaunay syndrome (0.8%) (Table 3).

Scores from standardized scales recorded at specific intervals (T0, T4w, T12w and T24w) revealed that the SALT score decreased from an average of 96.6 ( $\pm 8.23$  sd) at T0 to 48 ( $\pm 35.2$  sd) at T24w (Table 4). A total of 42.3% (50/118) patients achieved a SALT 30, 31.3% (37/118) a SALT 20 and 20.3% (24/118) a SALT 10 by Week 24. SALT  $\geq 50$  was seen in 44.1% (52/118) of patients (Figure 3), and SALT = 100 in 12.7% of patients (17/118) after 24 weeks of treatment (Figure 4). Trichoscopic signs observed throughout the study showed notable changes through time. The mean number of patients showing yellow dots decreased from 115 (97.5%) at T0 to 82 (69.5%) at T24w. Likewise, black dots declined

from 49 patients (41.5%) to 20 (16.9%) during the same period. Dystrophic hairs reduced from 20 (16.9%) to 7 patients (5.9%), exclamation mark hairs decreased from 18 (15.3%) to 5 (4.2%) patients, and regrowing hairs increased from 9 (7.6%) to 93 (82.3%) cases (Table 5). The correlation between SALT score and Skindex-16 at Week 24 was significant (Rho Spearman coefficient;  $p < 0.001$ ). The mean value of Skindex-16 decreased from 58 at T0 to 38 at T24w. Similarly, assessments using the HADS showed reductions in mean values regarding depression score (from 6.86 [T0] to 5.18 [T24w]) and anxiety score (from 7.36 [T0] to 5.65 [T24w]) over the study period.

Adverse events that emerged during the treatment period were reported in 15 of 118 patients (12.7%) with 4 mg baricitinib, and consisted in mild laboratory test abnormalities: hypertriglyceridaemia ( $>150$  mg/dL) was seen in 3 cases at T4w, and in 1 case it decreased without any measure at T24w; neutropenia was observed at T4w in 1 case, while transient



**FIGURE 4** Patient with SALT = 100 after 24 weeks of treatment: (a, b) clinical presentation and (c) trichoscopy.

**TABLE 5** Trichoscopic signs.

	Yellow dots, <i>n</i> (%)	Black dots, <i>n</i> (%)	Dystrophic hairs, <i>n</i> (%)	Exclamation mark hairs, <i>n</i> (%)	Regrowing hairs, <i>n</i> (%)
T0	115 (97.5%)	49 (41.5%)	20 (16.9%)	18 (15.3%)	9 (7.6%)
T4w	109 (92.4%)	34 (28.8%)	14 (11.9%)	8 (6.8%)	49 (41.5%)
T12w	93 (78.8%)	21 (17.8%)	8 (6.8%)	6 (5.1%)	88 (74.6%)
T24w	82 (69.5%)	20 (16.9%)	7 (5.9%)	5 (4.2%)	93 (82.3%)

increased creatine phosphokinase (CPK) was identified at T12w in 1 case; increased gamma-glutamyl transferase (gamma-GT) and serum creatinine were reported at T24w in 1 case, with no changes at other time points (Table 6).

Regarding adverse events, a mild acneiform reaction was reported in 5 patients, at T12w in 1 case and at T24w in 4. Headache of mild intensity and responding to non-steroidal anti-inflammatory drugs was reported by 6 patients: at T4w by 4 cases, at T12w by 1 and at T24w by 2 cases. Fatigue was reported by 1 patient at all follow-up visits: T4w, T12w, and T24w. Cystitis was seen in 1 case, at both T12w and T24w; high fever occurred at T12w and T24w in 1 case. One patient temporarily discontinued therapy due to an episode of cholecystitis. Aphthoid lesions were observed at T4w in 1 case. Benign paroxysmal positional vertigo occurred in 1 case at T12w. Constipation was reported in 2 cases at T24w. Other adverse events are reported in (Table 7). No permanent

treatment discontinuation of therapy was necessary, and all 118 patients are continuing treatment.

## DISCUSSION

This retrospective real-life study demonstrated an increasing in time effectiveness as well as good tolerability of baricitinib 4 mg at 24 weeks in adults with severe AA. Patients enrolled had a current AA episode lasting >6 months and <6 years, to evaluate also early stages of the disease. The response rates measured with the SALT score continuously increased over the 24 weeks and 42.3% (50/118) patients achieved a SALT 30, 31.3% (37/118) a SALT 20 and 20.3% (24/118) a SALT 10 at Week 24, confirming previous studies.<sup>7</sup> The percentages of patients who had a SALT score of 20 or less at Week 36, were 38.8% with 4 mg baricitinib, 22.8% with 2 mg baricitinib and

**TABLE 6** Blood exams.

	T4w	T12w	T24w
Hypertriglyceridaemia	3	1	–
Neutropenia	1	–	–
Transient increased CPK	–	1	–
Increased gamma GT	–	–	1
Increased creatinine	–	–	1
Hypertransaminasemia	–	–	–
Hypercholesterolaemia	–	–	–

**TABLE 7** Adverse events.

	T4w	T12w	T24w
Acneiform rash	–	1	4
Aphthoid lesions	1	–	–
Benign paroxysmal positional vertigo	–	1	–
Constipation	–	–	2
Cystitis	–	1	1
Fatigue	1	1	1
Fever	–	1	1
Focal epileptic seizure	–	1	–
Headache	4	1	2
Herpes simplex labial	1	1	2
Nasal abscess	–	1	–
Nausea	2	–	–
Prostatitis	–	1	–
Rosaceiform rash on the face	1	–	–
Trichodynia	–	–	2
Upper respiratory tract infection	–	1	–
Vaginal candidiasis	1	–	–
Vesicular rash	1	–	–
Weight gain	–	–	1

6.2% with placebo in BRAVE-AA1 and 35.9%, 19.4% and 3.3%, respectively, in BRAVE-AA2.<sup>7</sup> Looking at the trajectories of response to treatment, according to the post hoc analysis of the BRAVE-AA1 and AA2 studies, we divided our patients in early responders, that is, those who achieved SALT 30 within the first 12 weeks, and gradual responders, that is, those who achieved SALT 30 after Week 12 and up to Week 24<sup>9</sup>; 18.6% (22/118) of our patients were 'early responders', a percentage lower than that reported in the BRAVE study (32.6%), whereas 24.5% (29/118) were medium responders, a percentage similar to that of the BRAVE. This lower speed of response seen on our series can be explained by the severity scores of AA in our patients, as severity of AA influences speed of response, with more severe forms showing a slower response. In fact, we enrolled patients with very severe AA, with a mean SALT score of 96.6 ( $\pm 8.23$  SD) at baseline, compared to the SALT scores of 85.3 ( $\pm 18.2$  SD) and 84.8 ( $\pm 18.1$  SD) of the BRAVE-AA1 and AA2 studies.

Evidence indicates that patients with very severe AA (SALT score 95–100) have a lower chance of achieving an early response than patients with severe AA (SALT score 50 to <95).<sup>7</sup> The Italian Drug Agency (also known as AIFA) allowed the prescription of baricitinib treatment with public health funding, but it was not clear for which grade of severity. For this reason, we enrolled only very severe cases of AA.

This is the first time in which trichoscopy outcomes are evaluated in a study on effectiveness and safety of baricitinib in AA. From baseline to Week 24 we observed a progressive increase in the percentage of regrowing hair from 7.6% to 82.3% and a decrease of black dots from 41.5% to 16.9%. This indicates that trichoscopy can highlight signs of regrowth earlier than clinical evaluation with SALT, as the regrowing hair are not easy to see with the naked eye. The gradual disappearance of signs of AA activity like black dots, exclamation marks hair and dystrophic hair is another trichoscopy sign of hair regrowth.

The more the studies on baricitinib are prolonged the more we understand that hair regrowth may take weeks and even months to appear: most responses to baricitinib treatment are seen during the first months of treatment, but data at the 52-week follow-up show that response rates continue to increase over time, as some patients have a delayed response. Therefore, a longer follow-up is needed to confirm the optimal duration of treatment for gradual and late responders to achieve maximum benefit.

The mean value of Skindex-16 in our patients decreased from 58 at T0 to 38 at T24w, similarly to the data reported in the literature.<sup>7</sup> In the BRAVE studies, the Skindex-16 scores were reported dividing results between symptoms domain, emotions domain and functioning domain. Greater baseline impairment was reported in the emotions and functioning domains of Skindex-16.<sup>3</sup> Several studies have clearly established that AA can have a psychological and psychosocial impact on patients' quality of life, as confirmed by our results. The HADS scales showed reductions in mean values regarding depression score (from 6.86 [T0] to 5.18 [T24w]) and anxiety score (from 7.36 [T0] to 5.65 [T24w]) over the study period. At baseline 46% of patients had a borderline or abnormal HADS-D score, while the percentage decreased to 27.4% of patients after 24 weeks of treatment. Similar changes were seen in the HADS-A score, which was abnormal in 47.7% of patients at baseline, versus 34.5% of patients after 24 weeks of treatment. In the BRAVE studies only a limited number of patients presented with an abnormal HADS scores at baseline, maybe due to the exclusion of patients with significant uncontrolled neuropsychiatric disorders.<sup>3,7</sup> The correlation between SALT score and Skindex-16 at Week 24 was significant ( $p < 0.001$ ), confirming that improvement in Skindex-16 AA and HADS is associated with scalp hair regrowth only.

Regarding adverse events, our data showed that there is not an increase of adverse events during time: most of the side effect were reported at Week 4 and the incidence did not rise over time. Adverse events were reported in 12.7% of our patients, with most being mild laboratory abnormalities,

while in the published trials they were reported in 59.6% of patients over a 52-week treatment period. A recent systematic review showed that laboratory abnormalities represented 40.1% of adverse events in patients treated with JAK inhibitors, not only baricitinib.<sup>13</sup> No serious adverse events that led to discontinuation were reported, just one patient out to 118 (0.84%) temporarily discontinued the treatment due to an episode of cholecystitis, a side effect also reported in the Phase 3 BRAVE clinical trial with a incidence of 2.1% of 280 patients.<sup>7</sup>

The most reported adverse event in our cohort was an acneiform rash,<sup>14</sup> while in the clinical trials the most reported one were respiratory infections.<sup>7</sup> Perhaps climatic differences between Italy and the US may explain this different prevalence and further studies will show if type and prevalence of side effects of baricitinib vary in the different climatic regions.

Our study has several limitations. First, assessment of alopecia in other body areas, that is, eyebrows and eyelashes as well as nail changes was not assessed, and the contribution of their regrowth/improvement on quality of life and levels of anxiety and depression. The retrospective nature of the study and the absence of a control group limit the ability to draw definitive conclusions on the efficacy and safety of baricitinib compared to standard treatments or placebo. Moreover, the relatively small sample size and the short-term follow-up duration might restrict the generalizability of our findings. However, our study included several centres across the country, reducing the possible bias of interpretation of the results and several clinical parameters were evaluated.

## CONCLUSIONS

These preliminary data, on the effectiveness and safety of baricitinib in real-life setting among a cohort of over 100 patients are very promising and support the use of this drug in severe forms of AA. Early start of therapy, especially when duration of the disease is short, may be suggested, as well as performing trichoscopy to reveal responses to therapy earlier than clinical examination.

## AUTHOR CONTRIBUTIONS

Conceptualization and methodology: BMP and MS. Data curation and project management: All authors. Formal analysis and writing—original draft: BMP, MS, FP, SC, LR and FQ. Writing—review and editing: BMP, MS, FP, AR, FL, GM, FDO, MTC, LB, AS, GC, GG, PG, FP, NP, CF, AVM, MCF, EC and CF.

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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.

## ETHICAL APPROVAL

This study was conducted in accordance with the Declaration of Helsinki.

## ETHICS STATEMENT

The patients in this manuscript have given written informed consent to the publication of their case details.

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## REFERENCES

- Zhou C, Li X, Wang C, Zhang J. Alopecia areata: an update on etiopathogenesis, diagnosis, and management. *Clin Rev Allergy Immunol*. 2021;61(3):403–23.
- Dainichi T, Iwata M, Kaku Y. Alopecia areata: What's new in the epidemiology, comorbidities, and pathogenesis? *J Dermatol Sci*. 2023;112(3):120–7.
- Piraccini BM, Ohyama M, Craiglow B, Bewley A, Ding Y, Chen YF, et al. Scalp hair regrowth is associated with improvements in health-related quality of life and psychological symptoms in patients with severe alopecia areata: results from two randomized controlled trials. *J Dermatolog Treat*. 2023;34(1):2227299.
- Alessandrini A, Bruni F, Piraccini BM, Starace M. Common causes of hair loss – clinical manifestations, trichoscopy and therapy. *J Eur Acad Dermatol Venereol*. 2021;35(3):629–40.
- Freitas E, Guttman-Yassky E, Torres T. Baricitinib for the treatment of alopecia areata. *Drugs*. 2023;83(9):761–70.
- Rossi A, Muscianese M, Piraccini BM, Starace M, Carlesimo M, Mandel VD, et al. Italian guidelines in diagnosis and treatment of alopecia areata. *G Ital Dermatol Venereol*. 2019;154(6):609–23.
- King B, Ohyama M, Kwon O, Zlotogorski A, Ko J, Mesinkovska NA, et al. BRAVE-AA investigators. Two phase 3 trials of Baricitinib for alopecia areata. *N Engl J Med*. 2022;386(18):1687–99.
- King B, Zhang X, Harcha WG, Szepletowski JC, Shapiro J, Lynde C, et al. Efficacy and safety of ritlecitinib in adults and adolescents with alopecia areata: a randomised, double-blind, multicentre, phase 2b-3 trial. *Lancet*. 2023;401(10387):1518–29.
- King B, Shapiro J, Ohyama M, Egeberg A, Piraccini BM, Craiglow B, et al. When to expect scalp hair regrowth during treatment of severe alopecia areata with baricitinib: insights from trajectories analyses of patients enrolled in two phase III trials. *Br J Dermatol*. 2023;189(6):666–73.
- Olsen EA, Hordinsky MK, Price VH, Roberts JL, Shapiro J, Canfield D, et al. National Alopecia Areata Foundation. Alopecia areata investigational assessment guidelines—Part II. National Alopecia Areata Foundation. *J Am Acad Dermatol*. 2004;51(3):440–7.
- Chren MM. The Skindex instruments to measure the effects of skin disease on quality of life. *Dermatol Clin*. 2012;30(2):231–6. xiii.
- Snaith RP. The hospital anxiety and depression scale. *Health Qual Life Outcomes*. 2003;1:29.
- Sechi A, Song J, Dell'Antonia M, Heidemeyer K, Piraccini BM, Starace M, et al. Adverse events in patients treated with Jak-inhibitors for alopecia areata: a systematic review. *J Eur Acad Dermatol Venereol*. 2023;37:1535–46.
- Avallone G, Mastorino L, Tavoletti G, Macagno N, Barei F, Schena D, et al. Clinical outcomes and management of JAK inhibitor-associated acne in patients with moderate-to-severe atopic dermatitis undergoing upadacitinib: a multicenter retrospective study. *J Am Acad Dermatol*. 2024;90(5):1031–4.

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