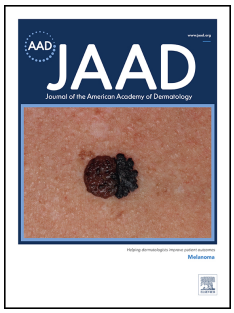

Relapse of Alopecia Areata During Ongoing JAK Inhibitor Therapy Is Not Uncommon and Usually Occurs in Previously Affected Areas: A Multicentre Italian Real-World Study.

Andrea Sechi, MD, PhD, Luca Rapparini, MD, Luca Valtellini, MD, Francesca Pampaloni, MD, Stephano Cedirian, MD, Francesca Bruni, MD, PhD, Federico Quadrelli, MD, Ginevra Martelli, MD, Mauro Barbareschi, MD, PhD, Angelo Valerio Marzano, MD, Bianca Maria Piraccini, MD, PhD, Michela Starace, MD, PhD, on behalf of the Alopecia Areata Relapse Study Group

PII: S0190-9622(26)03312-8

DOI: https://doi.org/10.1016/j.jaad.2026.08.031

Reference: YMJD 21726

To appear in: *Journal of the American Academy of Dermatology*

Received Date: 15 March 2026

Revised Date: 8 August 2026

Accepted Date: 10 August 2026

Please cite this article as: Sechi A, Rapparini L, Valtellini L, Pampaloni F, Cedirian S, Bruni F, Quadrelli F, Martelli G, Barbareschi M, Marzano AV, Piraccini BM, Starace M, on behalf of the Alopecia Areata Relapse Study Group, Relapse of Alopecia Areata During Ongoing JAK Inhibitor Therapy Is Not Uncommon and Usually Occurs in Previously Affected Areas: A Multicentre Italian Real-World Study., *Journal of the American Academy of Dermatology* (2026), doi: https://doi.org/10.1016/j.jaad.2026.08.031.

errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Article type: Brief Report

Title: Relapse of Alopecia Areata During Ongoing JAK Inhibitor Therapy Is Not Uncommon and Usually Occurs in Previously Affected Areas: A Multicentre Italian Real-World Study.

Running title: Relapse of Alopecia Areata During Ongoing JAK Inhibitor Therapy

Authors: Andrea Sechi, MD, PhD [1]*, Luca Rapparini, MD [2,3]*, Luca Valtellini, MD [1,4 #], Francesca Pampaloni, MD [2,3], Stephano Cedirian, MD [2,3], Francesca Bruni, MD, PhD [2,3], Federico Quadrelli, MD [2,3], Ginevra Martelli, MD [2,3], Mauro Barbareschi, MD, PhD [1,4], Angelo Valerio Marzano, MD [1,4], Bianca Maria Piraccini, MD, PhD [5], Michela Starace, MD, PhD [2,3] on behalf of the Alopecia Areata Relapse Study Group

* Authors equally contributed to the Manuscript as Co-First Author.

Affiliations:

1 Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.

2 Dermatology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy.

3 Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy.

4 Department of Physiopathology and Transplantation, Università degli Studi di Milano, Milan, Italy.

5 Private Dermatology Practice, Bologna, Italy.

 # Corresponding Author: Luca Valtellini, Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.

Email: luca.valtellini@unimi.it

Supplemental Material: https://data.mendeley.com/datasets/tprw6ktnwr/1

Acknowledgments: The authors thank the investigators of the Alopecia Areata Relapse Study Group for their contribution to this study. A complete list of the Alopecia Areata Relapse Study Group members is provided in Supplementary Material.

Fundings: None.

Conflicts of Interest: Angelo Valerio Marzano: consultancy/advisory boards disease-relevant honoraria from AbbVie, Amgen, Boehringer-Ingelheim, Bristol Myers Squibb, Galderma, Incyte, Johnson & Johnson, Leopharma, Novartis, MSD, Otsuka, Pfizer, Sanofi-Regeneron, Takeda and UCB. Bianca Maria Piraccini: consulting fees from Pierre Fabre-Ducray, Difa Cooper, Dercos-L'Oréal, Legacy Healthcare, Pfizer, and Eli Lilly. Michela Starace: fees for advisory board meetings and support for attending meetings from Almirall, Eli Lilly, Pierre Fabre, and L'Oréal. All the other authors have no relevant financial or non-financial interests to disclose.

Ethics statement: The patients in this manuscript have given written informed consent to the publication of their case details and photos according to the Declaration of Helsinki principles.

Ethical Approval: The study was approved by the local IRB (protocol n° 641/2024/Oss/AOUBo)

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.

Declaration of generative AI and AI-assisted technologies in the writing process: the authors declare that no generative AI or AI-assisted technologies were used in the preparation of this manuscript.

Manuscript word count: 500

References count: 5

Table count: 1

Figure count: 1

Keywords: alopecia areata; relapse; JAK inhibitors; baricitinib; ritlecitinib.

Key Message: Relapse during ongoing JAK inhibitor therapy is not uncommon in real-world alopecia areata management, and rescue outcomes are heterogeneous and not reliably predicted by baseline clinical features or the selected rescue approach, supporting individualized management.

Relapse during ongoing Janus kinase inhibitor (JAKi) therapy in alopecia areata (AA) is clinically relevant but poorly characterized. A systematic review and meta-analysis found an overall recurrence rate of 54% among JAKi-treated patients, with most relapses occurring after withdrawal rather than during active treatment[1]. Long-term extension data similarly showed durable maintenance of response in most patients receiving continued baricitinib or ritlecitinib[2,3].

We conducted a retrospective multicentre study to describe the timing, pattern, and management of AA relapse occurring despite continued JAKi treatment (**Supplementary**). Eligible patients had confirmed AA, were receiving oral JAKi, achieved a Severity of Alopecia Tool (SALT) score ≤20, and subsequently developed relapse without treatment interruption or dose reduction. Relapse was defined as the appearance of new patches in previously regrown or unaffected scalp areas after achieving SALT≤20.

A total of 142 patients were included. Baseline mean SALT score was 89.8±16.7; 66.2% were female, mean age was 37.8±13.6 years, and 74.6% had alopecia totalis or universalis. Most patients received baricitinib 4 mg/day (83.1%), followed by ritlecitinib 50 mg/day (13.4%) and baricitinib 2 mg/day (3.5%). SALT ≤20 was achieved after 27.1±15.5 weeks, and relapse occurred a mean of 29.5±20.6 weeks later. Overall, 54.9% relapsed within 52 weeks from treatment initiation.

Relapse-free survival differed across treatment groups in unadjusted analyses (log-rank p=0.002), with the longest mean survival observed in patients receiving baricitinib 4 mg/day

(31.7 weeks), compared with ritlecitinib 50 mg/day (20.1 weeks) and baricitinib 2 mg/day (13.2 weeks). Early relapse (≤52 weeks) was less frequent with baricitinib 4 mg/day than with ritlecitinib 50 mg/day (43.2%vs73.7%; adjusted OR 0.32, 95%CI 0.10–1.01) (**Fig. 1**). However, in multivariable Cox analysis, no clinical or treatment-related factor independently predicted time to relapse.

Relapses were most located in the occipital and parieto-temporal regions, and involved previously affected scalp areas in 97.9% of patients. Identifiable trigger factors were reported in 23.9% of cases, mainly psychological stress and infection. Diffuse hair shedding preceded patch recurrence in 26.1%. Relapse was limited to the scalp in 66.9%, whereas concomitant involvement of eyelashes, eyebrows, and body hair occurred in 28.9%, 25.4%, and 7.7%, of patients. First-line rescue strategies were heterogeneous, although topical clobetasol proprionate and intramuscular triamcinolone acetonide were the most frequently used approaches (**Table 1**). At first follow-up after rescue therapy, complete regrowth was achieved in 60.6% of patients, partial regrowth in 21.8%, and no regrowth in 17.6%. Among responders, mean time to regrowth of relapsed areas was 27.4±27.5 weeks. Neither rescue strategy, route of corticosteroid administration, AA subtype, JAKi regimen, nor relapse distribution was independently associated with outcome. Longer time to regrowth was the only factor associated with lower odds of complete response (OR per week 0.97, 95%CI 0.93–0.999).

These findings show that relapse during ongoing JAKi therapy is not uncommon in real-world AA management and usually occurs in scalp areas previously affected by disease[4]. Rescue outcomes are heterogeneous and not reliably predicted by baseline clinical features or the selected rescue approach, supporting individualized management and the need for biomarkers of relapse risk and retreatment responsiveness[5].

References

1. Yan D, Fan H, Chen M, Xia L, Wang S, Dong W, et al. The efficacy and safety of JAK inhibitors for alopecia areata: A systematic review and meta-analysis of prospective studies. Front Pharmacol. 2022 Aug 24;13:950450. doi:10.3389/fphar.2022.950450

2. Senna M, Mostaghimi A, Sinclair R, Ohyama M, Chiasserini C, Yu G, et al. Maintenance of long-term efficacy with continuous baricitinib treatment in patients with severe alopecia areata: 3-year results from BRAVE-AA1 and BRAVE-AA2. J Am Acad Dermatol. 2025 Nov 26;S0190-9622(25)03277-3. doi:10.1016/j.jaad.2025.11.064 PubMed PMID: 41314424.

3. Piliang M, Lynde C, King B, Mirmirani P, Sinclair R, Senna M, et al. Sustained hair regrowth with continued ritlecitinib treatment through week 48 in patients with alopecia areata with or without early target responses: Post hoc analysis of the ALLEGRO phase 2b/3 trial. J Am Acad Dermatol. 2025 Feb;92(2):276–84. doi:10.1016/j.jaad.2024.09.064 PubMed PMID: 39423930.

4. Dai Z, Chen J, Chang Y, Christiano AM. Selective inhibition of JAK3 signaling is sufficient to reverse alopecia areata. JCI Insight. 2021 Apr 8;6(7):e142205, 142205. doi:10.1172/jci.insight.142205 PubMed PMID: 33830087; PubMed Central PMCID: PMC8119218.

5. Kazmi A, Moussa A, Bokhari L, Bhoyrul B, Joseph S, Chitreddy V, et al. Switching between tofacitinib and baricitinib in alopecia areata: A review of clinical response. J Am Acad Dermatol. 2023 Dec;89(6):1248–50. doi:10.1016/j.jaad.2023.03.041 PubMed PMID: 37024053.

Figure legend

Figure 1. Kaplan–Meier survival curves depicting relapse-free survival after achievement of a SALT score ≤ 20 according to JAK inhibitor therapy (baricitinib 4 mg/day, baricitinib 2 mg/day, and ritlecitinib 50 mg/day). A statistically significant difference in time to relapse was observed among treatment groups (log-rank test, $\chi^2 = 12.392$, df = 2, p = 0.002). Numbers at risk are shown below the x-axis.

Tables

Table 1. Characteristics of the enrolled patients and assessment of response to first-line rescue therapy.

Characteristics of the enrolled patients				
Center, n	22			
Patients enrolled, n (%)	142 (100.0%)			
Sex: - Female, n (%) - Male, n (%)	 94 (66.2%) 48 (33.8%)			
Age, years	37.8 ± 13.6			
Age at diagnosis of AA, years	25.1 ± 13.9			
Duration of AA, years	12.1 ± 11.5			
Duration of the current episode, months	51.2 ± 67.6			
Severity of AA: - Patchy alopecia, n (%) - AT, n (%) - AU, n (%)	 36 (25.4%) 70 (49.2%) 36 (25.4%)			
Autoimmune comorbidities, n (%)	59 (41.6%)			
Family history for AA, n (%)	25 (17.6%)			
First line rescue therapy	**Response**			
	NR	**PR**	**CR**	**Total**
CP foam	12 (23.5%)	9 (17.6%)	30 (58.8%)	51 (100.0%)
CP cream	3 (8.6%)	9 (25.7%)	23 (65.7%)	35 (100.0%)
IMTAC	3 (18.8%)	3 (18.8%)	10 (62.5%)	16 (100.0%)
ILTAC	1 (8.3%)	4 (33.3%)	7 (58.3%)	12 (100.0%)
No therapy	0 (0.0%)	2 (40.0%)	3 (60.0%)	5 (100.0%)
OCS	1 (25.0%)	1 (25.0%)	2 (50.0%)	4 (100.0%)
OM	1 (33.3%)	0 (0.0%)	2 (66.7%)	3 (100.0%)
Other approaches*	4 (25.0%)	3 (18.8%)	9 (56.2%)	16 (100.0%)
Total	**25 (17.6%)**	**31 (21.8%)**	**86 (60.6%)**	**142 (100.0%)**

*Switch to ritlecitinib, TM, phototherapy, CP cream + IMTAC, CP cream + OCS, topical antralin.

Abbreviations. AA: alopecia areata; AT: alopecia totalis; AU: alopecia universalis; CP: clobetasol propionate; CR: complete response; ILTAC: intralesional triamcinolone acetonide; IMTAC: intramuscular

triamcinolone acetonide; NR: nonresponse; OCS: oral corticosteroids; OM: oral minoxidil; PR: partial response; TM: topical minoxidil.