UC Irvine

UC Irvine Previously Published Works

Title

Switching between Janus kinase inhibitors for treatment of alopecia areata: A multicenter retrospective review

Permalink

https://escholarship.org/uc/item/1jx4v1bz

Journal

Journal of the American Academy of Dermatology, 94(6)

ISSN

0190-9622

Authors

Martin, Aubrey

Chen, Li-Chi

Kreytak, Caroline

et al.

Publication Date

2026-06-01

DOI

10.1016/j.jaad.2026.01.055

Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at https://creativecommons.org/licenses/by/4.0/

Peer reviewed

eScholarship.org Powered by the California Digital Library
University of California

Switching between Janus kinase inhibitors for treatment of alopecia areata: A multicenter retrospective review

Aubrey Martin, BS,[a] Li-Chi Chen, MD, MPH,[b] Caroline Kreytak, BS,[a] Ronda Farah, MD,[c] Maria Hordinsky, MD,[c] Kristen I. Lo Sicco, MD,[d] Lindsey Bordone, MD,[e] Farah Moustafa, MD,[f] Gabriela Cobos, MD,[f] Crystal Aguh, MD,[g] Natasha Mesinkovska, MD,[h] John Meisenheimer, MD,[c] Maria Teachout, MS,[c] Anna Brinks, BA,[d] Carli Needle, BA,[d] Allison Bai, BS,[f] Jiana Wyche, BS,[g] Milan Hirpara, BA,[h] and Maryanne M. Senna, MD[a,i]

Background: Janus kinase inhibitors (JAKis) have transformed the treatment of alopecia areata (AA), but not all patients respond to initial therapy. The utility of switching between JAKis in treatment-refractory AA remains underexplored.

Objective: To evaluate the efficacy and safety of switching between JAKis in patients with severe AA.

Methods: In this multicenter retrospective study, we analyzed 108 patients with severe AA who switched between oral JAKis after a minimum treatment duration of 6 months. Treatment response was assessed using the Severity of Alopecia Tool (SALT). Multivariable logistic regression was used to identify predictors of response to a second JAKi.

Results: Overall, 48.8% of patients achieved SALT ≤20 on their second JAKi, and 32.6% achieved SALT ≤10. Of 21 patients who received a third JAKi, 52.4% achieved SALT ≤20 and 38.1% achieved SALT ≤10. Patients who responded to their first JAKi were more likely to respond to a second (odds ratio, 3.33; 95% CI, 1.22-9.68; P = .022). Adverse events were mild and consistent with prior reports.

Limitations: Retrospective design, treatment heterogeneity, and potential selection bias.

Conclusions: Switching between JAKis appears to be a viable strategy for severe AA patients, especially those responding to prior JAKi. Prior response may help guide treatment sequencing. (J Am Acad Dermatol 2026;94:1662-70.)

Key words: alopecia areata; baricitinib; JAK inhibitors; Janus kinase inhibitors; ritlecitinib; switching; tofacitinib.

From the Department of Dermatology, Lahey Hospital & Medical Center, Burlington, Massachusetts[a]; Department of Dermatology, University of Massachusetts Chan Medical School, Worcester, Massachusetts[b]; Department of Dermatology, University of Minnesota, Minneapolis, Minnesota[c]; Department of Dermatology, NYU Grossman School of Medicine, New York, New York[d]; Department of Dermatology, Vagelos College of Physicians and Surgeons, Columbia[e]; Department of Dermatology, Tufts Medicine, Boston, Massachusetts[f]; Department of Dermatology, Johns Hopkins, Baltimore, Maryland[g]; Department of Dermatology, University of California Irvine, Irvine, California[h]; and Department of Dermatology, Harvard Medical School, Boston, Massachusetts.[i]

Author Martin and Dr Chen are co-first authors.

Funding sources: Dr Martin received a Student Internship Award from the National Alopecia Areata Foundation (NAAF) in support of this study.

Patient consent: The authors obtained written consent from patients for their photographs and medical information to be published in print and online with the understanding that this information may be publicly available.

IRB approval status: Exempt.

Accepted for publication January 27, 2026.

Correspondence to: Maryanne M. Senna, MD, Department of Dermatology, Lahey Hospital and Medical Center, 67 S Bedford St, #100, Burlington, MA 01803. E-mail: Maryanne.M.Senna@lahey.org.

Published online January 30, 2026..

0190-9622/$36.00

© 2026 by the American Academy of Dermatology, Inc.

https://doi.org/10.1016/j.jaad.2026.01.055

INTRODUCTION

Alopecia areata (AA) is a chronic autoimmune disease characterized by nonscarring hair loss ranging from localized patches to complete scalp and/or body loss.[1] Nearly 7 million people in the United States and 147 million globally are affected.[2,3] Underlying pathology involves lymphocytic infiltrates around the hair follicle in the anagen phase, with the JAK-STAT pathway playing a key inflammatory role.[4-6]

Janus kinase inhibitors (JAKis) have shown promise in treating moderate-to-severe AA and are associated with an acceptable safety profile.[6] Although baricitinib, ritlecitinib, and deuruxolitinib are currently the only JAKis approved by the US Food and Drug Administration for AA, others are prescribed off-label.[7] While JAKis have revolutionized the treatment landscape for AA, not all patients respond to initial therapy or maintain significant regrowth longitudinally, prompting consideration of switching agents within the same class. Switching JAKis has been proposed as a potential strategy for managing refractory cases; however, data regarding this approach, either for lack of efficacy or insurance barriers, remain sparse.

Emerging evidence suggests the benefit of JAKi switching, particularly when nonresponse, partial response, or relapse occurs.[6-8] In a retrospective study of 26 patients who switched from tofacitinib (most commonly 10 mg daily) to baricitinib (predominantly 4 mg daily) due to inadequate response, side effects, or relapse, 66.6% (6 of 9) of prior nonresponders demonstrated clinical improvement.[7] Similarly, in a cohort of 77 patients, the mean daily doses of the second JAKi were 9.9 mg (SD 4.5) for tofacitinib and 5.2 mg (SD 1.9) for baricitinib. Switching from tofacitinib to baricitinib maintained remission in 53% (16 of 30) of prior responders, resulted in complete or partial regrowth in 100% (9 of 9) of relapsed responders, and produced partial regrowth in 28.6% (10 of 35) of partial responders, while providing limited benefit in 25% (2 of 8) of initial nonresponders.[8] A case series of 3 women with moderate-to-severe AA who failed tofacitinib 11 mg extended-release or upadacitinib 15-30 mg daily subsequently showed Severity of Alopecia Tool (SALT) improvement with baricitinib 4 mg daily, highlighting that patients may respond differently to distinct JAKis and doses.[6] Importantly, although all patients in these studies were treated with their first JAKi for at least 6 months, suggesting a fair trial period, these studies were limited by their single-center design and modest sample sizes. It remains unclear whether clinical improvements observed after switching were attributable to the new agent itself or simply a result of longer treatment duration. Additionally, most studies examined only a narrow set of JAKi combinations, offered limited data regarding third-line switches, and did not assess predictors of response. These gaps highlight the need for larger, multicenter studies to better define the utility, safety, and timing of JAKi switching in AA.

CAPSULE SUMMARY

- This multicenter study expands on prior evidence that switching between Janus kinase inhibitors can yield meaningful clinical improvement in patients with severe alopecia areata.
- Clinicians should consider switching as a viable strategy in prior responders who relapse, lose efficacy, or must change therapy due to side effects or insurance constraints.

This current multicenter study aims to investigate the efficacy and safety of switching between JAKis in patients with recalcitrant AA to provide clinicians with evidence-based treatment guidance. By leveraging data from 6 specialized hair loss clinics across the United States, this study aims to address the current knowledge gaps and offers real-world insights into the clinical utility of JAKi switching in refractory AA.

METHODS

Study design and setting

Institutional review board approval was obtained at all 6 participating institutions prior to initiating data collection. Data were retrospectively collected from 6 US specialty alopecia clinics from October 2024 to January 2025.

Patient selection

Patients were identified through retrospective chart review at each institution. Inclusion criteria required patients to have a confirmed diagnosis of severe AA, as defined by the Alopecia Areata Scale,[9] treatment with an oral JAKi for ≥6 months before switching to another oral JAKi (a minimum treatment duration of 6 months was required for the first, second, and third JAKi to allow adequate time for evaluation of treatment response); and complete medical records documenting treatment history, efficacy assessments, and follow-up outcomes. Patients were excluded if they had received less than 6 months of treatment with the initial JAKi or

Abbreviations used:

AA: alopecia areata
JAKi: Janus kinase inhibitor
OR: odds ratio
SALT: Severity of Alopecia Tool

were concurrently treated with systemic immunosuppressants or biologic therapies other than JAKis.

Data collection

Data were collected using a standardized data extraction form to ensure uniformity across all sites. The form captured demographics (age, sex, and race/ethnicity), disease characteristics (duration and severity of AA and duration of current episode), and comorbidities. Treatment information encompassed the type, dosage, and duration of the initial JAKi, the type and dosage of the subsequent JAKi, and the interval between therapies. Efficacy metrics included scalp hair loss assessments using the SALT score from baseline prior to any JAKi therapy, prior to switching JAKis, and at follow-up. A clinically meaningful response was defined as a SALT score of 20 or less (SALT ≤20), whereas partial to no response was defined as SALT >20.[10] The percentage of SALT improvement from baseline/response to the previous JAKi (50% [$SALT_{50}$] and 90% [$SALT_{90}$]) was also evaluated. Safety was assessed via documented adverse events associated with each JAKi, noting severity and whether they resulted in treatment discontinuation. In addition, the reason for switching—whether due to lack of efficacy or insurance overage—was recorded.

Statistical analysis

We used descriptive statistics to summarize demographic and clinical characteristics, reporting continuous variables as means with SDs and categorical variables as counts with percentages. Response rates to JAKi therapy, defined as achieving a SALT score ≤20, were compared across subgroups using chi-square or Fisher's exact tests, depending on cell sizes.

To identify factors associated with response to a second JAKi, purposeful selection of variables was conducted using univariate screening. We first performed univariate logistic regression assessing the association of achieving a SALT score ≤20 with each variable of interest, including age group, sex, race/ethnicity, AA subtype, duration of the current episode of AA, presence of autoimmune or atopic comorbidities, concurrent use of oral minoxidil or intralesional corticosteroids, first and second JAKi types, duration of first JAKi treatment, and whether the patient had responded to their first JAKi. Variables with a P value < .15 in univariate analysis, as well as confounders (defined as variables that led to a >15% change in odds ratio (OR) of another variable when added to the model), were included in the multivariable model.[11]

Multivariable logistic regression model with the selected variables was then used to estimate adjusted ORs with 95% CIs for achieving a SALT score ≤20 on the second JAKi. A two-sided P value < .05 was considered statistically significant. All analyses were conducted using R software, version 4.1.2 (R Foundation).

Ethical considerations

This study complied with the Declaration of Helsinki. Institutional review board approval was obtained at all participating institutions, and all patient data were anonymized to protect confidentiality. Efforts to minimize bias included blinding reviewers assessing clinical outcomes to patient treatment history.

RESULTS

Patient characteristics

A total of 108 patients with AA who switched between JAKis were included (Table I). The mean age was 38.5 years (SD, 16.5), and 66.7% were female. The cohort was predominantly White (66.7%), with smaller proportions identifying as Black (7.4%), Asian (7.4%), Hispanic (1.9%), or other (3.7%); 13.0% did not report their race or ethnicity. The mean duration of AA was 12.1 years (SD, 10.4), and the average duration of the current episode of AA was 65.8 months (5.5 years) (SD, 82.1). At baseline, the mean SALT score was 78.0 (SD, 28.7; range 25-100); 85% of patients had a SALT score ≥50, and 48% had a SALT score of 100. The most common AA subtype was alopecia universalis (45.4%), followed by patchy AA (16.7%), totalis (16.7%), and ophiasis (12.0%). Atopic comorbidities were reported in 15.7%, and 17.6% had other autoimmune diseases. Oral minoxidil was used concurrently in 54.6% (mean dose, 2.97 mg/day [SD, 1.30]), and 28.7% received intralesional corticosteroids.

Response to initial JAKi

Tofacitinib was the most commonly prescribed initial JAKi (71.3%), followed by baricitinib (25.0%) (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/ttbcvrtr96/2). Deuruxolitinib, ritlecitinib, and ruxolitinib were each used in ≤2 patients. Overall, 66.7% of patients experienced any improvement with their first JAKi; 35.8% achieved SALT ≤20, and 27.4% achieved SALT

Table I. Characteristics of patients with alopecia areata switching between Janus kinase inhibitors (JAKis) (*N* = 108)

Characteristic	Value
Age, y, mean (SD)	38.5 (16.5)
Sex, *n* (%)	
Female	72 (66.7)
Male	36 (33.3)
Race/ethnicity, *n* (%)	
White	72 (66.7)
Black	8 (7.4)
Asian	8 (7.4)
Hispanic	2 (1.9)
Other	4 (3.7)
Unreported	14 (13.0)
Duration of AA, y, mean (SD)	12.1 (10.4)
Duration of current episode of AA, month, mean (SD)	65.8 (82.1)
Baseline SALT score, mean (SD)	78.0 (28.7)
AA subtype, *n* (%)	
Patchy	18 (16.7)
Ophiasis	13 (12.0)
Totalis	18 (16.7)
Universalis	49 (45.4)
Diffuse	3 (2.8)
Sisaipho	1 (0.9)
Unspecified	6 (5.6)
Atopic disease, *n* (%)	17 (15.7)
Other autoimmune diseases*, *n* (%)	19 (17.6)
Family history of AA, *n* (%)	17 (15.7)
Concurrent treatment with oral minoxidil, *n* (%)	59 (54.6)
Dose of oral minoxidil (daily), mg, mean (SD)	2.97 (1.30)
Concurrent treatment with intralesional corticosteroids, *n* (%)	31 (28.7)
Initial oral JAKi treatment	
Tofacitinib, *n* (%)	77 (71.3)
Tofacitinib dose (daily), mg, mean (SD)	12.0 (4.1)
Duration of treatment with tofacitinib, month, mean (SD)	34.7 (35.0)
Baricitinib, *n* (%)	27 (25.0)
Baricitinib dose (daily), mg, mean (SD)	3.9 (0.4)
Duration of treatment with baricitinib, month, mean (SD)	12.1 (4.9)
Deuruxolitinib, *n* (%)	2 (1.9)
Deuruxolitinib dose (daily), mg, mean	16
Duration of treatment with deuruxolitinib, month, mean	16
Ritlecitinib, *n* (%)	1 (0.9)
Ritlecitinib dose (daily), mg	50
Duration of treatment with ritlecitinib, month	10
Ruxolitinib, *n* (%)	1 (0.9)
Ruxolitinib dose (daily), mg	50
Duration of treatment with ruxolitinib, month	72
Duration of treatment with first JAKi, month, mean (SD)	28.8 (31.6)
Duration of treatment with second, month, mean (SD)	17.9 (19.3)
Duration of treatment with third, month, mean (SD)	12.0 (5.1)

AA, Alopecia areata; *JAKi*, Janus kinase inhibitor; *SALT*, Severity of Alopecia Tool.
*Other autoimmune diseases include vitiligo, autoimmune thyroiditis, rheumatoid arthritis, lupus erythematosus, and inflammatory bowel disease.

≤10. Among those treated with tofacitinib, 75.8% showed improvement, with 47.8% achieving SALT ≤20 and 38.8% achieving SALT ≤10. In contrast, baricitinib yielded improvement in 41.7% of patients; however, only 8.3% achieved SALT ≤20, and none achieved SALT ≤10. Notably, the baricitinib-treated patients had a long mean duration of current episode of AA (53.8 months), which is associated with a reduced likelihood of achieving SALT ≤20.

Response to second JAKi

Overall, 48.8% of patients who switched from a first to a second JAKi achieved a SALT score ≤20, and 32.6% achieved a SALT score ≤10 (Table II). Most patients who initiated tofacitinib switched to a second JAKi due to inadequate response (58%) or insurance denial (26%) (Fig 1). Among the 59 patients who switched from tofacitinib to baricitinib, 40.4% showed further improvement, with 51.0% achieving SALT ≤20 and 29.4% achieving SALT ≤10 (Supplementary Table II, available via Mendeley at https://data.mendeley.com/datasets/ttbcvrtr96/2 and Supplementary Table III, available via Mendeley at https://data.mendeley.com/datasets/ttbcvrtr96/2). A lower proportion of patients achieving SALT ≤20 when switching to baricitinib 4 mg daily as the second JAKi was observed among those previously on tofacitinib 20 mg daily, compared with those previously on tofacitinib 10 mg daily (12.5% vs 59.5%; $P = .022$) (Table II). For the 9 patients who switched from tofacitinib to ritlecitinib, 37.5% showed improvement; of these, 87.5% achieved SALT ≤20 and 62.5% achieved SALT ≤10. None of the 3 patients who switched to upadacitinib improved. Of the 2 patients who switched to ruxolitinib, both improved—one achieving SALT ≤20 and 1 achieving SALT ≤10 (Supplementary Table II, available via Mendeley at https://data.mendeley.com/datasets/ttbcvrtr96/2).

Table II. Response to second JAKi treatment of patients with alopecia areata switching between JAKis, stratified by dosage (N = 101)

Initial JAKi	Initial JAKi daily dose	Second JAKi	Second JAKi daily dose	Any improvement in SALT (compared to the SALT score with first JAKi), *n* (%)	SALT score ≤20, *n* (%)	SALT score ≤10, *n* (%)	$SALT_{50}$ (compared to the SALT score with first JAKi), *n* (%)	$SALT_{90}$ (compared to the SALT score with first JAKi), *n* (%)
Tofacitinib *n* = 73	5 mg, *n* = 2	Baricitinib	4 mg, *n* = 1	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
		Ritlecitinib	50 mg, *n* = 1	1/1 (100)	1/1 (100)	0/1 (0)	1/1 (100)	0/1 (0)
	10 mg, *n* = 54	Baricitinib	2 mg, *n* = 2	0/1 (0)	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)
			4 mg, *n* = 45	17/34 (50.0)	22/37 (59.5)	13/37 (35.1)	13/32 (35.1)	3/32 (9.4)
		Ritlecitinib	50 mg, *n* = 3	2/3 (66.6)	3/3 (100)	2/3 (66.6)	2/3 (66.6)	1/3 (33.3)
		Upadacitinib	15 mg, *n* = 2	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)
		Ruxolitinib	40 mg, *n* = 2	2/2 (100)	1/2 (50.0)	1/2 (50.0)	2/2 (100)	1/2 (50.0)
	15 mg, *n* = 2	Baricitinib	4 mg, *n* = 2	1/2 (50)	2/2 (100)	0/2 (0)	0/2 (0)	0/2 (0)
	20 mg, *n* = 15	Baricitinib	2 mg, *n* = 1	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
			4 mg, *n* = 8	1/8 (12.5)	1/8 (12.5)	1/8 (12.5)	0/8 (0)	0/8 (0)
		Ritlecitinib	50 mg, *n* = 5	0/4 (0)	3/4 (75.0)	3/4 (75.0)	0/1 (0)	0/1 (0)
		Upadacitinib	30 mg, *n* = 1	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
	Overall			24/60 (40.0)	34/64 (53.1)	21/64 (32.8)	18/55 (32.7)	5/55 (9.1)
Baricitinib *n* = 24	2 mg, *n* = 1	Ritlecitinib	50 mg, *n* = 1	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)
	4 mg, *n* = 23	Ritlecitinib	50 mg, *n* = 19	5/13 (38.5)	3/13 (23.1)	2/13 (15.4)	3/13 (23.1)	2/13 (15.4)
		Tofacitinib	10 mg, *n* = 1	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)
			20 mg, *n* = 3	3/3 (100)	2/3 (66.6)	2/3 (66.6)	3/3 (100)	1/3 (100)
	Overall			10/18 (55.6)	7/18 (38.9)	6/18 (33.3)	8/18 (44.4)	5/18 (27.8)
Deuruxolitinib *n* = 2	16 mg, *n* = 2	Baricitinib	4 mg, *n* = 1	1/1 (100.0)	0/0 (0)	0/0 (0)	0/0 (0)	0/0 (0)
		Tofacitinib	10 mg, *n* = 1	0/0 (0)	0/0 (0)	0/0 (0)	0/0 (0)	0/0 (0)
	Overall			1/2 (50.0)	0/0 (0)	0/0 (0)	0/0 (0)	0/0 (0)
Ruxolitinib *n* = 1	50 mg, *n* = 1	Baricitinib	4 mg, *n* = 1	0/0 (0)	0/0 (0)	0/0 (0)	0/0 (0)	0/0 (0)
Ritlecitinib *n* = 1	50 mg, *n* = 1	Baricitinib	4 mg, *n* = 1	1/1 (100.0)	1/1 (100.0)	1/1 (100.0)	1/1 (100.0)	1/1 (100.0)
Total *N* = 101				36/82 (43.9)	42/86 (48.8)	28/86 (32.6)	27/77 (35.1)	11/77 (14.3)

The denominator of each category varies due to missing data of SALT score. $SALT_{50}$ and $SALT_{90}$ represent ≥50% and ≥90% improvement in scalp hair regrowth with the second JAKi relative to the response achieved with the first JAKi, as measured by the SALT score.
JAKi, Janus kinase inhibitor; *SALT*, Severity of Alopecia Tool.

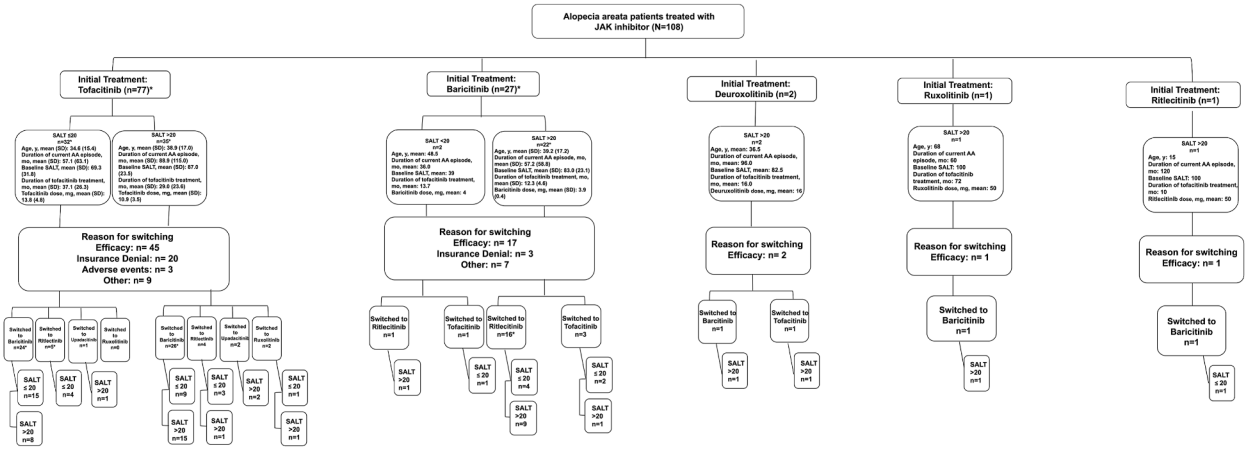


Fig 1. Characteristics and treatment response among patients with alopecia areata switching from an initial Janus kinase inhibitor (JAKi) to a second JAKi. *Denotes missing data on treatment response to JAKi in the group; therefore, downstream cell counts may be lower.

Among 24 patients initially treated with baricitinib, 20 switched to ritlecitinib and 4 to tofacitinib, primarily due to lack of efficacy. Among those switching to ritlecitinib, 42.9% achieved SALT ≤20 and 21.4% achieved SALT ≤10. Notably, all 4 patients who switched to tofacitinib responded, with 75.0% achieving SALT ≤10 (Supplementary Table II, available via Mendeley at https://data.mendeley.com/datasets/ttbcvrtr96/2). The mean interval between discontinuation of the first JAKi and initiation of the second was 2.7 months, and the mean duration of treatment with the second JAKi was 17.9 months.

Response to third JAKi

Twenty-one patients received a third JAKi with a mean treatment duration of 12 months. Overall, 75.0% showed any improvement, with 52.4% achieving SALT ≤20 and 38.1% achieving SALT ≤10 (Table III). However, 3 patients did not demonstrate adequate regrowth and maintained SALT ≥50 throughout treatment. The most common treatment sequence was tofacitinib → baricitinib → ritlecitinib, with 9 patients following this path; 55.6% achieved SALT ≤20 and 33.3% achieved SALT ≤10 (Supplementary Fig 1, available via Mendeley at https://data.mendeley.com/datasets/ttbcvrtr96/2). Additionally, all 3 patients who transitioned from ritlecitinib to tofacitinib as their third agent achieved SALT ≤10. Of the 3 patients switching from upadacitinib or tofacitinib to a third JAKi, 2 experienced any improvement, but none achieved SALT ≤20.

Predictors of response to second JAKi

In exploratory analyses, achievement of SALT ≤20 on a second JAKi was not significantly associated with age, sex, race/ethnicity, duration of current AA episode, comorbid autoimmune or atopic conditions, concurrent oral minoxidil or intralesional corticosteroid use, or identity of the second JAKi (Supplementary Table IV, available via Mendeley at https://data.mendeley.com/datasets/ttbcvrtr96/2). Patients without a family history of AA trended toward higher response rates compared to those with a family history (53.5% vs 26.7%, P = .087). Given that the duration of treatment with the initial JAKi may influence the therapeutic response to a subsequent JAKi, various treatment durations were analyzed to assess their association with improved response rates to the second JAKi. Notably, patients treated with their first JAKi for ≥18 months trended toward higher response to a second JAKi compared to those treated for less than 18 months (59.5% vs 28.3%, P = .085). This was not seen for other treatment durations including 6, 9, 12, and 15 months. Achieving SALT ≤20 on the first JAKi was significantly associated with achieving the same on a second JAKi (66.6% vs 38.5%, P = .025).

Multivariable analysis

On multivariable logistic regression, achieving SALT ≤20 on the initial JAKi was independently associated with increased odds of achieving SALT ≤20 on a second JAKi (OR, 3.33; 95% CI, 1.22-9.68; P = .022), after adjusting for age, which was identified as a confounder (Table IV). A reduced response was observed in patients with a family history of AA; however, this finding did not reach statistical significance (OR, 0.30; 95% CI, 0.07-1.13; P = .09).

Adverse events

The most commonly reported adverse events were hypercholesterolemia (7.4%, n = 8), acne (6.5%, n = 7), low-density lipoprotein cholesterol

Table III. Response to third JAKi treatment of patients with alopecia areata switching between JAKis, stratified by dosage ($N = 21$)

Second JAKi	Second JAKi daily dose	Third JAKi	Third JAKi daily dose	Any improvement in SALT (compared to the SALT score with second JAKi), *n* (%)	SALT score ≤20, *n* (%)	SALT score ≤10, *n* (%)	$SALT_{50}$ (compared to the SALT score with second JAKi), *n* (%)	$SALT_{90}$ (compared to the SALT score with second JAKi), *n* (%)
Baricitinib *n* = 14	4 mg, *n* = 14	Ritlecitinib	50 mg, *n* = 11	9/10 (90.0)	5/10 (50.0)	3/10 (30.0)	3/10 (30.0)	1/10 (10.0)
		Tofacitinib	10 mg, *n* = 1	1/1 (100.0)	1/1 (100.0)	1/1 (100.0)	1/1 (100.0)	0/1 (0)
			20 mg, *n* = 2	2/2 (100.0)	1/2 (50.0)	0/2 (0)	1/2 (50.0)	0/2 (0)
	Overall			12/13 (92.3)	7/13 (53.8)	4/13 (30.8)	5/13 (38.5)	1/13 (7.7)
Ritlecitinib *n* = 4	50 mg, *n* = 4	Tofacitinib	20 mg, *n* = 3	1/2 (50.0)	3/3 (100.0)	3/3 (100.0)	1/1 (100.0)	1/1 (100.0)
		Baricitinib	4 mg, *n* = 1	0/1 (0)	1/1 (100.0)	1/1 (100.0)	0/1 (0)	0/1 (0)
	Overall			1/3 (33.3)	4/4 (100.0)	4/4 (100.0)	1/2 (50.0)	1/2 (50.0)
Upadacitinib *n* = 2	15 mg, *n* = 2	Baricitinib	4 mg, *n* = 2	1/2 (50.0)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)
Tofacitinib *n* = 1	10 mg, *n* = 1	Baricitinib	4 mg, *n* = 1	1/1 (100.0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
Total *N* = 21				15/20 (75.0)	11/21 (52.4)	8/21 (38.1)	6/19 (31.6)	2/19 (10.5)

The denominator of each category varies due to missing data of SALT score. $SALT_{50}$ and $SALT_{90}$ represent ≥50% and ≥90% improvement in scalp hair regrowth with the third JAKi relative to the response achieved with the second JAKi, as measured by the SALT score.
JAKi, Janus kinase inhibitor; *SALT*, Severity of Alopecia Tool.

Table IV. Association between patient characteristic and achievement of a SALT score ≤20 after switching to a second JAKi

Characteristic	Adjusted odds ratio* (95% CI)	*P* value
Age, y, *n* (%)		
<18	5.14 (0.72-23.30)	.12
18-39	Reference	
≥40	0.95 (0.35-2.60)	.92
Family history of AA, *n* (%)		
No	Reference	
Yes	0.30 (0.07-1.13)	.09
Duration of first JAKi treatment		
<18 mo	Reference	
≥18 mo	1.99 (0.76-5.34)	.16
Achieving SALT ≤20 on first JAKi		
No	Reference	
Yes	**3.33 (1.22-9.68)**	**.022**

Bold odds ratio, 95% CI, and *P* value are statistically significant ($P < .05$).
AA, Alopecia areata; *JAKi*, Janus kinase inhibitor; *SALT*, Severity of Alopecia Tool.
*Multivariable-adjusted logistic regression model included age, family history of AA, duration of first JAK inhibitor treatment, and achieving SALT ≤20 on first JAK inhibitor.

level elevation (4.6%, $n = 5$), gastrointestinal symptoms (4.6%, $n = 5$), upper respiratory infection (4.6%, $n = 5$), headache (3.7%, $n = 4$), scalp folliculitis (3.7%, $n = 4$), and triglyceride elevation (2.8%, $n = 3$). Other less common adverse event (incidence <1%) included herpes simplex reactivation on the lip, leukopenia, weight gain, elevated liver function test, mild creatinine elevation, esophageal candidiasis, urinary tract infection, lower extremity tingling, epistaxis, night sweats, and cold intolerance.

DISCUSSION

In this multicenter retrospective study, we evaluated real-world outcomes in patients with severe AA who switched between oral JAKis, offering comprehensive data with the largest cohort to date on this increasingly common clinical scenario. Our findings suggest that JAKi switching can be a useful strategy in the management of severe AA, particularly among patients who demonstrate some degree of response to initial therapy.

Notably, 75% of patients who progressed to a third JAKi demonstrated improvement in SALT score, with over half achieving a SALT score ≤20 and approximately 40% achieving SALT ≤10. Sequential JAKi therapy may benefit select patients even after prior treatment failures. While previous studies have reported isolated successes when switching from

tofacitinib to baricitinib or vice versa,[7,8] our data expand on this. Compared to prior research, where patients were treated with their first JAKi for an average of 22.2 months on tofacitinib and 9.2 months on baricitinib, our cohort remained on initial therapy longer (mean 34.7 and 12.1 months, respectively), providing an extended trial period of first JAKi before switching.[8] Additonally, we explore a wider range of JAKi combinations, including sequences involving ritlecitinib, ruxolitinib, and upadacitinib, by providing insight into third-line switches, which have been largely understudied.

A key takeaway from our analysis is the predictive value of initial treatment response. Patients who achieved SALT ≤20 on their first JAKi were significantly more likely to respond again after switching, with adjusted odds nearly 4 times higher than those who did not respond initially. This suggests that treatment responsiveness may reflect an underlying disease biology that persists across different JAKi agents. In contrast, patients with a family history of AA appeared less likely to respond to a second agent, though this finding was not statistically significant. Clinical history and treatment trajectory remain important considerations when evaluating the potential benefit of switching. Dosage of the initial JAKi may also play a role in subsequent response. In our cohort, patients who transitioned from lower-dose tofacitinib to baricitinib appeared more likely to achieve favorable outcomes compared to those previously on higher-dose tofacitinib. However, these findings did not reach statistical significance on multivariable analysis, and stratification by dosage resulted in small sample sizes. As such, these trends should be considered exploratory and underscore the need for larger studies to clarify whether initial dosing influences subsequent efficacy.

Our results also highlight differences in outcomes between specific JAKi agents. While favorable responses were observed with tofacitinib, baricitinib, and ritlecitinib, outcomes were less favorable with upadacitinib. These differences may reflect variation in isoform selectivity, dosing, or tissue pharmacokinetics, as well as patient-level factors. Although some patients experienced improvement with certain sequences of JAKi use, our data are not sufficient to support conclusions about optimal sequencing strategies. Further studies are needed to determine whether sequencing influences efficacy or whether observed differences reflect pharmacologic properties, dose effects, or patient selection.

The safety profile observed across switches was consistent with prior studies of individual JAKis, with no unexpected adverse events. Common side effects included acne, hyperlipidemia, mild infections, and laboratory abnormalities that resolved without need for dose de-escalation. These findings suggest sequential JAKi use is generally well-tolerated with appropriate monitoring.

This study has several limitations. As a retrospective analysis, we cannot rule out the impact of confounding factors or selection bias. While all patients had at least 6 months of JAKi treatments, standardized switching criteria were not in place. The inclusion criterion of at least 6 months of treatment with an oral JAKi before switching is consistent with prior studies; however, delayed responses beyond this timeframe have been reported, and thus our results may underrepresent the benefit of longer treatment courses. Although our cohort of 108 patients represents one of the larger real-world series to date, the sample size remains relatively limited and may not provide sufficient power to detect more nuanced differences in treatment response, such as distinguishing between patients who initially responded to a JAKi and subsequently experienced disease relapse and those who did not demonstrate any response throughout the JAKi treatment. Additionally, given that data were collected from tertiary referral centers, results may not generalize to broader dermatology settings. Nevertheless, the multi-institutional design, data on switches involving up to 3 different JAKis, and inclusion of less commonly studied agents represent important strengths.

In conclusion, our findings support the clinical utility of JAKi switching in select patients with refractory AA, particularly those with a history of response to a prior oral JAKi treatment. These suggest that prior responses may help guide treatment decisions. Future large-scale prospective studies are needed to clarify optimal sequencing strategies, understand mechanisms of variable response, and identify predictors that can inform personalized care.

Conflicts of interest

None disclosed.

REFERENCES

1. Zhou C, Li X, Wang C, Zhang J. Alopecia areata: an update on etiopathogenesis, diagnosis, and management. *Clin Rev Allergy Immunol*. 2021;61(3):403-423.
2. Mesinkovska N, King B, Mirmirani P, Ko J, Cassella J. Burden of illness in alopecia areata: a cross-sectional online survey study. *J Investig Dermatol Symp Proc*. 2020;20(1):S62-S68.
3. Villasante Fricke AC, Miteva M. Epidemiology and burden of alopecia areata: a systematic review. *Clin Cosmet Investig Dermatol*. 2015;8:397-403.
4. Bertolini M, McElwee K, Gilhar A, Bulfone-Paus S, Paus R. Hair follicle immune privilege and its collapse in alopecia areata. *Exp Dermatol*. 2020;29(8):703-725.

5. Triyangkulsri K, Suchonwanit P. Role of janus kinase inhibitors in the treatment of alopecia areata. *Drug Des Devel Ther*. 2018;12:2323-2335.
6. Katamanin O, Ch'en PY, Song EJ. Exploring the efficacy of baricitinib in treating alopecia areata after failed janus kinase inhibitor therapy. *JAAD Case Rep*. 2024;43:36-39.
7. Ehsani A, Razavi Z, Rahimnia A, et al. Switching JAK inhibitors: evaluating baricitinib's effectiveness in alopecia areata after tofacitinib failure. *Arch Derm Res*. 2025;317(1):491.
8. Kazmi A, Moussa A, Bokhari L, et al. Switching between tofacitinib and baricitinib in alopecia areata: a review of clinical response. *J Am Acad Dermatol*. 2023;89(6):1248-1250.
9. King BA, Mesinkovska NA, Craiglow B, et al. Development of the alopecia areata scale for clinical use: results of an academic-industry collaborative effort. *J Am Acad Dermatol*. 2022;86(2):359-364.
10. Wyrwich KW, Kitchen H, Knight S, et al. The alopecia areata investigator global assessment scale: a measure for evaluating clinically meaningful success in clinical trials. *Br J Dermatol*. 2020;183(4):702-709.
11. Bursac Z, Gauss CH, Williams DK, Hosmer DW. Purposeful selection of variables in logistic regression. *Source Code Biol Med*. 2008;3(1):17.