JAMA Dermatology | Original Investigation

Baricitinib Withdrawal and Retreatment in Patients With Severe Alopecia Areata
The BRAVE-AA1 Randomized Clinical Trial

Brett King, MD, PhD; Justin Ko, MD; Ohsang Kwon, MD; Sergio Vañó-Galván, MD, PhD; Bianca Maria Piraccini, MD; Yves Dutronc, MD; Guanglei Yu, PhD; Chunyuan Liu, PhD; Najwa Somani, MD; Susan Ball, PhD; Natasha A. Mesinkovska, MD

IMPORTANCE Baricitinib has demonstrated efficacy for treating severe alopecia areata in adults. There is currently limited information about the need for continuous therapy after achieving scalp hair regrowth.

OBJECTIVE To report results from the randomized withdrawal period of the BRAVE-AA1 trial.

DESIGN, SETTING, AND PARTICIPANTS BRAVE-AA1 was a randomized, placebo-controlled, phase 3 randomized clinical trial with a treatment withdrawal substudy that was conducted at 70 centers in 3 countries beginning in March 2019. It included 654 adults with severe alopecia areata (AA) (Severity of Alopecia Tool [SALT] score ≥50) who were randomized 3:2:2 to receive treatment with baricitinib, 4 mg; baricitinib, 2 mg; or placebo. Data were analyzed in August 2023.

INTERVENTION At week 52, 154 patients who were responders (SALT score ≤20) were rerandomized 3:1 to continue to take their current dose of baricitinib or transition to placebo (randomized withdrawal). Responders randomized to placebo who experienced a loss of treatment benefit (>20-point worsening in SALT score) at any time after week 52 were retreated with their original baricitinib dose.

MAIN OUTCOME AND MEASURES The proportion of patients who lost treatment benefit through week 152 and the proportion of patients who recaptured response after retreatment. The last observation carried forward was used to impute missing or censored data.

RESULTS Of 654 patients who received treatment, the mean (SD) age was 37.1 (13.0) years, and there were 383 women (58.6%). At week 52, 10 of 39 responders taking baricitinib, 2 mg, and 30 of 115 responders taking baricitinib, 4 mg, were rerandomized to placebo. At 4 and 8 weeks of treatment withdrawal, 0% and 10% to 11% of patients, respectively, lost treatment benefit regardless of dose. At week 152, 80% of patients had lost benefit compared with 7% for those who continued baricitinib therapy for both dose groups. Within the follow-up observation periods, 5 of 8 patients taking 2 mg (63%) and 21 of 24 patients taking 4 mg (87.5%) recaptured a SALT score of 20 or less response after retreatment.

CONCLUSIONS AND RELEVANCE Severe AA is a chronic, relapsing condition, and this randomized clinical trial found that withdrawal of therapy for a patient population with severe AA who had achieved meaningful hair regrowth after 1 year of treatment with baricitinib resulted in loss of benefit for almost all patients, indicating that continued therapy is required to maintain hair regrowth.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03570749

Visual Abstract

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Brett King, MD, PhD, Department of Dermatology, Yale School of Medicine, New Haven, CT 06520 (brett.king@yale.edu).

JAMA Dermatol. doi:10.1001/jamadermatol.2024.2734
Published online August 14, 2024.

Alopecia areata (AA) is a chronic autoimmune disease characterized by patchy or complete hair loss of any hair-bearing site that results from the collapse of hair follicle immune privilege.[1] The oral Janus kinase (JAK) inhibitor baricitinib, administered at doses of 2 mg or 4 mg, once daily, demonstrated efficacy in achieving scalp hair regrowth over 52 weeks in 2 phase 3, double-blind, randomized clinical trials (BRAVE-AA1 and BRAVE-AA2) and has been approved for the treatment of adults with severe AA.[2-4] More recently, the oral JAK3/TEC family inhibitor ritlecitinib has been approved for treating adults and adolescents with severe AA.[5]

In patients with severe AA, the optimal duration of therapy or need for continuous treatment for maintenance of response are not well understood. Based on data from clinical trials, spontaneous remission is rare among patients with extensive scalp hair loss, in which placebo-response rates of 1% to 5% were reported.[3,5-7] Furthermore, clinical experience has shown that relapse is frequent on treatment discontinuation.[8] However, over the course of the disease, there may be circumstances in which clinicians and/or patients require interruption of therapy (eg, surgery or illness) or discontinuation of therapy (eg, planning for pregnancy) after response had been achieved. Therefore, it is important to understand the outcomes of treatment withdrawal and for clinicians to have data that can be applied to potential clinical scenarios in which treatment interruption or discontinuation is required.

In this article, we report the outcomes of randomized treatment withdrawal after 52 weeks of treatment with baricitinib, 2 mg and 4 mg, from the phase 3 clinical trial BRAVE-AA1. Understanding the effects of baricitinib treatment withdrawal and the factors that may influence continued response to treatment are important to inform clinicians in their long-term treatment of patients.

Key Points

Question What are the short-term and long-term relapse rates following treatment withdrawal in patients with severe alopecia areata who achieved a response after 52 weeks of baricitinib, 2 mg, or baricitinib, 4 mg, once daily?

Findings In this randomized clinical trial of 654 adults with severe alopecia areata, at 4 and 8 weeks, 0% and 10% to 11% of patients, respectively, experienced a loss of treatment benefit, which increased to 80% or more by week 152. With retreatment, most patients recaptured response during the follow-up observation period (2 mg, 63%; 4 mg, 85%).

Meaning The results of this trial suggest that severe alopecia areata is a relapsing condition requiring maintenance therapy after successful regrowth has been achieved.

Methods

Study Population

BRAVE-AA1 was an adaptive phase 2 to 3, double-blind, parallel-group, randomized, placebo-controlled trial with a randomized withdrawal substudy (Supplement 1 and Supplement 2). The primary trial design for the phase 3 portion was published previously.[2,3] Briefly, patients aged 18 to 60 years and 18 to 70 years for male and female individuals, respectively, with a Severity of Alopecia Tool (SALT)[9] score of 50 or greater (≥50% scalp hair loss) and a current AA episode lasting longer than 6 months to less than 8 years without spontaneous improvement (ie, ≤10-point reduction in SALT score) over the 6 months before screening were enrolled. Patients were randomized 3:2:2 to receive baricitinib, 4 mg; baricitinib, 2 mg; or placebo once daily for 52 weeks, with placebo nonresponder patients rescued at week 36. The primary outcome was a SALT score of 20 or less at week 36 (achievement of ≤20% scalp hair loss). All patients who completed the 36-week placebo-controlled period entered a long-term extension of up to 200 weeks. For the randomized withdrawal substudy, patients initially randomized to baricitinib, 4 mg or 2 mg, who had achieved a SALT score of 20 or less at week 52 were rerandomized 3:1 to continue taking their current dose of baricitinib or transition to placebo (randomized withdrawal).

BRAVE-AA1 was conducted in accordance with the ethical principles of the Declaration of Helsinki and Good Clinical Practice guidelines, and the trial protocol was approved by the institutional review board or ethics committee at each center. the trial was conducted in compliance with ICH guidelines, and the protocol provided additional guidance for safety reporting. All patients provided written informed consent for participation in the clinical studies.

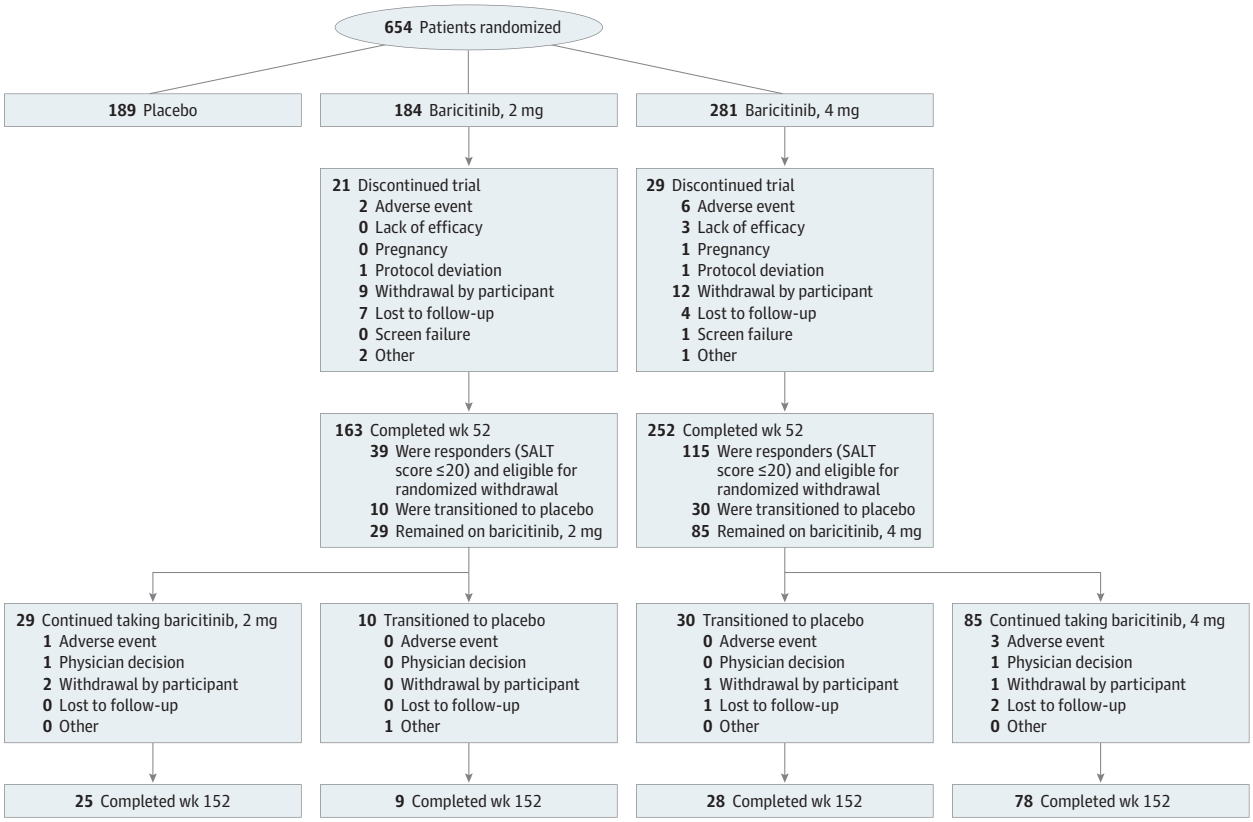
Randomized Withdrawal

The 3:1 randomization ratio was chosen to minimize the number of patients undergoing withdrawal due to the potential psychological effect of relapse. The randomized withdrawal occurred regardless of duration of response (SALT score ≤20) before randomization. Rerandomization for the substudy was performed in a masked manner by a computer-generated random sequence using an interactive web response system. Responders who were rerandomized to placebo at week 52 and subsequently experienced a loss of treatment benefit (defined as a greater than 20-point worsening from their week 52 SALT score) were retreated with their original baricitinib dose (retreated populations). Retreatment could occur at any visit (scheduled or unscheduled) after week 52. Patients who were rerandomized to remain taking their original dose of baricitinib at week 52 continued to receive the same initial dose. The analyses presented in this article include data collected up to week 152 (ie, 100 weeks of randomized withdrawal).

Main Outcomes and Measures

For all patients enrolled in the randomized withdrawal substudy, the proportion with a SALT score of 20 or less and the proportion with loss of treatment benefit is reported through week 152. For patients who met the criterion of loss of treatment benefit and were retreated, the proportion of patients who regained a SALT score of 20 or less during the follow-up observation period are reported. Achievement of a Clinician-Reported Outcome (ClinRO) Measures for Eyebrow (EB) or Eyelash (EL) score of 0 or 1 (ie, full coverage and no areas of

Figure 1. Trial Profile



CONSORT diagram for patients who were randomized to baricitinib, 4 mg, or baricitinib, 2 mg, at baseline in BRAVE-AA1 and randomized to placebo or remained taking their initial dose after achieving a Severity of Alopecia Tool (SALT) score of 20 or less at week 52.

hair loss to minimal gaps and even distribution) with a 2-point or greater improvement from baseline is reported for patients with a baseline ClinRO EB or EL score of 2 or 3 (ie, significant gaps and/or uneven distribution to no notable hair).[10]

Baseline demographic and disease characteristics for all patients eligible for rerandomization, including the proportion of patients with severe AA (SALT score, 50 to <95) vs very severe AA (SALT score, 95-100)[9] and duration of the current episode (<4 years vs ≥4 years), are reported. Additionally, these baseline characteristics are presented for patients who maintained benefit and those who lost treatment benefit during the randomized withdrawal.

Statistical Analysis

The statistical summaries of the efficacy data during the randomized withdrawal period and retreatment were performed using the randomized withdrawal population and the retreated population, respectively. The randomized withdrawal population included patients who achieved a SALT score of 20 or less at week 52, were eligible to participate in the randomized withdrawal period, and received at least 1 dose of treatment on or after the week 52 visit. The retreated population included patients who transitioned to placebo at week 52 but were retreated with their original dose of baricitinib after loss of treatment benefit. Recapture of a SALT score of 20 or less at least once throughout the follow-up observation period was assessed for the retreated population. Descriptive statistics were summarized, and data after retreatment or treatment discontinuation were censored for the randomized withdrawal period. The last observation carried forward imputation was used to impute the missing or censored data. Patients without a single observation after the randomized withdrawal were excluded from the analysis. The statistical analyses of the response recapture following retreatment used observed data. Any data collected after permanent treatment discontinuation were excluded. Statistical analyses were conducted using SAS Enterprise Guide, version 7.12 (SAS Institute). Statisitical significance was set at $\alpha = .05$.

Results

BRAVE-AA1 enrolled 654 patients, of whom 281 (43%) received 4 mg and 184 (28%) received 2 mg through week 52 (**Figure 1**). At week 52, 115 (41%) taking baricitinib, 4 mg, and 39 (21%) taking 2 mg had a SALT score of 20 or less and were eligible for randomized withdrawal. Among the responders to baricitinib, 4 mg, 30 of 115 (26%) were transitioned to placebo, and 85 of 115 (74%) remained taking their original dose; 28 (93%) and 78 (92%), respectively, completed the week 152

Table. Baseline Demographic and Disease Characteristics for All Patients in the Randomized Withdrawal Population

Entry	No. (%)			
	Initially randomized to baricitinib, 4 mg		Initially randomized to baricitinib, 2 mg	
	Continued baricitinib treatment (n = 85)	Transitioned to placebo (n = 30)	Continued baricitinib treatment (n = 29)	Transitioned to placebo (n = 10)
Age, mean (SD), y	37.2 (12.9)	35.5 (14.2)	38.8 (12.4)	36.0 (13.7)
Sex				
Female	57 (67)	20 (67)	22 (76)	7 (70)
Male	28 (33)	10 (33)	7 (24)	3 (30)
Race				
Asian	37 (44)	8 (27)	12 (41)	5 (50)
Black or African American	6 (7)	2 (7)	0	0
White	41 (48)	17 (57)	16 (55)	5 (50)
Age of onset of AA, mean (SD), y	27.0 (15.2)	27.6 (15.4)	27.2 (14.0)	26.0 (14.7)
Duration since AA onset, mean (SD), y	10.29 (10.4)	7.84 (9.8)	11.65 (11.3)	10.07 (8.8)
Duration of current AA episode, mean (SD), y	2.86 (2.6)	2.73 (2.3)	2.79 (5.7)	1.18 (0.4)
Duration of current AA episode				
<4 y	65 (77)	23 (77)	26 (90)	10 (100)
≥4 y	20 (24)	7 (23)	3 (10)	0
Baseline AA severity				
Severe (SALT score 50 to <95)	53 (62)	21 (70)	19 (66)	8 (80)
Very severe (SALT score 95-100)	32 (38)	9 (30)	10 (35)	2 (20)
SALT score, mean (SD)[a]	80.9 (18.6)	79.1 (18.5)	78.0 (19.1)	76.5 (18.2)
Atopic background[b]	33 (3)	13 (43)	11 (38)	5 (50)
Universalis[c]	34 (40)	8 (27)	16 (38)	3 (30)
ClinRO score of 2 or 3				
ClinRO eyebrow score of 2 or 3[d,e]	52 (61)	14 (47)	16 (55)	7 (70)
ClinRO eyelash score of 2 or 3[d,e]	47 (55)	13 (43)	12 (41)	4 (40)
Scalp hair PRO				
Scalp hair PRO of 3 (50%-94% loss)	37 (44)	16 (53)	15 (52)	5 (50)
Scalp hair PRO of 4 (95%-100% loss)	46 (54)	12 (40)	10 (34)	5 (50)
PRO score of 2 or 3				
PRO eyebrow score of 2 or 3[d,e]	54 (64)	12 (40)	18 (62)	7 (70)
PRO eyelash score of 2 or 3[d,e]	46 (54)	11 (37)	12 (41)	5 (50)

Abbreviations: AA, alopecia areata; ClinRO, clinician-reported outcome; PRO, Scalp Hair Assessment PRO; SALT, Severity of Alopecia Tool.

[a] Scores on the SALT range from 0 to 100, with 0 representing no scalp hair loss and 100 complete hair loss.

[b] Atopic background is defined as medical history or current atopic dermatitis, allergic rhinitis, allergic conjunctivitis, or allergic asthma.

[c] Diagnosis of alopecia universalis was according to the investigator's assessment.

[d] ClinRO/PRO score of 2 indicates substantial gaps in eyebrow(s)/eyelashes.

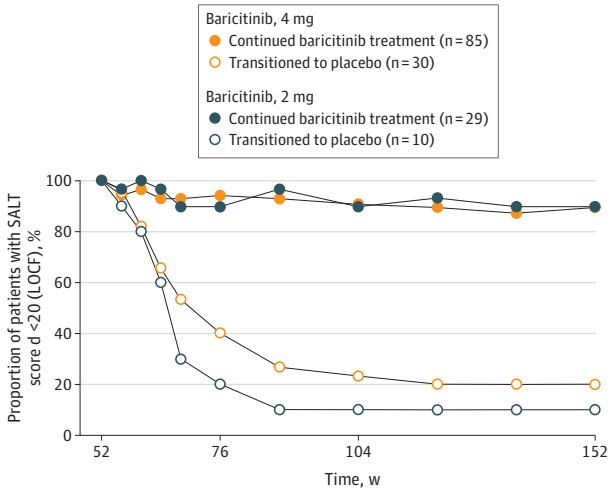
[e] ClinRO/PRO score of 3 indicates no notable eyebrow(s)/eyelashes.

treatment visit. Of the 39 responders to baricitinib, 2 mg, 10 of 39 (26%) were transitioned to placebo, and 29 of 39 (74%) remained taking their original dose; of these patients, 9 (90%) and 25 (86%), respectively, completed the week 152 treatment visit. Patient demographic and baseline disease characteristics were comparable across treatment arms (**Table**). Compared with the overall BRAVE-AA1 population reported previously,[3] week 52 responders to baricitinib, 2 mg and 4 mg, eligible for randomized withdrawal tended to have a shorter duration of their current episode and less severe AA (ie, greater proportion of patients having baseline SALT score of 50 to <95 vs baseline SALT score ≥95).

Among patients who remained taking baricitinib, 4 mg, at week 152, a SALT score of 20 or less was maintained by 90%. Similarly, among patients who remained taking baricitinib, 2 mg, a SALT score of 20 or less was maintained by 89% (**Figure 2**). A similar pattern was observed for the end points of SALT score of 10 or less from weeks 52 to 152 for both doses (eFigure 1 in Supplement 3). For patients who remained taking baricitinib, response rates for a ClinRO EB or EL score of 0 or 1 with a 2-point or greater improvement also remained stable from weeks 52 to 152, with 69% or greater and 67% or greater EB response rates and 50% or greater and 70% or greater EL response rates among patients who continued treatment with baricitinib, 2 mg and 4 mg, respectively (eFigure 2 in Supplement 3).

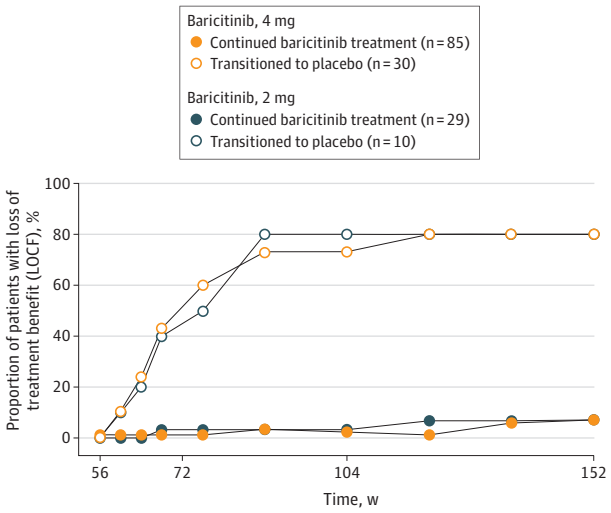
For patients who were withdrawn from baricitinib, 4 mg, 96% and 82% maintained a SALT score of 20 or less at weeks 4 and 8, respectively (Figure 2). At week 152, only 6 of 30 (20%) had maintained that response. Similarly, for those withdrawn from baricitinib, 2 mg, 9 of 10 (90%) and 8 of 10 (80%) maintained a SALT score of 20 or less at weeks 4 and 8, respectively, and 1 patient (10%) maintained that response at week 152. Similarly, the proportion of patients with a SALT score

Figure 2. Proportion of Patients With a Severity of Alopecia Tool (SALT) Score of 20 or Less From Weeks 52 to 152 for Patients Who Remained Taking Treatment and Who Were Withdrawn to Placebo



LOCF indicates last observation carried forward.

Figure 3. Proportion of Patients With Loss of Treatment Benefit From Weeks 56 to 152 for Patients Who Remained Taking Treatment and Who Were Withdrawn to Placebo



LOCF indicates last observation carried forward.

of 10 or less decreased from 23 of 30 (77%) to 5 of 30 (17%) (4-mg withdrawal) and 8 of 10 (80%) to 1 of 10 (10%) (2-mg withdrawal) during weeks 52 to 152 (eFigure 1 in Supplement 3). Among patients randomized to placebo at week 52, 43% were EB responders at week 52 (both doses), which decreased to 4 of 14 (29%) (baricitinib, 4 mg) and 1 of 7 (14%) (baricitinib, 2 mg) at week 152 (eFigure 2A in Supplement 3). For patients randomized to placebo at week 52, the EL response rate was 4 of 13 (31%) (baricitinib, 4 mg) and 1 of 4 (25%) (baricitinib, 2 mg), respectively, and this response was generally stable through week 152, although the number of patients was small (eFigure 2B in Supplement 3).

Loss of Treatment Benefit (Greater Than 20-Point SALT Score Worsening)

For patients who remained taking their initial dose of baricitinib, 2 mg or 4 mg, after week 52, 7% (2 mg, 2 of 29; 4 mg, 6 of 85) experienced a loss of treatment benefit at week 152 (**Figure 3**). For those who were withdrawn to placebo, loss of treatment benefit occurred during the shorter term, 4 and 8 weeks after treatment withdrawal, in 0% and 10% to 11% of patients, respectively, regardless of treatment allocation. By 24 weeks (6 months), at least half of patients withdrawn from baricitinib, 4 mg (18 of 30 [60%]) and 2 mg (5 of 10 [50%]), experienced a loss of treatment benefit. At week 152, the proportion of patients with loss of treatment benefit after treatment withdrawal was 80% (2 mg, 8 of 10; 4 mg, 24 of 30) for both doses. For those patients withdrawn from baricitinib, 4 mg, who did not experience a loss of treatment benefit, a higher proportion had shorter duration of current episode and shorter duration since disease onset compared with those who experienced a loss of treatment benefit (eTable in Supplement 3); fewer patients in this group had atopic background, alopecia universalis, and EB and EL loss.

Overall, most patients experienced hair regrowth (ie, decreasing SALT score) following retreatment with the initial dose of baricitinib, with varying trajectories (eFigures 3 and 4 in Supplement 3). The proportion of patients recapturing a SALT score of 20 or less increased over time. During the retreatment period, which varied by patient, 21 of 24 patients (87.5%) who were retreated with 4 mg and 5 of 8 patients (63%) who were retreated with 2 mg recaptured response after retreatment.

Discussion

In this randomized clinical trial, most patients who underwent baricitinib treatment withdrawal at week 52 experienced a loss of treatment benefit that was consistent with reports in the literature of relapses with withdrawal of other systemic therapies in AA.[8] Treatment withdrawal was dictated by the clinical trial design, which was distinctly different from clinical practice, in which the duration and/or depth of response and other parameters (baseline disease severity or chronicity) broadly inform treatment decisions, but may be especially important in guiding decisions to adjust the dose, interrupt therapy, or discontinue treatment. The current recommendation from expert consensus is to consider potential discontinuation of systemic treatment only after complete regrowth has been achieved and maintained for 6 months or when it is sufficient to be managed with topical treatments.[11] It is uncertain what the loss of treatment benefit would have been in the present study had patients been required to achieve full and stable regrowth of scalp hair for at least 6 months before treatment withdrawal.

Retreatment was triggered by a worsening of greater than 20 points in absolute SALT score. As illustrated by individual patient trajectories, not only is the time to disease recurrence

variable, but also the rate and extent of hair loss (once it begins) varies considerably across patients, with some losing most hair during a short period (eFigures 3 and 4 in Supplement 3). At the point of observation in this article, not all patients had recaptured efficacy, although recapture rates increased progressively over time. Similarly, in a trial of ritlecitinib, not all patients who underwent treatment withdrawal recaptured response.[12] If treatment discontinuation is considered in clinical practice, positive findings on a hair pull test may help to signal early shedding, although this tool has not been validated for this purpose or for disease monitoring during JAK inhibitor treatment withdrawal. Retreatment at the earliest sign of shedding would be important to stabilize the disease and recapture response. The loss of treatment benefit did not become noticeable until approximately 8 weeks after treatment withdrawal. Within the BRAVE-AA clinical trials, interruptions of treatment for 4 weeks or less did not appear to affect achievement or maintenance of a SALT score of 20 or less. Considering these 2 observations together, it seems prudent to limit interruptions of treatment to 4 weeks or fewer.[13] There was a small proportion of patients who did not lose treatment benefit even after 2 years of treatment withdrawal. While the baseline characteristics of patients with no loss of treatment benefit after withdrawal from baricitinib, 4 mg, indicated less disease activity in this subgroup compared with those who experienced a loss of treatment benefit, this trend could not be confirmed among patients withdrawn from baricitinib, 2 mg, with and without loss of treatment benefit due to the limited number of patients (eTable in Supplement 3). The observations should be taken with caution due to the small sample size; however, they provide some indication of potential disease characteristics of patients in whom long-term remission may be possible.

Limitations

A potential limitation of this study was the scheduling of patient visits, which were separated by longer intervals toward the end of the study. While patients were able to be retreated at unscheduled visits, some may have waited too long and lost considerably more than 20 points in their SALT score before retreatment was initiated, leading to longer times to recapture response (achieve a SALT score ≤20). Because the response to retreatment in some participants was gradual and the loss of treatment benefit could have occurred late during the postwithdrawal observation period, some patients may not have had sufficient time to recapture response during retreatment (eFigures 3 and 4 in Supplement 3). Nonetheless, there is a small but clinically important risk that some patients may not show a response to retreatment. Quality-of-life data were not collected during this portion of the study, and this effect would be necessary to assess before any discussion of treatment withdrawal.

Conclusions

In this randomized clinical trial, in patients with severe AA, withdrawal of therapy among patients who achieved meaningful hair regrowth after 1 year of treatment with baricitinib resulted in almost all patients losing their hair. Therefore, it is not recommended to discontinue therapy after achieving successful regrowth with 1 year of therapy (52 weeks). These data add to our growing knowledge of severe AA, showing that it is a chronic disease and similar to other autoimmune diseases and requires long-term maintenance therapy for most patients to maintain successful outcomes.

ARTICLE INFORMATION

Accepted for Publication: June 13, 2024.

Published Online: August 14, 2024. doi:10.1001/jamadermatol.2024.2734

Author Affiliations: Department of Dermatology, Yale School of Medicine, New Haven, Connecticut (King); Department of Dermatology, Stanford University School of Medicine, Palo Alto, California (Ko); Department of Dermatology, Seoul National University College of Medicine, Seoul, South Korea (Kwon); Hair Disorders Unit, Dermatology Service, Ramon y Cajal Hospital, TricoHRC Research Group, Instituto Ramón y Cajal de Investigación Sanitaria, University of Alcala, Madrid, Spain (Vañó-Galván); Dermatology Unit, Istituto di Ricovero e Cura a Carattere Scientifico Azienda Ospedaliero, Universitaria di Bologna, Bologna, Italy (Piraccini); Department of Experimental, Diagnostic and Specialty Medicine Alma Mater Studiorum, University of Bologna, Bologna, Italy (Piraccini); Eli Lilly and Company, Indianapolis, Indiana (Dutronc, Yu, Somani, Ball); Tigermed-BDM Inc, Somerset, New Jersey (Liu); Department of Dermatology, University of California, Irvine (Mesinkovska).

Author Contributions: Drs King and Dutronc had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: King, Ko, Vañó-Galván, Piraccini, Dutronc, Mesinkovska.
Acquisition, analysis, or interpretation of data: King, Ko, Kwon, Dutronc, Yu, Liu, Somani, Ball, Mesinkovska.
Drafting of the manuscript: Vañó-Galván, Somani, Ball.
Critical review of the manuscript for important intellectual content: All authors.
Statistical analysis: Yu, Liu.
Administrative, technical, or material support: King, Kwon, Somani.
Supervision: Vañó-Galván, Piraccini, Dutronc, Somani, Mesinkovska.

Conflict of Interest Disclosures: Dr King reported personal fees from Eli Lilly, Sun, and Pfizer and that his spouse has served as a consultant, speaker, and advisory board member for Pfizer, Eli Lilly, and Sun outside the submitted work. Dr Ko reported personal fees from Eli Lilly during the conduct of the study as well as personal fees from Pfizer and being a trial investigator for AbbVie and Concert/Sun outside the submitted work. Dr Vañó-Galván reported personal fees from Lilly during the conduct of the study and personal fees from Pfizer outside the submitted work. Drs Dutronc and Ball reported being an employee of and share holder in Eli Lilly during the conduct of the study. Dr Yu reported a salary from Eli Lilly and Company outside the submitted work. Dr Somani reported being an employee of and minor shareholder in Eli Lilly & Co. Dr Mesinkovska reported personal fees from Lilly, Pfizer, Sun Pharma, and AbbVie during the conduct of the study. No other disclosures were reported.

Funding/Support: Baricitinib is developed by Eli Lilly and Company under license from Incyte Corporation.

Role of the Funder/Sponsor: Eli Lilly and Company was involved in the study design, data collection, data analysis, data interpretation, manuscript preparation, and publication decisions.

Data Sharing Statement: See Supplement 4.

Additional Contributions: We thank the participants, caregivers, and investigators. Eric A. Rodriguez, PhD, and Lucy M. Gee, PhD, Eli Lilly and Company, provided writing and editorial assistance, for which they were compensated.

REFERENCES

1. Gilhar A, Etzioni A, Paus R. Alopecia areata. *N Engl J Med*. 2012;366(16):1515-1525. doi:10.1056/NEJMra1103442

2. Kwon O, Senna MM, Sinclair R, et al. Efficacy and safety of baricitinib in patients with severe alopecia

areata over 52 weeks of continuous therapy in two phase III trials (BRAVE-AA1 and BRAVE-AA2). *Am J Clin Dermatol*. 2023;24(3):443-451. doi:10.1007/s40257-023-00764-w

3. King B, Ohyama M, Kwon O, et al; BRAVE-AA Investigators. Two phase 3 trials of baricitinib for alopecia areata. *N Engl J Med*. 2022;386(18):1687-1699. doi:10.1056/NEJMoa2110343

4. Freitas E, Guttman-Yassky E, Torres T. Baricitinib for the Treatment of Alopecia Areata. *Drugs*. 2023;83(9):761-770. doi:10.1007/s40265-023-01873-w

5. King B, Zhang X, Harcha WG, 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):1518-1529. doi:10.1016/S0140-6736(23)00222-2

6. Harries MJ, Sun J, Paus R, King LE Jr. Management of alopecia areata. *BMJ*. 2010;341:c3671. doi:10.1136/bmj.c3671

7. King B, Mesinkovska N, Mirmirani P, et al. Phase 2 randomized, dose-ranging trial of CTP-543, a selective Janus Kinase inhibitor, in moderate-to-severe alopecia areata. *J Am Acad Dermatol*. 2022;87(2):306-313. doi:10.1016/j.jaad.2022.03.045

8. Egeberg A, Linsell L, Johansson E, Durand F, Yu G, Vañó-Galván S. Treatments for moderate-to-severe alopecia areata: a systematic narrative review. *Dermatol Ther (Heidelb)*. 2023;13(12):2951-2991. doi:10.1007/s13555-023-01044-5

9. 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. doi:10.1111/bjd.18883

10. Wyrwich KW, Kitchen H, Knight S, et al. Development of clinician-reported outcome (ClinRO) and patient-reported outcome (PRO) measures for eyebrow, eyelash and nail assessment in alopecia areata. *Am J Clin Dermatol*. 2020;21(5):725-732. doi:10.1007/s40257-020-00545-9

11. Meah N, Wall D, York K, et al. The Alopecia Areata Consensus of Experts (ACE) study: Results of an international expert opinion on treatments for alopecia areata. *J Am Acad Dermatol*. 2020;83(1):123-130. doi:10.1016/j.jaad.2020.03.004

12. Peeva E, Guttman-Yassky E, Banerjee A, et al. Maintenance, withdrawal, and re-treatment with ritlecitinib and brepocitinib in patients with alopecia areata in a single-blind extension of a phase 2a randomized clinical trial. *J Am Acad Dermatol*. 2022;87(2):390-393. doi:10.1016/j.jaad.2021.12.008

13. Lilly. When should Olumiant (baricitinib) treatment be interrupted and what are the effects of treatment interruption? Accessed May 1, 2024. https://medical.lilly.com/us/products/answers/when-should-olumiant-baricitinib-treatment-be-interrupted-and-what-are-the-effects-of-treatment-interruption-167089